APPENDIX AVAILABLE ON THE HEI WEB SITE

Research Report 178

National Particle Component Toxicity (NPACT) Initiative Report on Cardiovascular Effects

Sverre Vedal et al.

Section 1: NPACT Epidemiologic Study of Components of Fine Particulate Matter and Cardiovascular Disease in the MESA and WHI-OS Cohorts

Appendix H. MESA Exposure and Health Analysis: Additional Text, Tables, and Figures

Note: Appendices that are available only on the Web have been assigned letter identifiers that differ from the lettering in the original Investigators' Report. HEI has not changed the content of these documents, only their identifiers.

Appendix H was originally Appendix G

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APPENDIX G: MESA exposure and health analysis: additional text, tables and figures

- **MESA nearest neighbor and inverse-distance weighting (IDW): exposure estimation**
- **MESA nearest neighbor and IDW: health analysis**
- **Cross-sectional effects on CIMT in MESA by proximity to nearest monitor**
- **Analyses of SO_4, SO_2, and NO_3**
    - **Cross-validation statistics**
    - **Cross-sectional and longitudinal analyses adjusting for NO2 and SO2**
    - **Cross-sectional and longitudinal analyses for sulfate, nitrate, SO2, and NO2**
- **Cross-sectional effects of sulfur on CAC and CIMT with the interaction of traffic variables**

MESA nearest neighbor, IDW and city-wide average: exposure estimation

Monitoring at MESA Air sites began in July, 2005 and ended in August 2009. $PM_{2.5}$ speciation data were measured from April 2007 through August 2008. Data from the one year period from May 2, 2007 to April 16, 2008 was used for this analysis. The mean for each monitoring site over that period was calculated as the 10 percent trimmed mean (i.e., the top and bottom 5 percent of data were excluded for the calculation of the mean).

Three different secondary approaches were used to estimate MESA Air study participant exposure to $PM_{2.5}$ components: (1) the annual average concentration of the two-week measurements at the monitor nearest to each study participant's residence (nearest monitor); (2) inverse distance weighting (IDW) of all annual average monitor concentrations in each city relative to each subject's residence; and (3) city-wide average concentrations based on all monitors within each city. For all three approaches, subjects within each city residing within 100 meters of either an A1 road (primary limited access or interstate highway) or an A2 road (primary US or state highway, without limited access), or within 50 meters of an A3 road (secondary state or county highway), were assigned the average $PM_{2.5}$ and EC concentrations measured at that city's MESA Air roadside monitor. The roadside monitors in these cases were not used in calculating the exposures of subjects not living close to an A1, A2 or A3 road. For OC, silicon and sulfur, roadside monitors were included in the calculations for all three of the exposure estimation methods.

The following $PM_{2.5}$ component concentrations were included in this analysis: elemental carbon [EC], organic carbon [OC], silicon and sulfur.EC and OC were selected as reflecting combustion sources, silicon as an indicator of crustal dust and sulfur as an indicator of sulfate, a secondary aerosol. To obtain information on temporal trends, $PM_{2.5}$ component data were

obtained from the Health Effects Institutes (HEI) Air Quality Database website (https://hei.aer.com/login.php) for 2002 and 2007.

208 subjects (3.3 %) lived within 100 meters of an A1 road, 243 (3.9%) with 100 meters of an A2 road, and 1,459(23.3%) within 50 meters of an A3 road. A total of 1,774 subjects (28.4%) were therefore classified as living close to a large roadway. Using the criteria for living close to a large roadway, the following in each city lived close to a large roadway: 18.5% in Winston-Salem, 59.5% in New York, 20.8% in Baltimore, 22.8% in St.Paul, 31.2% in Chicago, and18.1% in Los Angeles. Among those not living close to a large roadway, median distance to the nearest MESA Air monitor was 4.1 km (IQR 4.3). Most (90.3%) of the participants resided within 10 km of an air pollution monitor.

Appendix Table G.1 shows $PM_{2.5}$ and $PM_{2.5}$ component annual average concentrations (µg /m^3) by city and monitor. Appendix Table G.2 and Appendix Figure G.1 shows median (IQR) and mean (SD), respectively, study subject $PM_{2.5}$ and component concentrations over all six cities according to the three exposure metrics. Mean $PM_{2.5}$ concentrations for the six study sites based on nearest monitor ranged from 16.22µg/m^3(Los Angeles) to 10.26µg/m^3(St. Paul); EC ranged from 2.67µg/m^3 (New York City) to 0.70µg/m^3 (St. Paul); OC ranged from 4.37µg/m^3 (Winston-Salem) to 2.74µg/m^3 (St. Paul); silicon ranged 0.15µg/m^3 (Los Angeles) to 0.08µg/m^3 (Baltimore); and sulfur ranged from 1.65µg/m^3 (Baltimore) to 0.85µg/m^3 (St. Paul). Medians (IQRs) for IDW and city average are also shown.

Appendix Figure G.2 shows the correspondence between mean $PM_{2.5}$ and $PM_{2.5}$ component concentrations from the CSN for 2002 and 2007 in the MESA cities with available CSN data. There was generally good correspondence between concentrations over that five year span except for silicon, which showed a decrease, except in Los Angeles and Winston-Salem.

MESA nearest neighbor, IDW and city average: health effects analysis

Statistical Analysis:

Multiple linear regression was used to estimate the associations between $PM_{2.5}$ measures and CIMT and CAC (among persons with Agatston scores greater than zero). Agatston scores were analyzed after log transformation. Binomial regression was used to estimate the associations between $PM_{2.5}$ measures and the presence of CAC (Agatston Scores>0). All measures of association were expressed per inter-quartile range (IQR) of each concentration measure.

Covariates in the regression analyses were selected a priori as known or suspected cardiovascular risk factors for CHD. Models progressed from less to more rich in covariates:

Model 1: covariates include age, gender, race-ethnicity

Model 2: Model 1 + total cholesterol, HDL cholesterol, smoking status, hypertension, lipid-lowering medication

Model 3: Model 2 + education, income, waist circumference, body surface area, BMI, BMI^2, diabetes, LDL, triglycerides

Model 4: Model 2 + metropolitan area

Race/ethnicity was categorized as white non-Hispanic of European ancestry, Chinese, African American, and Hispanic. BMI was include d as a continuous variable. Cigarette smoking status was categorized as never, former or current smoker. Annual family income was categorized into 5 categories. Education was classified as: high school not completed, high school completed, some college but no degree, or completed bachelor's degree or more. Current use of lipid-lowering medications was classified as either some or none. Diabetes was categorized as not diabetic, impaired fasting glucose, untreated diabetes and treated diabetes. Diabetes was defined as fasting glucose of $\geq$ 7.0mmol/L ($\geq$ 126 mg/dL) or use of hypoglycemic medication. Impaired

fasting glucose was defined as fasting glucose =5.5-6.9mmol/L (100-125mg/dL). Hypertension was defined as systolic blood pressure ≥140 mmHg, diastolic blood pressure ≥ 90 mmHg or taking antihypertensive medications.

Models using the nearest monitor concentration estimates and the base set of covariates model (Model 2) were considered as the primary models. Sensitivity analysis consisted in comparing findings across the four models and the three alternative exposure measures, as well as assessing estimates from selected two-pollutant models and models that controlled for ultrasound sonographer.

Mean age of the study participants was 62 years, 47.5 percent were male, and 39.1 percent were non-Hispanic white, 11.7 percent Chinese, 27.4 percent African American, and 21.7 percent Hispanic. Additional characteristics of the study sample are shown in Appendix Table G.3. The prevalence of current smoking was low (12.7%), and approximately half of the cohort reported never having smoked.

Median CIMT was 0.84mm (IQR 0.23mm). 49.0% of subjects had a CAC Agatston score > 0; among those, the median score was 86.0 Agatston units (IQR 270.5).

CIMT

Appendix Table G.4 shows estimates of effects of $PM_{2.5}$ and $PM_{2.5}$ components on CIMT by the several exposure estimation methods and analysis models. Appendix Figure G.4 shows estimated effects on CIMT based on our primary exposure approach (nearest monitor) and Model 2. Increases in predicted $PM_{2.5}$, OC, EC and sulfur, but not silicon, were associated with increased CIMT; CIMT increases per IQR concentration increases were 14.7 μm (95% CI [9.0,20.5]), 35.1μm (26.8,43.3), 9.6μm (3.6,15.7), 22.7μm (15.0,30.4) and 5.2 μm (-9.8,20.1) for

$PM_{2.5}$, OC, EC, sulfur and silicon, respectively. The size of the effect estimates for OC and sulfur was higher than that for EC.

In sensitivity analyses, findings were generally consistent across the three exposure estimation approaches and were largely unchanged when controlling for more covariates in the extended model (Model 3). In addition to controlling for lipid-lowering medications in our primary model, we carried out an analysis restricted to those who reported never having been on statin medications (n= 4,754); findings in this subgroup were essentially identical to those in the larger group (results not shown). Effects of adding variables for each metropolitan area to the model (Model 4), effectively removing between-area effects and allowing assessment of only within-area effects, were also examined. Metropolitan area variables could not be added to models in which city-wide average was used as the exposure metric. Several findings were sensitive to control for area. For our primary exposure method and model, none of associations of $PM_{2.5}$ and $PM_{2.5}$ components with CIMT were significant when metropolitan areas were included as covariates in model 2 (Model 4) (Appendix Table G.4), although the size of the effect estimates for EC and sulfur remained essentially unchanged, and the effect of $PM_{2.5}$ was only moderately reduced. We also included ultrasound sonographer as an indicator variable in place of metropolitan area in the CIMT models for sonographers who performed at least 10 studies. Since sonographers were unique to study site, this effectively also controlled for study area. Results with sonographer in the CIMT models were essentially no different from those controlling for metropolitan area (results not shown).

For CIMT, estimates from two-pollutant models were examined using nearest monitor and primary analysis model that included each pair of the $PM_{2.5}$ components. Only the association of

CIMT with OC was not sensitive to inclusion in the model of the other components or total $PM_{2.5}$ (results not shown).

