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Long-term exposure to PM2.5 major components and mortality in the southeastern United States 2000-2016: a population-based cohort study

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Abstract

Long-term exposure to PM2.5 major components and mortality in the southeastern United States 2000-2016: a population-based cohort study

By Siyao Xiao

Background

Long-term exposure to fine particulate matter (PM2.5) has been widely linked to adverse health effects in cardiovascular and pulmonary system. However, the association regarding to specific PM2.5 component has been less studied. Research on the relative distribution of PM2.5 component is imperatively needed to better understand the relationship to design effective interventions and environmental policies.

Methods:

We conducted a population-based cohort study comprised of all elder Medicare enrollees (aged ≥65, N=13,590,387) in the southeastern United States from 2000-2016 to explore the association between long-term exposure to PM2.5 and the all-cause mortality among the elderly. We applied well-validated prediction models to estimate the ZIP code level of annual mean concentration of five major PM2.5 components including black carbon (BC), nitrate (NIT), organic matter (OM), sulfate (SO4) and soil particles. Relevant data were analyzed using Cox proportional hazard model adjusting for potential confounders.

Results:

In the cohort of 13,590,387 Medicare enrollees and a total of 107,191,652 person-years, we observed significantly elevated all-cause mortality in all the five PM2.5 components (BC, NIT, OM, SO4 and soil particles) in their single-pollutant models. Hazard ratios (HR) of 1.025 (95%CI: 1.023-1.027), 1.027 (95% CI: 1.025-1.030), 1.012 (95% CI: 1.010-1.013), 1.018 (95% CI: 1.017-1.020), 1.021 (95% CI: 1.017-1.024), and 1.004 (95% CI: 1.003-1.006) were observed respectively.

Conclusions:

Among the cohort of elder Medicare enrollees residing Southeastern US 2000-2016, our study provided epidemiologic evidence that long-term exposure to major PM2.5 components is significantly associated with higher mortality.

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Contents

Introduction

Air pollution is a significant public health issue, leading to a variety of adverse health effects that were well documented worldwide.1 There are numerous epidemiologic studies suggesting an association of long-term exposure to PM2.5 with mortality. 2 In previous cohort studies of large number of Medicare beneficiaries, long-term exposure of PM2.5 was reported to associate with elevated all-cause mortality3-5, hospital admissions, gestational age, and neurological diseases. However, the relative contribution of PM2.5 components still remains unclear. An increasing number of studies reported a variation in the association between PM2.5 mass concentrations and health outcomes regarding to different geographical region and seasons, which could be largely explained by the difference in PM2.5 composition. Therefore, understanding the relative contribution of PM2.5 components is crucial to interpret the incidence of PM2.5-related morality and to design targeted policies.

The health effects of PM2.5 have widely been a concern crossing many countries and regions in the world. Recent epidemiological and toxicological studies have discovered associated adverse health effects besides pulmonary disorder and impairments.6,7 Even at very low level of exposure that is far below the national standard, PM2.5 is still believed to induce adverse outcomes. For instance, some researchers found that both short-term and long-term exposure to PM2.5 were associated with all-cause mortality at exposure levels below the newly revised U.S. EPA standards.7 In addition, the PM2.5 components and the relative proportion of each chemical were found to have effect modification effects on mortality since certain PM2.5 components significantly modified the association8. Thus, it’s not sufficient to rely on PM2.5 mass alone to evaluate health effects of PM2.5 exposure.

The health effect of PM2.5 exposure among the older adults has grown into a big concern in the Southeastern U.S. According to a publication about prescribed fire by United States Department of Agriculture (USDA), in 2011, over 6.4 million acres of forest were burned by prescription in the 13 Southern states. Prescribed fire emitted abundant smoke from biomass burning, therefore having a significant impact on PM2.5 concentrations. In addition, retirement migration has significant impacts on the percentage of elder residents in the southeastern U.S.

Accurate estimates of human exposure to PM2.5 components is essential for such research.10 The exposure assessments in previous studies were usually limited by the geographic locations of air quality monitoring stations, which meant the spatial variation of PM2.5 component exposure was poorly captured. As a result, it lacked epidemiological studies that were conducted based on high-resolution PM2.5 component estimates. To address these needs, we conducted a population-based cohort study that was based on fine-resolution PM2.5 components data and Medicare enrollees to investigate the association between long-term exposure to five major components (BC, NIT, OM, SO4, and soil particles) and all-cause mortality in the southeastern U.S. from 2000-2016. This study aimed to explore the association between each PM2.5 component and mortality.