CAC

Appendix Table G.5 shows estimated effects of $PM_{2.5}$ and $PM_{2.5}$ components on presence of CAC by the several estimation methods and models. Appendix Figure G.4 shows estimated effects on presence of CAC based on our primary exposure approach (nearest monitor) and Model 2. For this model, there were no statistically significant associations between presence of CAC and $PM_{2.5}$ or $PM_{2.5}$ components. In sensitivity analyses, using IDW or city-wide average, presence of CAC was negatively associated with EC in Model 2 and in Model 3 with the extended set of covariates. With adjustment for metropolitan region (Model 4), EC was no longer negatively associated with presence of CAC.

Appendix Table G.6 shows estimated effects of $PM_{2.5}$ and $PM_{2.5}$ components on log-transformed CAC (in those with detectable calcium) by estimation method and models. Appendix Figure G.4 shows estimated effects on CAC in those with measurable CAC based on our primary exposure and analysis model. For the primary exposure and analysis model, no significant positive association of any PM measure and amount of CAC was observed. In sensitivity analyses, silicon was associated with amount of CAC using city-wide average and IDW, but in the negative direction; this negative association was no longer present after adjustment for city region (Model 4).

Appendix Table G.1, Part 1. Participant characteristics at the baseline examination 2000-2002.

	N	%		N	%
Gender			Diabetes		
Male	2974	47.5	Normal	4635	74.1
Female	3282	52.5	IFG	855	13.7
Age(years)			Treated diabetes	157	2.5
45-54	1828	29.2	Untreated diabetes	589	9.4
55-64	1755	28.1	Missing	20	0.3
65-74	1838	29.4	Education		
75-84	835	13.3	Incomplete high school	1057	16.9
Race-ethnicity			Complete high school	1135	18.1
White	2449	39.1	Some college	1776	28.4
Chinese	735	11.7	Complete college	2269	36.3
Black	1714	27.4	Missing	19	0.3
Hispanic	1358	21.7	Lipid lowering medication		
Income($/year)			No	5238	83.7
<12,000	655	10.5	Yes	1015	16.2
12,000-24,999	1161	18.6	Missing	3	0.05
25,000-49,999	1748	27.9	Hypertension		
50,000-74,999	1048	16.8	No	3504	56.0
≥75,000	1410	22.5	Yes	2752	44.0
Missing	234	3.7	MESA city		
Cigarette smoking			Winston-Salem	999	16.0
Never	3145	50.3	New York	1021	16.3
Former	2299	36.7	Baltimore	975	15.6
Current	794	12.7	St. Paul	982	15.7
Missing	18	0.3	Chicago	1088	17.4
BMI			Los Angeles	1191	19.0
18.5-22.9	1796	28.7			
23-27.5	2459	39.3			
27.6-40	1777	28.4			
>40	224	3.6	Total	6256	

BMI=body mass index; IFG=impaired fasting glucose

Appendix Table G.1, Part 2. Summary statistics of log(CAC), presence of CAC, and CIMT by gender and race-ethnicity for MESA exam 1 participants used in the cross-sectional analysis.

Variable		Log(CAC)			Presence of CAC			CIMT	
		N	Mean	SD	N	%	N	Mean (mm)	SD
Gender	Female	1103	3.96	1.76	2872	38	2872	0.67	0.18
	Male	1581	4.57	1.83	2621	60	2621	0.69	0.20
Race-ethnicity	White	1215	4.53	1.88	2179	56	2179	0.67	0.18
	Chinese American	325	4.03	1.70	673	48	673	0.65	0.19
	Black, African-American	601	4.12	1.81	1452	41	1452	0.72	0.20
	Hispanic	543	4.22	1.77	1189	46	1189	0.66	0.18
Total		2684			5493		5493		

Appendix Table G.2. $PM_{2.5}$ and $PM_{2.5}$ component annual average concentrations (μg /m^3) by city and MESA Air monitor, May 2, 2007 – Apr 16, 2008.

City	monitor ID	Type	$PM_{2.5}$	EC	OC	Silicon	Sulfur
LA	L001	non-roadside	16.33	1.97	3.99	0.15	1.18
	L002	Roadside	16.75	2.17	3.77	0.16	1.22
	LC001	non-roadside	13.43	1.46	3.02	0.13	1.20
	LC002	non-roadside	15.31	1.60	3.54	0.14	1.23
	LC003	Roadside	13.25	1.40	2.79	0.12	1.18
Chicago	C001	non-roadside	12.18	1.15	3.24	0.10	1.13
	C002	non-roadside	13.66	1.27	3.15	0.13	1.19
	C004	non-roadside	14.61	1.57	3.70	0.10	1.31
	C006	non-roadside	13.83	1.31	3.30	0.12	1.26
	C007	Roadside	15.45	1.69	3.71	0.12	1.30
Baltimore	B001	Roadside	15.62	2.13	3.61	0.11	1.69
	B003	non-roadside	14.71	1.42	3.65	0.09	1.69
	B004	non-roadside	13.86	1.36	3.25	0.08	1.67
	B005	non-roadside	12.67	0.96	2.90	0.07	1.53
St.Paul	S001	Roadside	10.96	1.07	3.20	0.12	0.87
	S002	non-roadside	10.23	0.68	2.67	0.11	0.85
	S003	non-roadside	10.54	0.84	3.15	0.11	0.83
NY	N001	non-roadside	13.24	2.32	3.77	0.11	1.46
	N002	Roadside	15.35	3.00	3.96	0.15	1.36
Winston-Salem	W001	non-roadside	13.22	1.46	4.99	0.09	1.62
	W002	non-roadside	13.23	1.05	3.51	0.10	1.59
	W003	Roadside	13.92	1.22	3.84	0.10	1.66
	W004	non-roadside	13.01	0.99	3.62	0.09	1.67

*$PM_{2.5}$, particulate matter<2.5 μm in aerodynamic diameter; EC, element carbon; OC, organic carbon

Appendix Table G.3. Distribution (median and inter-quartile range [IQR]) of $PM_{2.5}$ and $PM_{2.5}$ component concentrations ($\mu g/m^3$) by three estimation approaches

Approach	$PM_{2.5}$		EC		OC		Silicon		Sulfur	
	median	IQR	median	IQR	median	IQR	median	IQR	median	IQR
Nearest monitor	13.66	2.340	1.36	0.825	3.61	0.724	0.11	0.074	1.30	0.409
Inverse-distance weighting (IDW)	13.69	1.314	1.32	0.570	3.50	0.624	0.12	0.039	1.26	0.425
City-wide average	13.57	1.143	1.32	0.509	3.42	0.517	0.11	0.031	1.24	0.435

*$PM_{2.5}$, particulate matter<2.5 μm in aerodynamic diameter; EC, element carbon; OC, organic carbon.

Appendix Table G.4. Difference in CIMT* (μm) for pollutant IQR increases by analysis model and exposure estimation approach

	$PM_{2.5}$*	EC*	OC*	Silicon	Sulfur
	CIMT difference (95% CI)	CIMT difference (95% CI)	CIMT difference (95% CI)	CIMT difference (95% CI)	CIMT difference (95% CI)
Model 1**					
Nearest Monitor	13.7 (8.0,19.5)	8.2 (2.2,14.2)	36.5 (28.3,44.7)	3.1 (-11.9,18.0)	22.6 (14.9,30.2)
IDW	8.8 (4.8,12.7)	4.8 (0.0,9.5)	25.4 (19.9,30.8)	-0.6 (-10.2,9.0)	23.8 (15.8,31.8)
City-Wide Average	7.6 (3.7,11.3)	2.6 (-1.9,7.1)	21.3 (16.4,26.2)	-0.2 (-9.9,9.5)	22.9 (14.8,31.0)
Model 2**					
Nearest Monitor	14.7 (9.0,20.5)	9.6 (3.6,15.7)	35.1 (26.8,43.3)	5.2 (-9.8,20.1)	22.7 (15.0,30.4)
IDW	9.6 (5.7,13.5)	6.0 (1.3,10.8)	24.9 (19.4,30.3)	1.3 (-8.3,10.9)	24.0 (16.0,32.0)
City-Wide Average	8.5 (4.7,12.3)	3.9 (-0.5,8.4)	20.6 (15.7,25.5)	1.8 (-7.9,11.4)	23.3 (15.2,31.4)
Model 3**					
Nearest Monitor	15.8 (9.9,21.7)	10.8 (4.6,16.9)	36.5 (28.0,44.9)	7.3 (-8.0,22.5)	23.9 (16.0,31.7)
IDW	10.6 (6.5,14.6)	7.2 (2.3,12.0)	26.9 (21.2,32.6)	2.4 (-7.4,12.2)	25.4 (17.2,33.5)
City-Wide Average	9.6 (5.7,13.5)	5.0 (0.4,9.6)	21.8 (16.7,26.9)	2.8 (-7.1,12.7)	24.8 (16.5,33.1)
Model 4**					
Nearest Monitor	5.9 (-10.3,22.0)	6.3 (-11.4,23.8)	-2.3 (-26.2,21.5)	-10.1 (-41.0,20.6)	27.4 (-19.3,73.8)
IDW	6.0 (-9.8,21.8)	12.1 (-11.0,35.0)	***	-8.5 (-47.2,30.0)	***

*$PM_{2.5}$, particulate matter less than or equal to 2.5 μm in aerodynamic diameter; EC, element carbon; OC, organic carbon; CIMT, carotid intima-media thickness

**Model 1: covariates include age, gender, race-ethnicity

Model 2: Model 1 + total cholesterol, HDL cholesterol, smoking status, hypertension, lipid-lowering medication

Model 3: Model 2 + education, income, waist circumference, body surface area, BMI, BMI^2, diabetes, LDL, triglycerides

Model 4: Model 2 + metropolitan area

***unstable estimate

Appendix Table G.5.

CAC* relative risk (RR) for pollutant IQR increases by analysis model and exposure estimation approach.