Material and Methods

Study population

Our study population comprised of Medicare enrollees aged 65 or older residing in seven Southeastern states (Alabama, Florida, Georgia, Mississippi, North Carolina, South

Carolina, and Tennessee). We constructed the cohort from January 1, 2000, to December 31, 2016, with all-cause mortality as the outcome. Each participant in this cohort was marked with a unique ID and were assigned their PM2.5 exposure in each follow-up year. Based on the Medicare beneficiary denominator file that we obtained from the Center for Medicare and Medicaid Services, we extracted varieties of demographic information of Medicare enrollees, including age, gender, race, date of death, ZIP code of residence, the year of Medicare enrollment, and Medicaid eligibility as an indicator of socioeconomical background.

Exposure

We estimated the annual average concentrations of total PM2.5 mass and the five major PM2.5 components of interest at the ZIP code level using well-validated PM2.5 composition prediction models.9 Briefly, we divided the satellite-derived total PM2.5 mass into individual chemical components based on the relative PM2.5 component distribution that we estimated via chemical transport model fused with ground-based measurements of chemical composition.13 In estimating ground-level PM2.5 mass, we used North American Regional Estimates (V4.NA.03), which modified the V4.NA.02 GWR method with additional geographically weighted regression as part of the MAPLE (Mortality–Air Pollution Associations in Low-Exposure Environments) project. Besides, in applying the relative contribution of each PM2.5 component, we used V4.NA.02, which demonstrated significant long-term cross validated R2 of PM2.5 components of 0.59, 0.86, 0.57, 0.96 and 0.60 for BC, NIT, OM, SO4 and soil particles, respectively. We calculated the annual

mean concentration for each PM2.5 component of interest in each ZIP code between 2000 and 2016. Based on the ZIP code of residence in each calendar year, we could capture annual residential mobility.

Covariates

We collected neighborhood-level covariates, including eight ZIP code tabulation area (ZCTA) level variables that were derived from the 2000 U.S. Census, 2010 U.S. Census and 2005-2012 American Community Survey (ACS), and we assigned them to participants based on ZIP code residence. The variables included proportion of Hispanic resident, proportion of Black resident, percentage of participant who received less than high school education, proportion of participant who lived under poverty line, proportion of owner-occupied housing units, population density, median house value, and median annual household income. If information was missing at given year while available at adjacent years, we interpolated it though linear interpolation. Body mass index (BMI) and percentage of ever-smokers at the county level between 2000 and 2016 were obtained from the Behavioral Risk Factor Surveillance System (BRFSS). The data of daily air temperature and relative humidity at 32 km × 32 km spatial resolution were obtained from the North American Regional Reanalysis data (NARR). These daily gridded meteorological data were averaged for each ZIP code, and then we further calculated the annual means and assigned them to participants based on ZIP code of residence.

Statistical analysis

We fit Cox proportional hazard models for each PM2.5 component after adjusting for potential confounders including sociodemographic information, socioeconomic status, behavioral risk factors, and meteorological variables. Namely, we created five single-pollutant models to evaluate the association between long-term exposure to each PM2.5 component and all-cause mortality, respectively. We used a Generalized Estimating Equation (GEE) to adjust for residual autocorrelation within each ZIP code region and used robust standard errors to calculate the 95% confidence interval (CIs). We took the potential lag effect of each PM2.5 component on mortality into consideration; thereby we linked current health records to the PM2.5 exposure in the previous year to build one-year lag models. All the results in the study were presented as hazard ratios with 95% CIs per interquartile range increase in annual mean concentration in exposure. We investigated the potential nonlinearity between each PM2.5 component and all-cause mortality by fitting penalized spline models for each PM2.5 component after adjusting for the same covariates. In single-pollutant models, we characterized the concentration-response (C-R) relationship for each specific PM2.5 component.

We conducted several sensitivity analyses to evaluate the robustness of the main results. First, we made additional adjustments for the total PM2.5 mass and the difference of total PM2.5 mass concentration and each component.12 Second, we fitted the multi-pollutant model, which included all five PM2.5 component of interest and adjusted for the same covariates . Third, we performed multi-component penalized spline models to identify if the C-R relationship holds in both single- and multi-component models.

The computations of the analyses were conducted on the Rollins HPC Cluster at Emory University, and relevant statistical analyses were conducted using R software, version 4.0.2.

Result

Our study included an open cohort of 13,590,387 Medicare enrollees and a total of 107,191,652 person-years of follow-up in the southeastern U.S. from 2000-2016, with a median of 8 years of follow-up. During the study period, 4,898,015 deaths were observed, which accounted for 36.0% of total population. 99.50% of study participants were enrolled between 65 and 74 years old. 43.7% of participants were males and 56.3% of participants were females. White population was the majority among study participants, which accounted for 82.5% of total population, and Black population and other races accounted for 12.8% and 4.6%, respectively. In addition, 12.6% of participants were eligible for Medicaid.

The overall annual mean concentration of PM2.5 mass in the seven targeted states between 2000 and 2016 was 9.6 μg/m3. The annual mean concentrations of five PM2.5 components of interests were 0.8 μg/m3 (IQR: 0.3 μg/m3), 0.5 μg/m3 (IQR: 0.3 μg/m3), 3.6 μg/m3 (IQR:1.2 μg/m3), 2.7 μg/m3 (IQR: 1.5 μg/m3) and 0.7 μg/m3 (IQR: 0.3 μg/m3) for black carbon, nitrate, organic matter, sulfate, and soil particles, respectively. The spatial distribution of total PM2.5 mass and each component were included in the study. The highest PM2.5 mass concentrations were observed in the North-central regions of Alabama, Georgia, and along the Tennessee-North Carolina border.7 For black carbon, Alabama and Georgia had higher concentrations than other states, and a similar distribution was observed

in organic matter. Higher nitrate concentrations were found in western Tennessee and eastern North Carolina regions. In contrast, areas with higher levels of soil particles were concentrated in the southernmost Florida. For sulfate, observations of high concentration were mainly distributed among regions in central North Carolina, north-central areas of Alabama and Georgia, and the Tennessee-North Carolina border. During the study period, we observed a declining trend in total PM2.5 mass concentrations and sulfate levels overall, and the temporal trends of BC, NIT and soil particles were relatively flat. For OM, there was a constant fluctuation in the annual mean concentrations during the 17 years of study period, but the overall change was not significant.

In single-pollutant models, we found a significant positive association between long-term exposure to PM2.5 components and all-cause mortality. In the analyses with no lag effect, each IQR increase in the concentrations of PM2.5 mass, BC, NIT, OM, SO4 and soil particles was associated with mortality with HRs of 1.025 (95% CI: 1.023-1.027), 1.027 (95% CI: 1.025-1.030), 1.012 (95% CI: 1.010-1.013), 1.018 (95% CI: 1.017-1.020), 1.021 (95% CI: 1.017-1.024), and 1.004 (95% CI: 1.003-1.006), respectively. Similar results were observed in one-year lag effect analyses, where the hazard of PM2.5 mass, BC, NIT, OM, SO4, and soil particles increased by 2.7% (95% CI: 2.4-2.9%), 3% (95% CI: 2.8-3.3%), 1.1% (95% CI: 1.0-1.3%), 1.9% (95% CI: 1.7-2.1%), 2.5% (95% CI: 2.2-2.9%) and 0.3% (95% CI: 0.2-0.5%) , respectively, for each IQR increase in the concentration.

We also investigated the C-R relationships between each PM2.5 component and all-cause mortality in single-component models. The association between BC and OM exposure appeared to approach linearity. For NIT exposure, we observed a significant threshold at 0.8 μg/m3. The association between NIT exposure and mortality below 0.8 μg/m3 was not

clear. However, at exposure levels above 0.8 μg/m3, a rising linear association was observed. For sulfate, a linear rising association was found at exposure levels below 2.5 μg/m3, while the C-R curve became flat and presented a weak positive association as sulfate exposure rose. The C-R curve of soil particle was distinct from other four PM2.5 components. We observed a rising trend of morality below the threshold of soil particle exposure at 1 μg/m3, while it went downward and negative at exposure levels above.

Discussion

In our prospective population-based cohort study comprised of 13,590,387 Medicare enrollees, we found significant and independent associations between the long-term exposure to BC, NIT, OM, and soil particles and elevated all-cause mortality in both single- and multiple-component models. The association between SO4 exposure and increased morality was only observed in single-pollutant models, while an inverse association was found after we adjusted for total PM2.5 mass or other PM2.5 components.