	$PM_{2.5}$*	EC*	OC*	Silicon	Sulfur
	RR (95% CI)	RR (95% CI)	RR (95% CI)	RR (95% CI)	RR (95% CI)
Model 1**					
Nearest Monitor	1.00 (0.99,1.01)	0.96 (0.93,0.99)	1.03 (0.96,1.09)	0.84 (0.33,2.14)	0.98 (0.91,1.07)
IDW	0.99 (0.98,1.01)	0.95 (0.91,0.99)	0.98 (0.90,1.06)	0.49 (0.16,1.53)	0.98 (0.90,1.06)
City-Wide Average	0.99 (0.98,1.00)	0.94 (0.90,0.98)	1.01 (0.09,1.55)	0.37 (0.09,1.55)	0.97 (0.89,1.05)
Model 2**					
Nearest Monitor	1.00 (0.99,1.01)	0.97 (0.94,1.00)	1.01 (0.95,1.07)	0.92 (0.37,2.32)	0.98 (0.90,1.06)
IDW	1.00 (0.98,1.01)	0.96 (0.92,1.00)	0.96 (0.89,1.04)	0.64 (0.21,1.96)	0.97 (0.90,1.05)
City-Wide Average	0.99 (0.98,1.01)	0.95 (0.91,0.99)	0.99 (0.91,1.08)	0.51 (0.12,2.09)	0.97 (0.89,1.05)
Model 3**					
Nearest Monitor	1.00 (0.99,1.01)	0.97 (0.94,1.01)	1.03 (0.97,1.09)	1.02 (0.39,2.64)	0.99 (0.91,1.07)
IDW	1.00 (0.99,1.01)	0.96 (0.92,1.00)	0.99 (0.91,1.07)	0.70 (0.22,2.22)	0.98 (0.90,1.06)
City-Wide Average	1.00 (0.98,1.01)	0.96 (0.91,0.99)	1.01 (0.93,1.10)	0.57 (0.13,2.44)	0.97 (0.90,1.06)
Model 4**					
Nearest Monitor	1.01 (0.98,1.05)	1.04 (0.94,1.15)	1.08 (0.91,1.28)	***	1.35 (0.79,2.30)
IDW	1.02 (0.97,1.09)	1.11 (0.91,1.34)	***	***	2.04 (0.62,6.66)

*$PM_{2.5}$, particulate matter less than or equal to 2.5 μm in aerodynamic diameter; EC, element carbon; OC, organic carbon; CAC, coronary artery calcification.

**Model 1: covariates include age, gender, race-ethnicity

Model 2: Model 1 + total cholesterol, HDL cholesterol, smoking status, hypertension, lipid-lowering medication

Model 3: Model 2 + education, income, waist circumference, body surface area, BMI, BMI^2, diabetes, LDL, triglycerides

Model 4: Model 2 + metropolitan area

***unstable estimate

Appendix Table G.6.

Percentage change in CAC* for pollutant IQR increases by analysis model and exposure estimation approach.

	$PM_{2.5}$*	EC*	OC*	Silicon	Sulfur
	% change (95% CI)	% change (95% CI)	% change (95% CI)	% change (95% CI)	% change (95% CI)
Model 1**					
Nearest Monitor	-1.52 (-3.31,0.26)	-1.65 (-3.54,0.24)	-0.59 (-3.14,1.96)	-3.96 (-8.62,0.70)	0.61 (-1.67,2.89)
IDW	-1.00 (-2.21,0.21)	-1.26 (-2.76,0.24)	-0.61 (-2.29,1.08)	-3.14 (-6.09,-0.19)	0.70 (-1.68,3.08)
City-Wide Average	-0.85 (-2.02,0.32)	-1.11 (-2.52,0.30)	0.19 (-1.32,1.70)	-3.41 (-6.36,-0.45)	0.66 (-1.76,3.07)
Model 2**					
Nearest Monitor	-1.56 (-3.34,0.21)	-1.61 (-3.49,0.27)	-0.98 (-3.52,1.57)	-3.08 (-7.73,1.58)	0.05 (-2.22,2.33)
IDW	-1.03 (-2.23,0.17)	-1.22 (-2.71,0.28)	-0.86 (-2.54,0.83)	-2.52 (-5.47,0.43)	0.12 (-2.25,2.50)
City-Wide Average	-0.63 (-1.84,0.58)	-0.83 (-2.28,0.63)	0.13 (-1.44,1.70)	-3.66 (-6.71,-0.61)	1.13 (-1.34,3.60)
Model 3**					
Nearest Monitor	-1.37 (-3.22,0.48)	-1.43 (-3.37,0.52)	-0.86 (-3.51,1.78)	-3.35 (-8.18,1.47)	0.58 (-1.76,2.92)
IDW	-0.89 (-2.14,0.37)	-1.06 (-2.61,0.49)	-0.90 (-2.67,0.86)	-3.07 (-6.13,0.00)	0.67 (-1.77,3.12
City-Wide Average	-0.72 (-1.94,0.49)	-0.90 (-2.36,0.57)	-0.05 (-1.63,1.53)	-3.21 (-6.27,-0.14)	0.64 (-1.85,3.12)
Model 4**					
Nearest Monitor	-3.10 (-8.08,1.89)	-3.40 (-8.76,1.97)	-1.05 (-8.03,5.93)	4.13 (-5.43,13.68)	-2.32 (-16.91,12.27)
IDW	-3.78 (-8.75,1.19)	-5.42 (-12.52,1.69)	***	3.24 (-8.59,15.07)	8.51 (-24.75,41.77)

*$PM_{2.5}$, particulate matter less than or equal to 2.5 μm in aerodynamic diameter; EC, element carbon; OC, organic carbon; CAC, coronary artery calcification.

**Model 1: covariates include age, gender, race-ethnicity

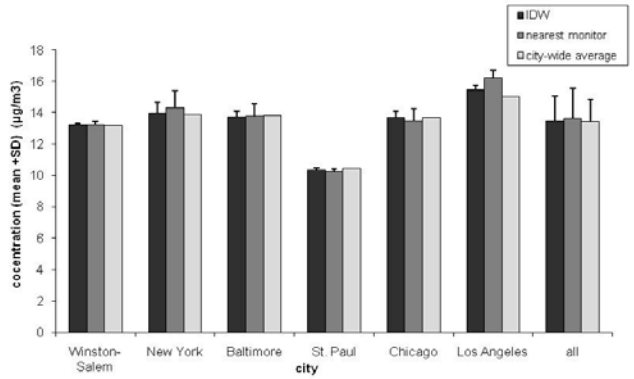
Model 2: Model 1 + total cholesterol, HDL cholesterol, smoking status, hypertension, lipid-lowering medication

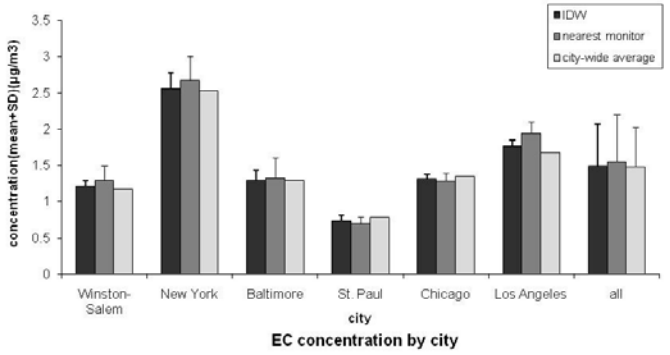
Model 3: Model 2 + education, income, waist circumference, body surface area, BMI, BMI^2, diabetes, LDL, triglycerides

Model 4: Model 2 + metropolitan area

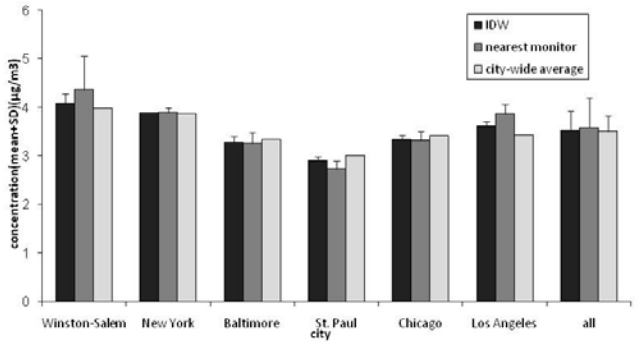
***unstable estimate

Appendix Figure G.1. $PM_{2.5}$ and $PM_{2.5}$ component concentrations (mean and standard deviation bar) by city and exposure estimation approach. $PM_{2.5}$, particulate matter <2.5 µm in aerodynamic diameter; EC, elemental carbon; OC, organic carbon; IDW = inverse distance weighting; Si = silicon; S = sulfur