Black carbon is derived largely from the incomplete combustion of fossil fuels, wood, and biomass, and is a good indicator of combustion-related air pollution, which was only recently recognized as a short-lived climate-forcer.13,14 The associations between BC exposure and all-cause mortality in our study were consistent with other epidemiological studies.15-18 A Canadian population-based cohort study (n = 299,165) using single- and multi-component models found that the risk of non-accidental death increased by 3.7% for each 1 μg/m3 increase in BC exposure. In addition, the pattern of C-R curve at BC exposure below 1 μg/m3 was similar to our results. It is notable that there is relatively limited evidence of health effects from long-term exposure to PM2.5, as most previous studies

focused on the short-term exposure effects. For the risk of acute exposure to BC, a study conducted in Southern Europe found that the all-cause mortality increased by 1.8% (95% CI: 0.3% to 3.3%) in Athens and 1.8% (95% CI: −0.3% to 4.0%) in Barcelona at 1-day lag15, which was close to our results, 2.4% increase in mortality. Beside European studies, a study conducted in Shanghai also reported a 2.3% (95% CI: 0.6–4.1%) increase in all-cause mortality for each IQR increase in BC exposure.19 Previous studies attribute the health effects of BC to its toxicity to human cardiopulmonary system.20-22 These in-vivo and animal experiments had suggested that exposure to BC may induce cytotoxic morphological changes, inflammatory responses, and inhibition of cell growth, which were associated with mechanisms behind environmental air pollution-mediated atherosclerosis and ischemic heart disease.

Organic matter is a chemically complex compound based on organic carbon and primarily generated through the process of biomass and fossil fuel combustion. In the Southeastern U.S, there is a long tradition of prescribed fire, which is associated with a large production of organic matter especially during later winter and early spring. The health effect of OM has been studied in both short-term and long-term studies.16 In long term studies, Ostro et al. reported that higher all-cause mortality is associated with the increase in organic carbon concentration per IQR in both 8-km and 30-km buffer zones, with the hazard ratios of 1.70 (95% CI: 1.53–1.87) and 1.73 (95% CI: 1.64–1.82), respectively.23 Their results were approximately consistent with ours, in the same direction but different magnitude because Ostro et al mainly focused on organic carbon, which was a component of organic matter, while organic matter that we studied, included both organic carbon and other organic substances. Crouse et al. also found a positive association between organic matter and

increased morality, although it reversed to negative in multi-pollutant models.16 OM was found to be associated with cancer development in multiple toxicologic studies.24-26 It was partially explained as tumor initiators and tumor promotors after being inhaled into the respiratory tract and undergoing metabolic activation. Electrophile epoxides, the oxide as a product, then formed adducts with respiratory cell DNA, causing DNA damage and increasing the risk of cancer in consequence.

Sulfate and nitrate, as the predominant components of secondary inorganic aerosols, are mainly formed by photochemical reactions by ultraviolet, ozone, hydroxyl radical, etc. In the southeastern U.S, gasoline-powered vehicles, diesel engines, natural gas and coal burning generated most of sulfate and nitrate. For nitrate, most studies we found were consistent with our study that the exposure was positively associated with higher mortality. For instance, Li et al.,27 reported that an IQR increase was associated with 0.32% (95% CI: 0.09–0.87%) increase in totally mortality in the full year. Similarly, studies in Houston28 and California23, and a meta-analysis of 63 studies29 also found a positive effect from nitrate exposure. However, the health effect of sulfate exposure is less conclusive. Gwynn et al.30, Liu et al.28, and Ostro et al.23 all reported that higher sulfate exposure was associated with higher all-cause mortality, while Son et al.31 found less contribution of sulfate exposure in the eastern U.S . In our study, we found a significantly positive association in single-pollutant models, it reversed after we adjusted for total PM2.5 mass or other PM2.5 components. R Reiss et al. used the toxicologic characteristics of sulfate to explain it.32 Sulfate could be explained to be less potent than PM2.5 generally, or sulfate was not toxic and was acting as a surrogate for other constituents. Also, the health effects of sulfate exposure might be indirect. There were several hypotheses on the indirect

effects of sulfate regarding to its impacts on bioavailability of metallic species33, enhancement of lung deposition of more toxic compounds34, and catalysis of organic aerosol formation.35 However, it still needs more evidence to draw a general conclusion.

Soil particles are usually suspended in the air by mechanical movements and are one of the major components of fine particulate matter.10 The health effects of soil particle exposure mainly come from the heavy metal and silica components, which were both well documented.36-37 Heavy metal was likely to accumulate in human blood and bones, causing damages to the nervous system, while silica usually deposited in the lungs and impaired the normal function of respiratory system. To the best of our knowledge, there has no literature that explored the association between soil particle exposure and all-cause mortality, but our study provided some insights of views. We found a linear association between soil particle and increased mortality at concentration levels below 1 μg/m3 in the C-R curve, which compromised >90% of our sample size. Namely, for most population in the study, their exposure to soil particle was associated with higher mortality.

There are several strengths in our study. As most previous studies focused on the health effect of total PM mass, few studies specifically investigated on the relative contribution of individual PM2.5 components. There were some literature indicated that variation in PM2.5 components might lead to inconsistency.38-39 In the context, our study advanced the evidence base and specifically focused on individual effects of each PM2.5 component. In exposure assessment, our air pollution data were derived from fine-resolution surface of chemical composition models that had decent accuracy of estimation. In terms of spatial coverage, our study included all regions in the seven states, which included both urban and rural areas. In statistical analysis, we used a combination of multiple analytical methods to

make our results robust. We used the Cox proportional hazard models and penalized spline models, based on both linear and non-linear assumption, to investigate the C-R relationship in single- and multi-pollutant models.

There are also noteworthy limitations in our study. First, we were unable to obtain residential address for each subject, i.e., we had to assign the annual mean levels of exposure at ZIP code level to approximate their true exposure levels, and thus exposure measurement error is likely. Second, we are subject to residual confounding because our models failed to include individual-level behavior risk factors due to lack of available information, such as alcohol consumption, substance use, and exercise frequency.10 Third, our study included five major PM2.5 components, which accounted for most of chemicals in the total PM2.5 mass42. However, this study didn't take the rest of components into consideration and their individual effects on morality remained unclear. Forth, our study only included residents in the southeastern U.S., which meant we might not be able to present the true association at national level. Due to the heterogeneity in PM2.5 components and demographic information, our results might not be applicable to other regions of the U.S. In addition, we were unable to access the cause of mortality among deceased Medicare enrollees. Finally, due to the potential confounding effects by other PM2.5 components and the variation of total PM2.5 mass, most previous studies chose multi-pollutant models18,43 or adjusted for total PM2.5 mass afterward.18,19,44,45 However, because of the intercorrelation among PM2.5 components, multicollinearity was an issue in multi-pollutant models in our large-scale study.

Conclusion

In our study, we found a statistically significant and positive association between long-term exposure to major PM2.5 components (BC, NIT, OM and soil particles) and elevated all-cause mortality among older adults in the southeastern U.S.

Appendix

Table 1. Cohort characteristics

	Number	Percentage %
Demographic Information		
Death	4,898,015	36.00
Total Population	13,590,387	100
Total person-years	107,191,652	100
Age at entry (years)		
65-74	13,527,082	99.50
75-84	53,181	0.40
85+	10,122	0.07
Gender		
Male	5,943,391	43.70
Female	7,646,996	56.30
Race		
White	11,217,509	82.50
Black	1,745,096	12.80
Other	627,782	4.60
Medicaid Eligibility		
Eligible	1,718,169	12.60
Not Eligible	11,872,218	87.40
Air pollutant ($\mu g/m^3$)*		
$PM_{2.5}$ mass	9.56	2.10
Black carbon	0.82	0.27
Nitrate	0.54	0.20
Organic matter	3.56	0.93
Sulfate	2.71	1.02
Soil particles	0.72	0.29
Area-level covariates*		
Annual mean temperature, Celsius	19.40	3.60
Relative Humidity, %	76.30	4.00
Smoking rate, %	47.60	7.10
Below Poverty Level, %	10.80	6.80
Not graduated from high school, %	26.80	15.10
Owner-occupied housing units, %	70.40	13.40
Population density, people per mile squared	1516.40	2170.20
Body-mass index, kg/m^2	27.50	1.00