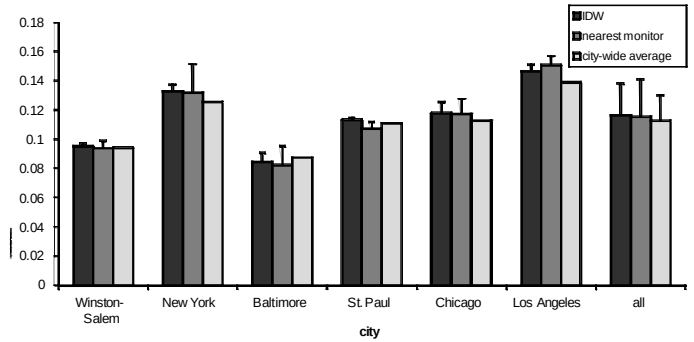




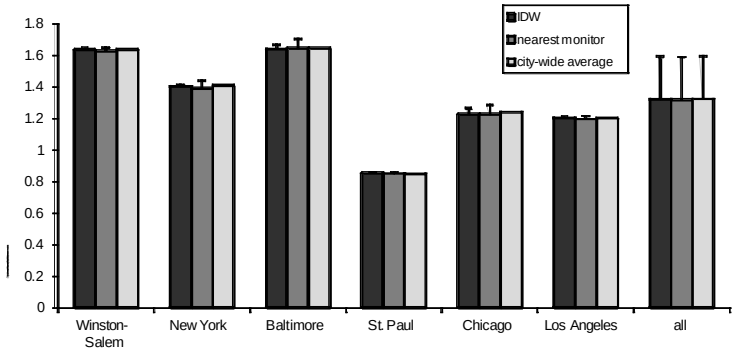
EC concentration by city



OC concentration by city

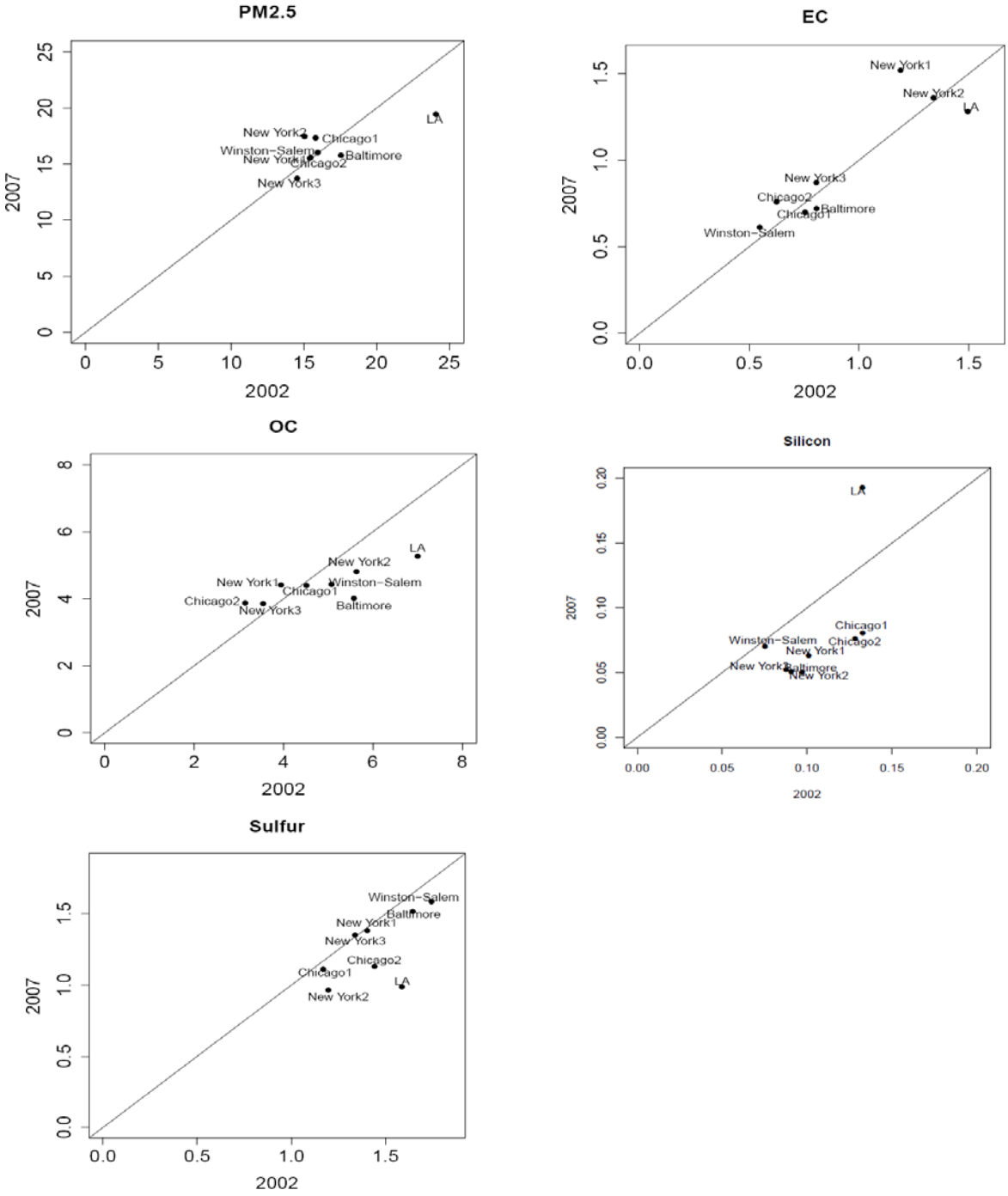


Silicon concentration by city

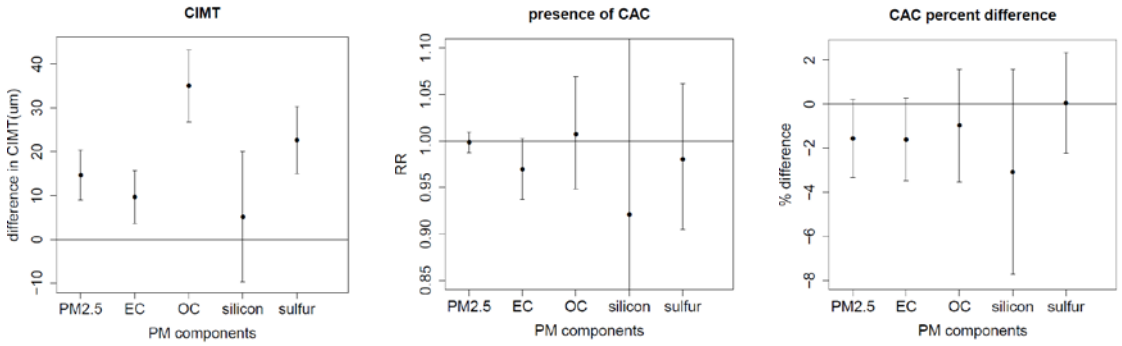


Sulfur concentration by city

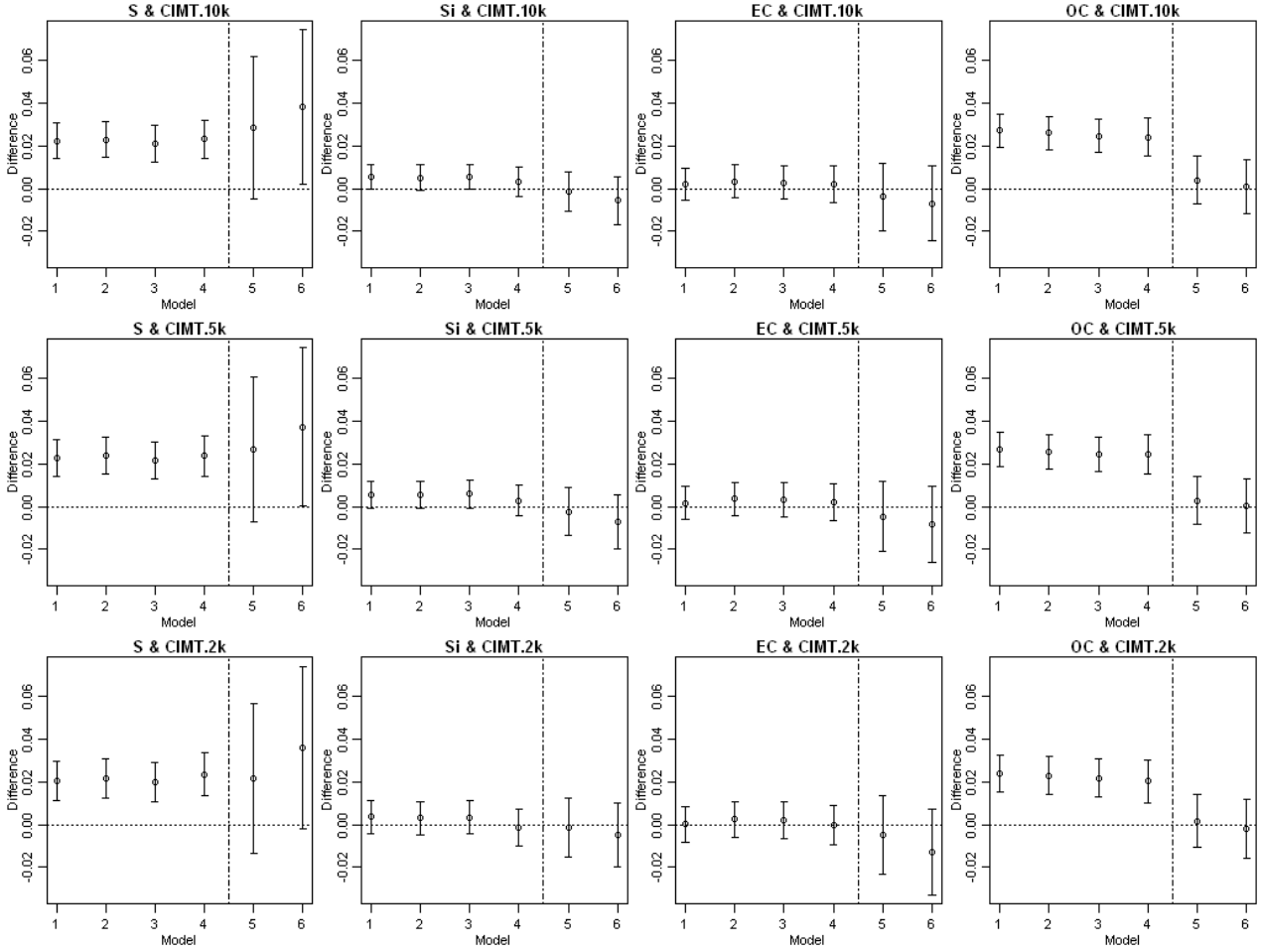
Appendix Figure G.2. Correspondence of mean $PM_{2.5}$ and $PM_{2.5}$ component concentrations in 2002 and 2007 from CSN monitoring sites in the MESA cities (https://hei.aer.com/login.php). $PM_{2.5}$ = particulate matter <2.5 µm in aerodynamic diameter; EC = elemental carbon; OC = organic carbon.



Appendix Figure G.3. Estimated effects of $PM_{2.5}$ and $PM_{2.5}$ components (per IQR) on difference in CIMT (µm), relative risk (RR) of CAC, and percent difference in CAC based on nearest monitor exposure estimates and the base model (Model 2, see Methods). $PM_{2.5}$ = particulate matter <2.5 µm in aerodynamic diameter; EC = elemental carbon; OC = organic carbon.



By proximity to MESA monitoring site



Appendix Figure G.4. Cross-sectional effects on CIMT in MESA at exam 1 for an interquartile increase (0.51, 0.02, 0.89, and 0.69 for sulfur, silicon, EC, and OC, respectively) in predicted $PM_{2.5}$ component concentrations from the NPACT spatio-temporal spatial model in six cross-sectional models for three prediction areas; 1) participant addresses within 10 kilometers of any monitor from one year prior to exam 1 through exam 3 participants (primary approach); 2) address within 5 kilometers; 3) address within 2 kilometers

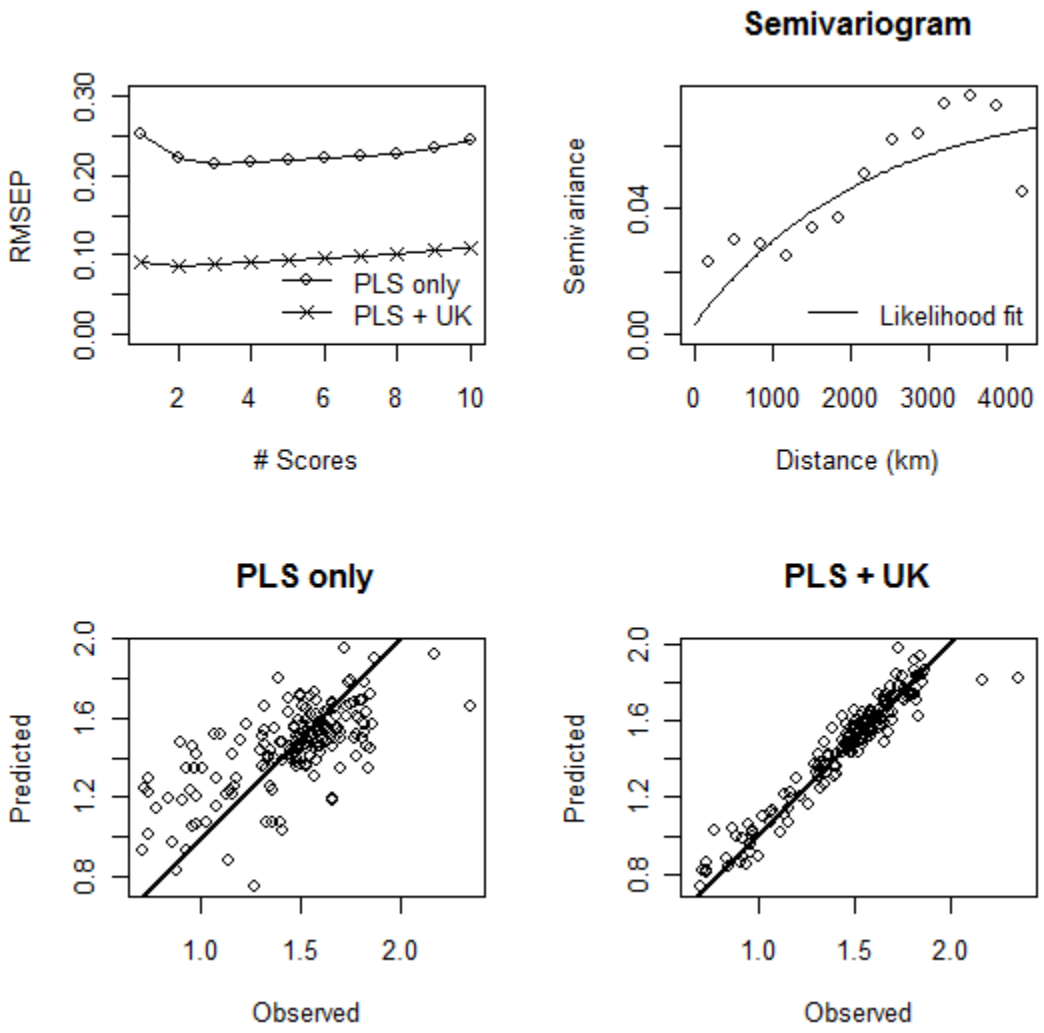
Appendix Figure G.5: SO4 10-fold CV results. Fitted variogram and predicted vs. observed plots correspond to using PLS with 2 components as the mean model.

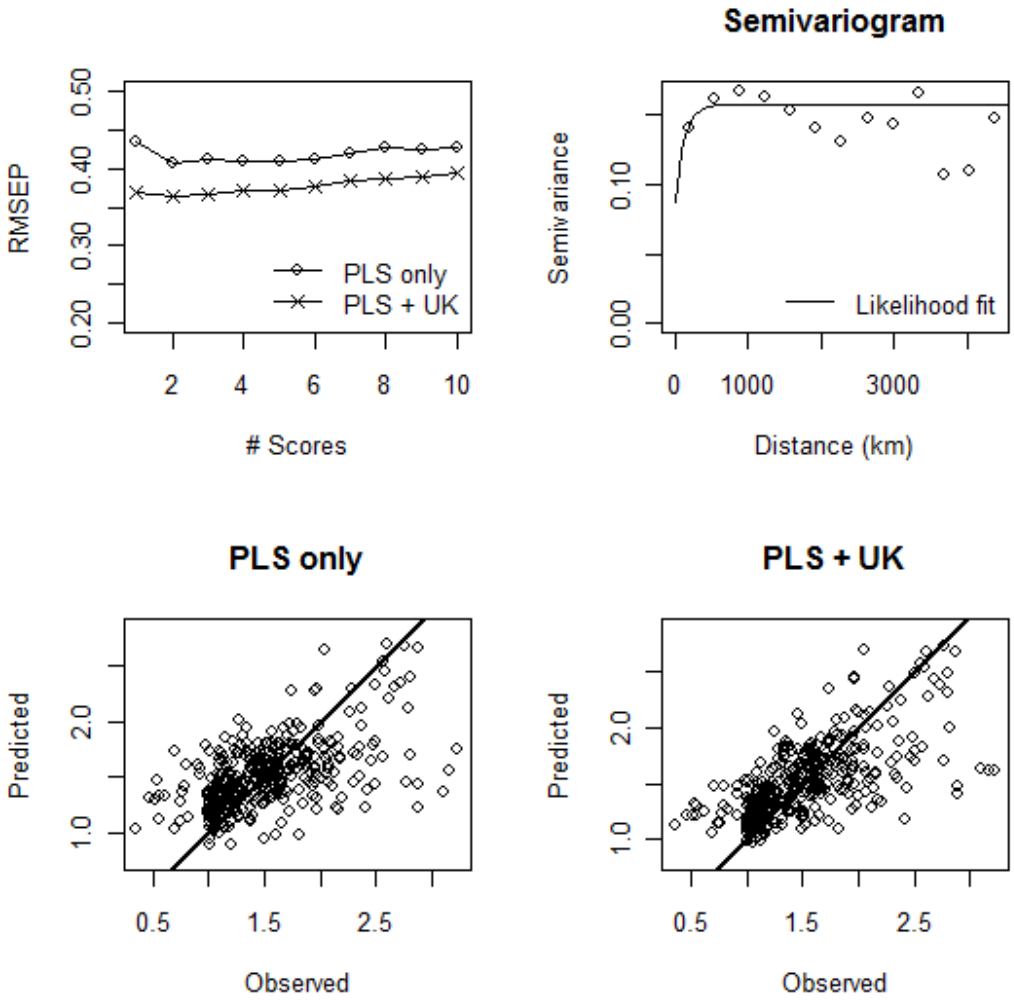
RMSEP = root mean squared error of prediction

PLS=partial least squares

UK= universal kriging; UK Pars= UK parameters

CV= cross-validation





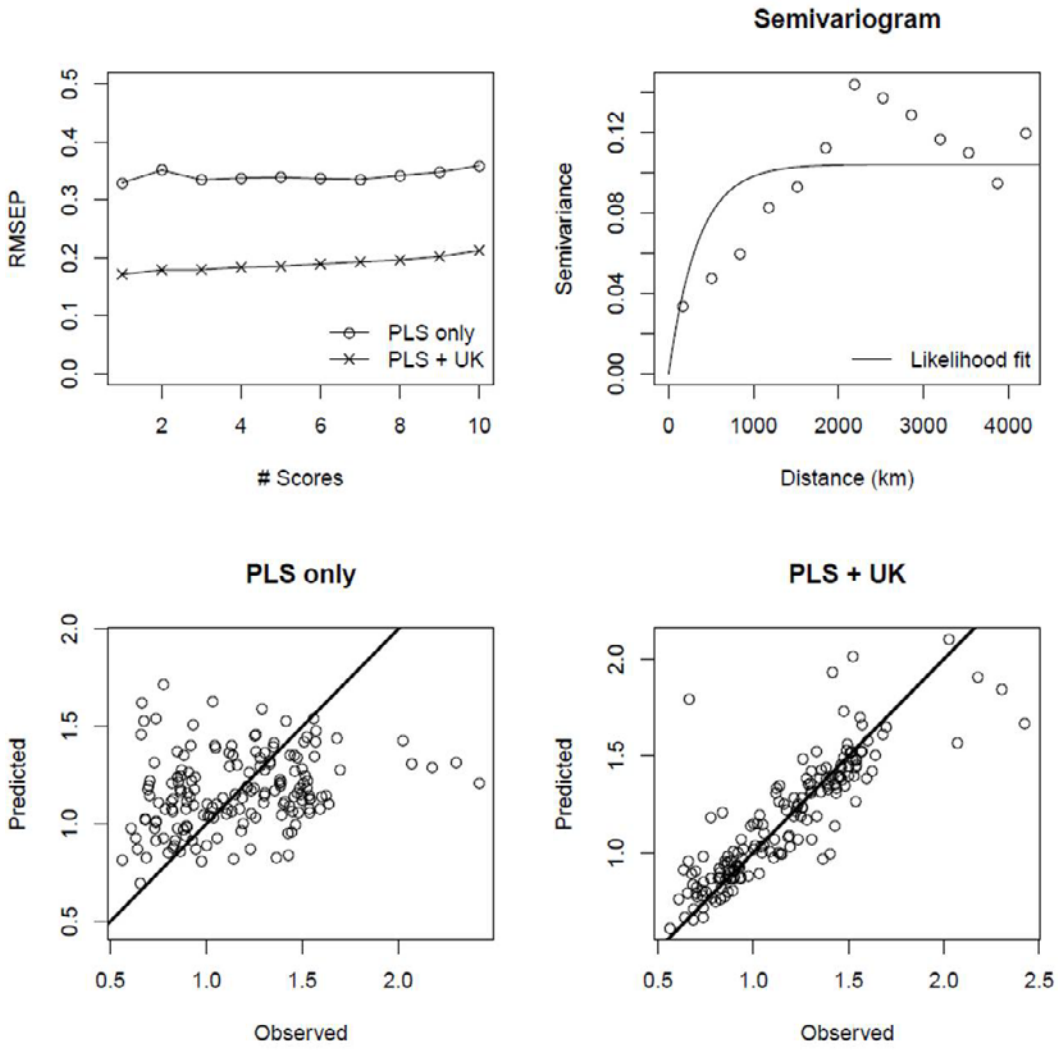
Appendix Figure G.6: SO2 10-fold CV results. Fitted variogram and predicted vs. observed plots correspond to using PLS with 2 components as the mean model.