Median house value, US$1000	149.20	85.90
Median household income, US$1000	46.00	15.80

Table 2. Mortality associated with per interquartile range increase in the concentrations of PM2.5 mass and major components

	Single-component Models (Lag 0)	Single-component Models (Lag 1)
	Hazard Ratio (95% CI)	
$PM_{2.5}$ mass	1.025 (1.023,1.027)	1.027 (1.024,1.029)
Black Carbon	1.027 (1.025, 1.030)	1.030 (1.028,1.033)
Nitrate	1.012 (1.010, 1.013)	1.011 (1.010,1.013)
Organic Matter	1.018 (1.017, 1.020)	1.019 (1.017,1.021)
Sulfate	1.021 (1.017, 1.024)	1.025 (1.022,1.029)
Soil Particles	1.004 (1.003, 1.006)	1.003 (1.002,1.005)

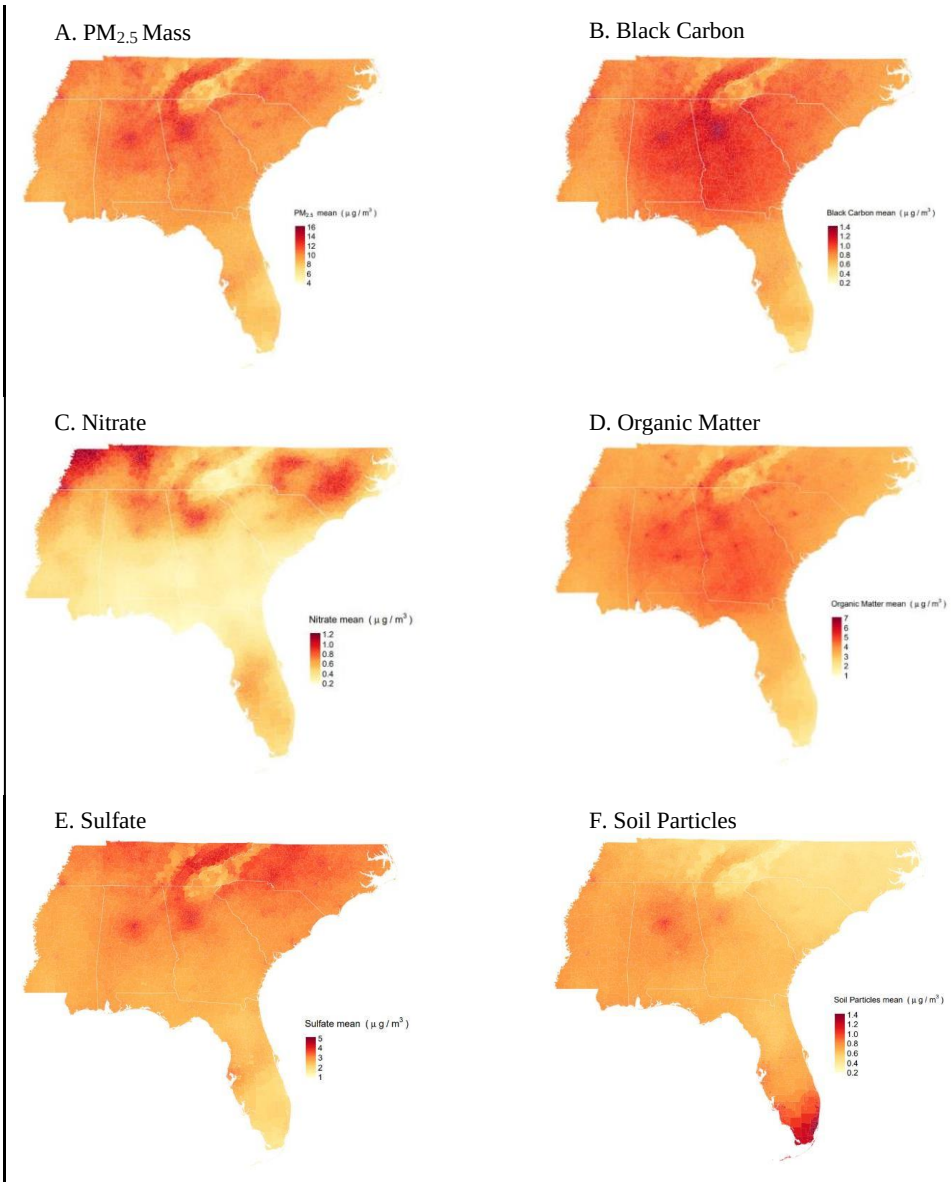

Figure 1. Average concentrations (µg/m3) of PM2.5 mass and major components in the southeastern United States from 2000-2016.