RMSEP = root mean squared error of prediction

PLS=partial least squares

UK= universal kriging; UK Pars= UK parameters

CV= cross-validation



Appendix Figure G.7: NO3 10-fold CV results. Fitted variogram and predicted vs. observed plots correspond to using PLS with 2 components as the mean model.

RMSEP = root mean squared error of prediction

PLS=partial least squares

UK= universal kriging; UK Pars= UK parameters

CV= cross-validation

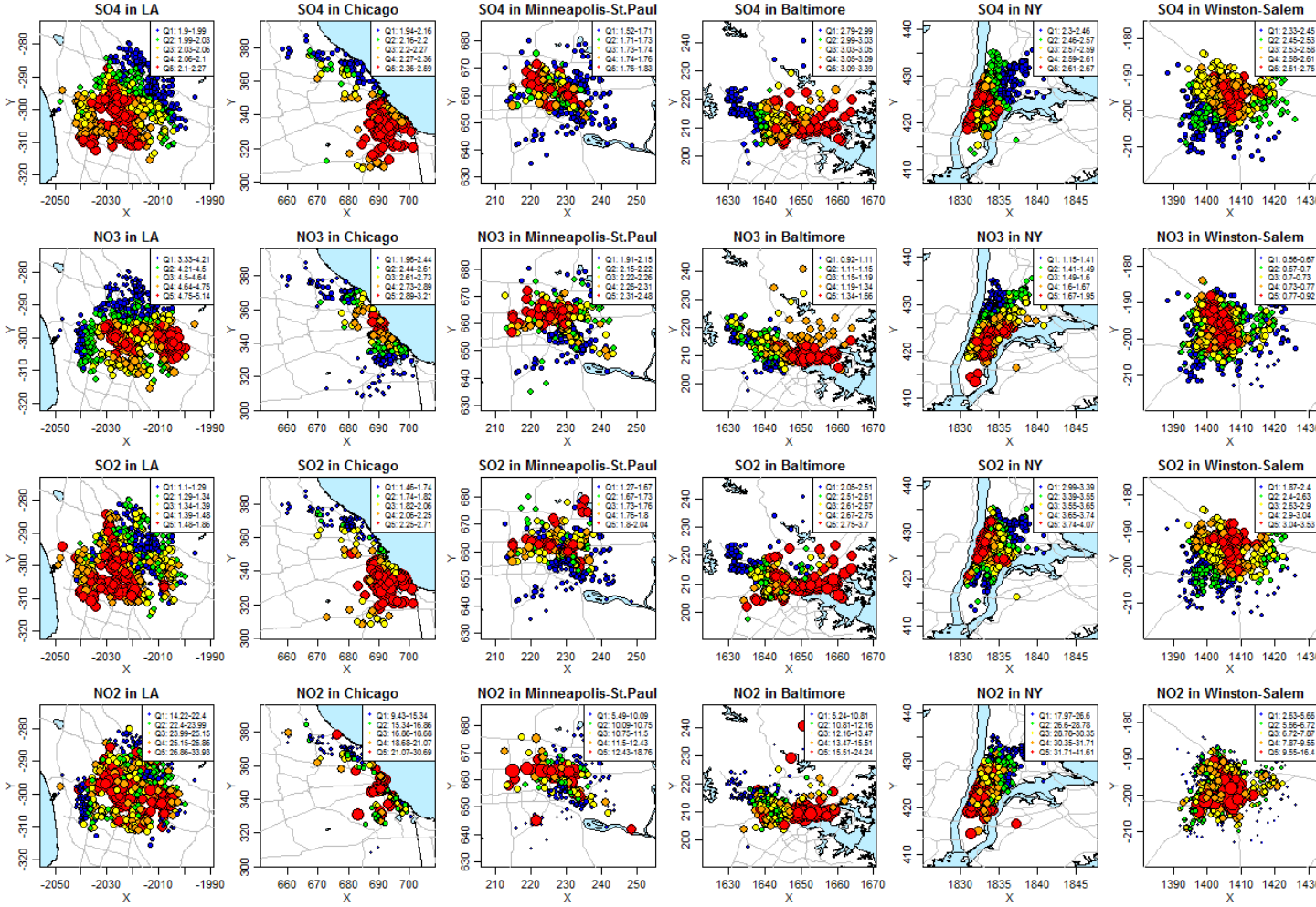
Appendix Table G.7. Cross-validation statistics for predicted sulfate, nitrate, and SO_2 concentrations from the national model

	Nation-wide				MESA Air 6 city area*			
	PLS only		PLS + Universal kriging		PLS only		PLS + Universal kriging	
	RMSE	R^2	RMSE	R^2	RMSE	R^2	RMSE	R^2
Sulfate	0.22	0.47	0.08	0.93	0.17	0.00	0.06	0.86
Nitrate	0.34	0.06	0.17	0.76	0.34	0.00	0.15	0.79
SO_2	0.41	0.31	0.36	0.45	0.34	0.18	0.30	0.35

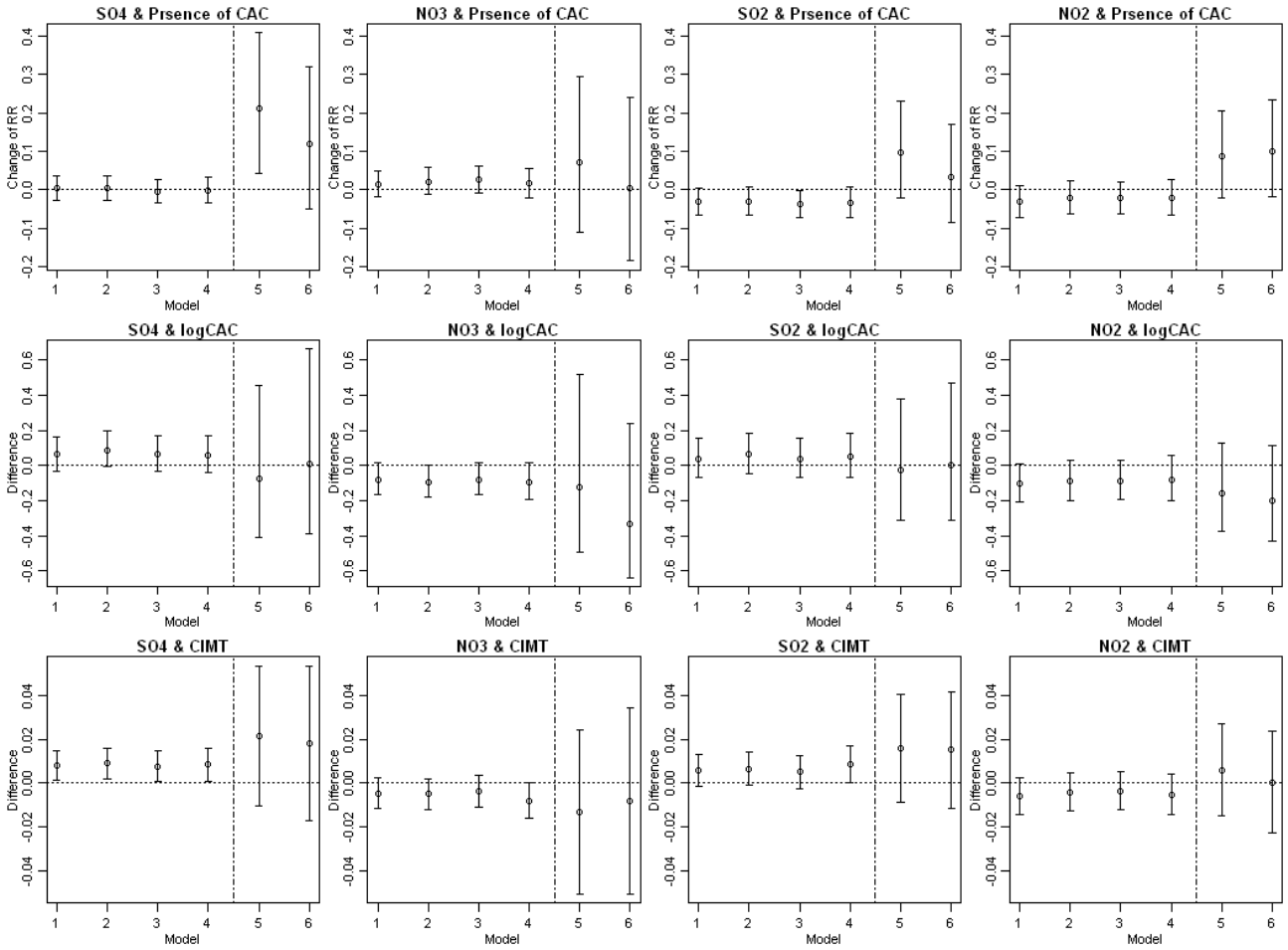
* Defined by 200 kilometer buffers from each city center

Cross-validation statistics for NO_2 predictions from the spatio-temporal model by city is shown in Appendix C

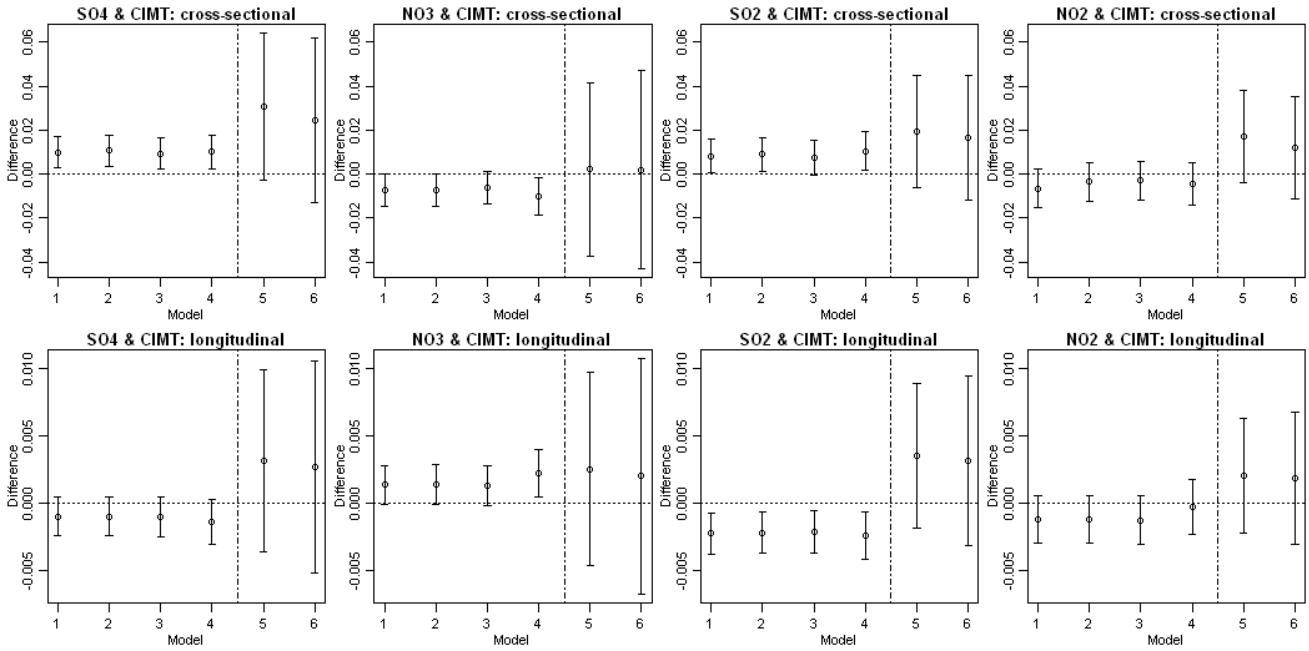
Cross-sectional and longitudinal analyses for sulfate, nitrate, SO_2, and NO_2



Appendix Figure G.8. Predicted long-term concentrations of sulfate, nitrate, and SO_2 from the national spatial model, and NO_2 from the spatio-temporal model at participant locations by 6 cities (different colors represent quintiles of the range of concentrations for a component in each city; blue, green, yellow, orange, and red display 1st, 2nd, 3rd, 4th, and 5th quintiles).

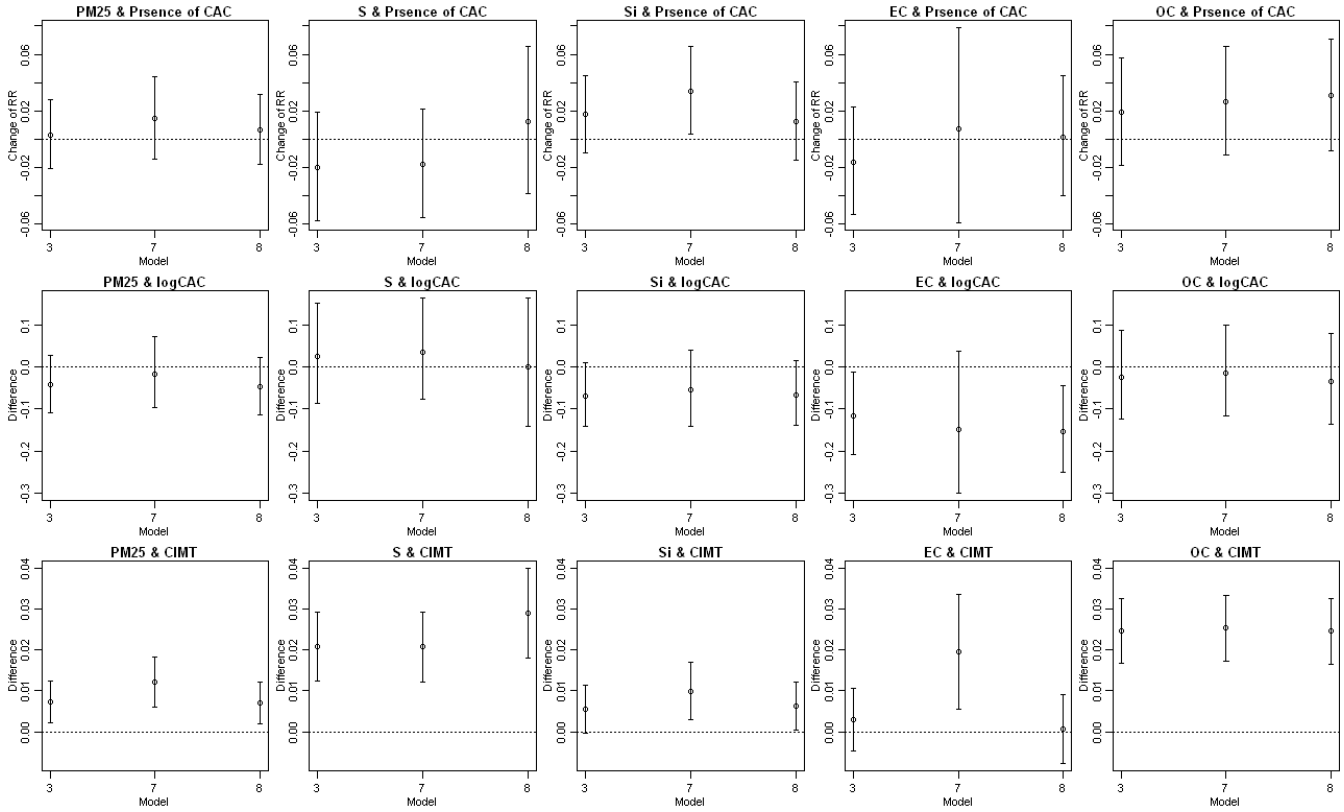


Appendix Figure G.9. Cross-sectional associations for presence of CAC, log(CAC) and CIMT in MESA at exam 1 for an interquartile increase (0.56, 1.65, 1.14, and 13.46 for sulfate, nitrate, SO_2, and NO_2, respectively) in predicted sulfate, nitrate, and SO_2 concentrations from the national spatial model and NO_2 from spatio-temporal model in six cross-sectional models. (See Table 38 in the Section 1 main text for description of the six models.)

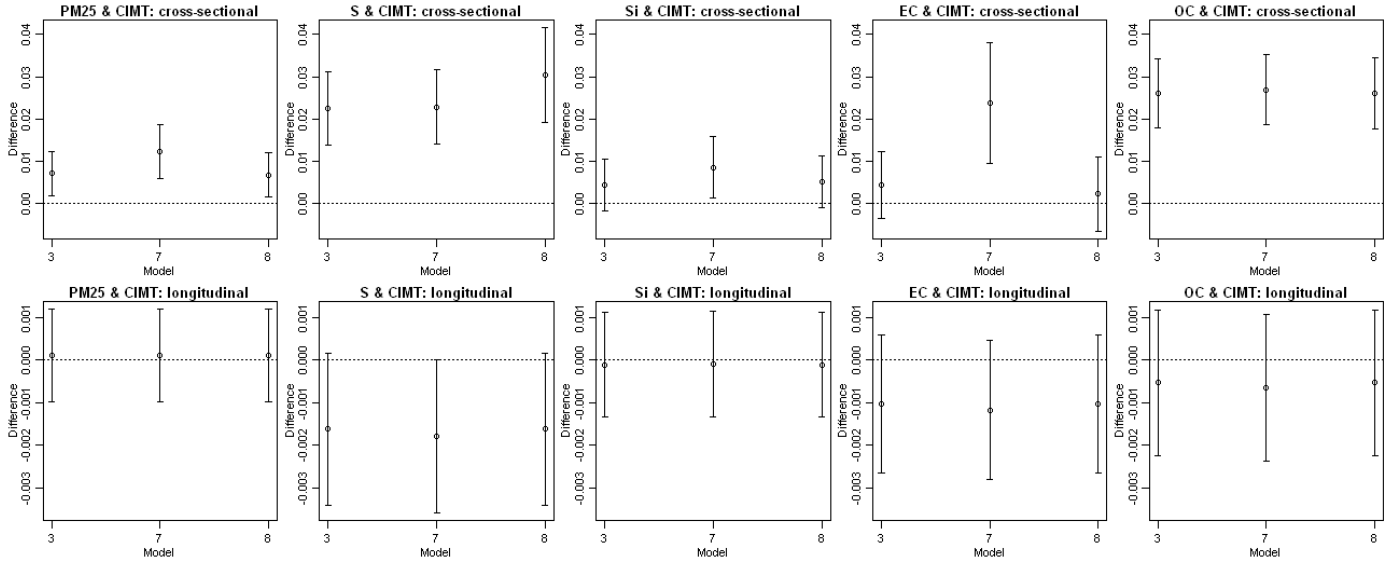


Appendix Figure G.10. Cross-sectional and longitudinal associations from the longitudinal model for CIMT in MESA for an interquartile increase (0.56, 1.65, 1.14, and 13.46 for sulfate, nitrate, SO_2, and NO_2, respectively) in predicted sulfate, nitrate, and SO_2 concentrations from the national spatial model and NO_2 from spatio-temporal model in six models. (See Table 38 in the Section 1 main text for description of the six models.)