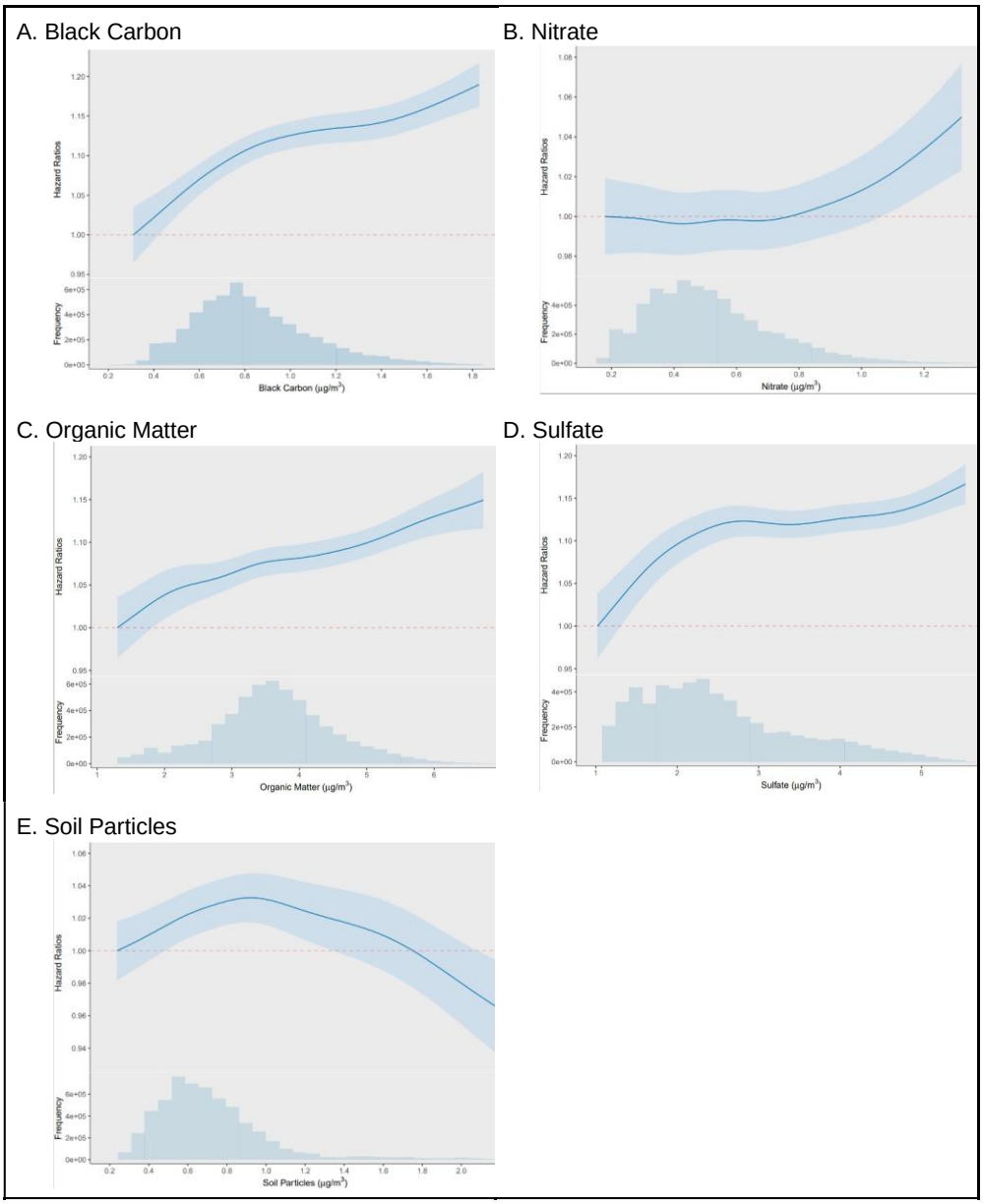

Figure 2. Concentration-response curves for five major components (BC, OM, NIT, SO4 and soil particles) from single-pollutant models.

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