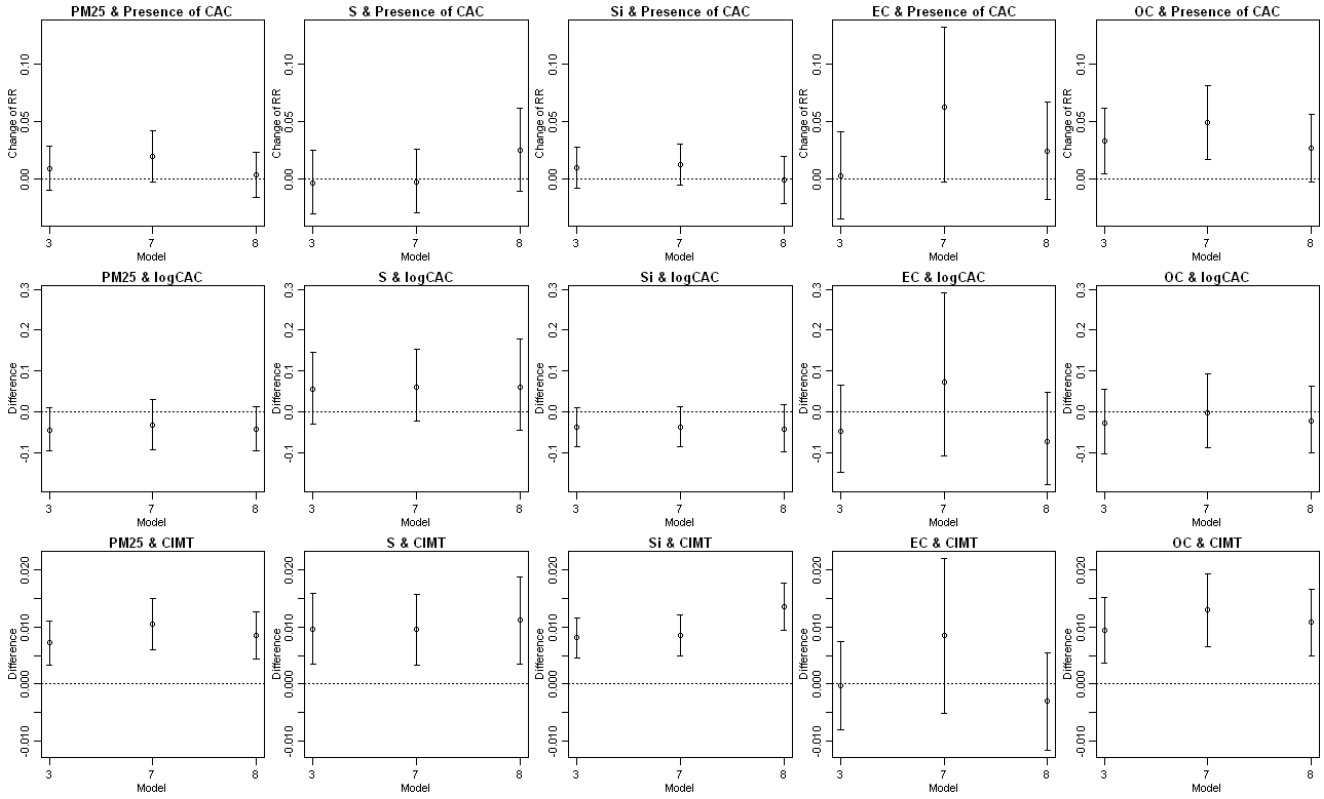
Cross-sectional and longitudinal analyses adjusting for NO_2 and SO_2



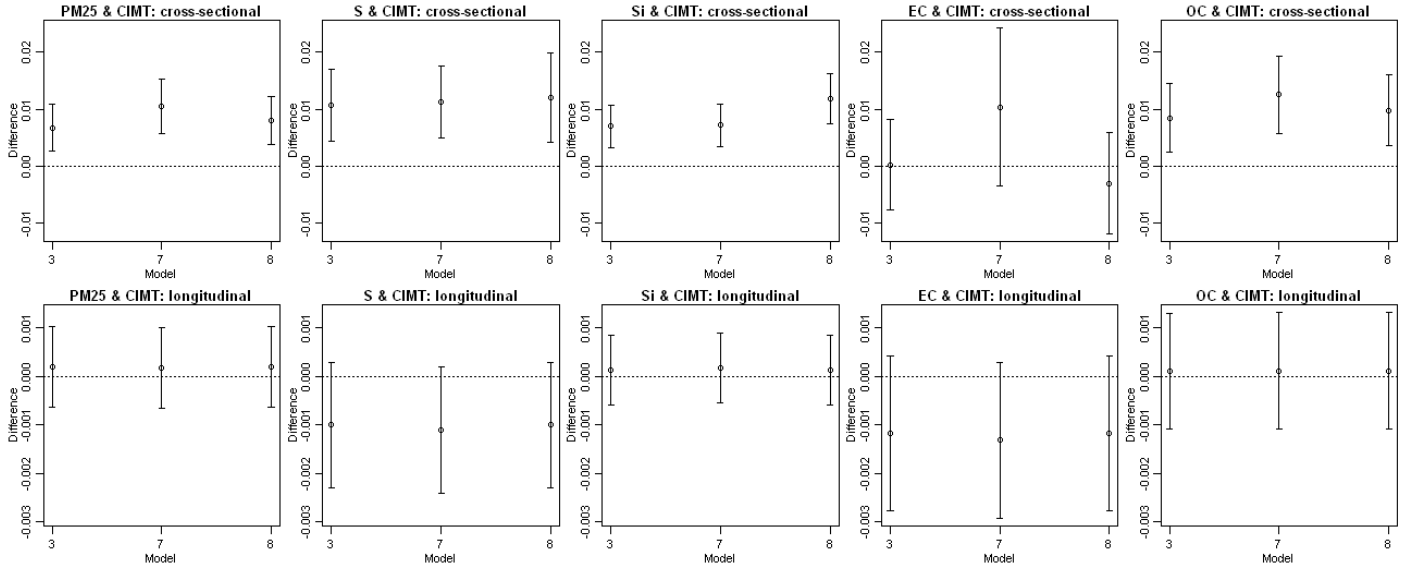
Appendix Figure G.11. Cross-sectional associations for presence of CAC, log(CAC) and CIMT in MESA at exam 1 for an interquartile increase (1.51, 0.51, 0.02, 0.89, and 0.69 for $PM_{2.5}$, sulfur, silicon, EC, and OC, respectively) in predicted $PM_{2.5}$ and $PM_{2.5}$ component concentrations from the NPACT spatio-temporal model in the primary model (model 3) adjusting for NO_2 (model 7) and SO_2 (model 8)



Appendix figure G.12. Cross-sectional and longitudinal associations from the longitudinal model for CIMT in MESA for an interquartile increase (1.51, 0.51, 0.02, 0.89, and 0.69 for $PM_{2.5}$, sulfur, silicon, EC, and OC, respectively) in predicted $PM_{2.5}$ and $PM_{2.5}$ component concentrations from the NPACT spatio-temporal model in the primary model (model 3) adjusting for NO_2 (model 7) and SO_2 (model 8)



Appendix Figure G.13. Cross-sectional associations for presence of CAC, log(CAC) and CIMT in MESA at exam 1 for an interquartile increase (2.19, 0.18, 0.02, 0.28, and 0.39 for $PM_{2.5}$, sulfur, silicon, EC, and OC, respectively) in predicted $PM_{2.5}$ and $PM_{2.5}$ component concentrations from the national spatial model in the primary model (model 3) adjusting for NO_2 (model 7) and SO_2 (model 8)



Appendix figure G.14. Cross-sectional and longitudinal associations from the longitudinal model for CIMT in MESA for an interquartile increase (2.19, 0.18, 0.02, 0.28, and 0.39 for $PM_{2.5}$, sulfur, silicon, EC, and OC, respectively) in predicted $PM_{2.5}$ and $PM_{2.5}$ component concentrations from the national spatial model in the primary model (model 3) adjusting for NO_2 (model 7) and SO_2 (model 8)

Cross-sectional effects of sulfur on CAC and CIMT with the interaction of traffic variables

Appendix Table G.8. Cross-sectional association for presence of CAC, log(CAC) and CIMT in MESA at exam 1 for an interquartile increase in predicted of sulfur from spatio-temporal model and national spatial with the interaction with NO_2 and road proximity variable

			Presence of CAC			Log CAC			CIMT		
Exposure model	Health model	Pollutant	RR*	95% CI		exp(B)	95% CI		B	95% CI	
Spatio-temporal	Interaction with NO_2	Sulfur	1.028	0.943	1.121	0.892	0.689	1.156	0.016	-0.002	0.034
		S*NO_2	0.996	0.990	1.003	1.012	0.994	1.031	-0.002	-0.003	-0.001
	Interaction with road+	Sulfur	0.985	0.944	1.028	1.029	0.904	1.171	-0.006	-0.015	0.003
		S*road	0.976	0.892	1.068	0.995	0.772	1.283	-0.003	-0.020	0.015
National Spatial	Interaction with NO_2	Sulfur	1.002	0.926	1.085	0.890	0.705	1.123	0.011	-0.005	0.027
		S*NO_2	1.000	0.994	1.005	1.013	0.997	1.030	-0.001	-0.003	0.000
	Interaction with road	Sulfur	0.994	0.964	1.025	1.049	0.957	1.150	-0.007	-0.013	0.000
		S*road	1.016	0.951	1.085	1.030	0.859	1.236	0.001	-0.012	0.014

* Effect estimates (RR and beta coefficients) and 95% CIs were presented per interquartile increase in sulfur: 1.51 for the spatio-temporal model and 0.18 for national spatial model

+ Indicator variable for proximity to roads defined by addresses within 100 meters from the closest A1 or A2 road or 50 meters from the closest A3 road