**Air Pollution Epidemiology to Support Environmental Regulations and Policies**

by

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## Dedication

To my mom. I love you and miss you terribly.

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Thank you to Sara for all of her support and mentorship over these years, and for her unwavering patience and compassion when things were so hard.

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## ABSTRACT

Research shows that air pollutants such as particulate matter (PM) are associated with heart and lung disease and other adverse health effects. A primary way the US Environmental Protection Agency (EPA) reduces air pollutant concentrations is by setting National Ambient Air Quality Standards (NAAQS), which regulate the maximum pollutant levels allowed in ambient air. The EPA also establishes source-specific emissions standards and pollution-reduction policies.

Currently, the NAAQS regulates $PM_{2.5}$ (<2.5 μm) and $PM_{10}$ particles (<10 μm). Importantly, however, $PM_{10}$ includes $PM_{2.5}$ particles. As such, the EPA would rather replace the $PM_{10}$ standard with a standard specifically for $PM_{10-2.5}$ (≤ 10 μm and >2.5). Yet, the EPA has not done so, deciding that there was inadequate information on the causal impacts of $PM_{10-2.5}$ on health. The limited amount of $PM_{10-2.5}$ health research is largely due to an insufficient availability of exposure data. However, data from National Aeronautics and Space Administration (NASA) satellites creates opportunities to estimate $PM_{10-2.5}$ levels to use in assessing $PM_{10-2.5}$ health impacts.

The first two aims of this dissertation were designed to inform the science used by the EPA to set a $PM_{10-2.5}$ NAAQS. In Aim 1, we estimated $PM_{10-2.5}$ exposure using highly resolved satellite data and advanced spatiotemporal statistical modeling in six US metropolitan areas. In Aim 2, we paired these $PM_{10-2.5}$ estimates with the detailed health data in the Multi-Ethnic Study of Atherosclerosis (MESA) to estimate cross-sectional

associations between long-term $PM_{10-2.5}$ exposure and levels of inflammation and coagulation, which are subclinical markers of cardiovascular disease.

Aim 3 was designed to inform the EPA in its setting of a source-specific emissions reduction program. We focused on a diesel school bus program since they transport more than 25 million children – a highly sensitive subpopulation – in the US each year. The EPA developed the Diesel Emissions Reduction Act (DERA) School Bus Rebate Program, which randomly awards funding to replace older, more polluting diesel school buses with cleaner buses. In Aim 3 I quantified the attendance impacts of this EPA program.

In Aim 1, our final predictions captured the long-term spatial patterns of $PM_{10-2.5}$ very well in four of our study areas, and well to modestly in the others. Additionally, it outperformed two alternative exposure prediction methods spatially in all six areas. In Aim 2, we found no evidence that long-term $PM_{10-2.5}$ exposure was associated with greater levels of inflammation and coagulation in the MESA cohort. In fact, contrary to our hypothesis, we found greater inflammation and coagulation with lower $PM_{10-2.5}$, although results were sensitive to adjustment for chronic health conditions. In Aim 3, we found suggestive evidence that receiving rebate funds to replace or retrofit older school buses with cleaner buses was associated with increases in school district attendance. The attendance effects were strongest when larger proportions of students were impacted and when the oldest, most polluting buses were replaced.

This dissertation provides evidence that using satellite data in spatiotemporal prediction modeling can successfully generate long-term average spatially resolved $PM_{10-2.5}$ estimates. It also highlights the strengths and limitations of using satellite-based

predictions to study the health impacts of $PM_{10-2.5}$ exposure. Additionally, it provides evidence that a source-specific emissions reduction program, such as the EPA's DERA School Bus Rebate Program, can have measurable impacts based on the suggestive evidence we saw of the program's role in improving school district attendance.

# CHAPTER 1 :

# Introduction

## Background:

### *Air Pollution is Associated with Adverse Health Outcomes*

Air pollution has been ranked as one of the top ten risk factors for morbidity and mortality in the world, largely due to its impacts on cardiovascular and respiratory disease (US EPA 2019). Importantly, the observed exposure-response relationships with air pollution are near-linear (Pope et al. 2015) at levels observed in the United States (US) with no evidence of a threshold below which there is no impact on health (Pope et al. 2020). As such, even at current low levels, it is estimated that nearly 80,000 lives are lost prematurely each year in the US due to the cardiovascular impacts of these exposures (Brauer 2016) while nearly 1,000 lives are lost prematurely each year due to the respiratory impacts of these exposures (WHO 2016).

One of the most ubiquitous forms of air pollution is particulate matter (PM), which includes a broad class of "chemically and physically diverse substances that exist as discrete particles (liquid droplets or solids) over a wide range of sizes" (US EPA 2019). The most common sizes studied include $PM_{2.5}$ (aerodynamic diameter $\leq 2.5$ μm), $PM_{10}$ (aerodynamic diameter $\leq 10$ μm), and $PM_{10\text{-}2.5}$ (aerodynamic diameter $\leq 10$ μm and $> 2.5$ μm). Yet the current understanding of the population burden of airborne particles is driven almost exclusively by the rich literature on $PM_{2.5}$ (Lim et al. 2010).

The US Environmental Protection Agency's (EPA's) most recent review of the science concluded that short- and long-term $PM_{2.5}$ exposure is causally linked to all-cause mortality as well as system- and organ-specific adverse outcomes (US EPA 2019). In this review, the EPA concluded that short- and long-term $PM_{2.5}$ exposure is causally linked to many cardiovascular effects, including myocardial infarction, hospital admissions or emergency department visits for cardiovascular disease, and cardiovascular-related mortality (US EPA 2019). The EPA also found likely causal relationships between short- and long-term $PM_{2.5}$ exposure and respiratory effects, including hospital admissions or emergency department visits for endpoints such as asthma, chronic obstructive pulmonary disease (COPD), respiratory infection, and respiratory-related mortality (US EPA 2019). For many of these associations, there was evidence of increased risk by factors such as race/ethnicity, socioeconomic status, and age (US EPA 2019). While these heterogeneous associations by race/ethnicity and socioeconomic status might exist due to factors such as differences in proximity to and types of local emissions sources, housing quality, and occupation, heterogeneous effects by age are likely due to biological differences.

In terms of $PM_{10-2.5}$, the recent EPA review of the science determined that the evidence was suggestive of, but not sufficient to infer, a causal relationship between both short- and long-term $PM_{10-2.5}$ exposures and cardiovascular effects, such as cardiovascular-related emergency department visits, hospital admissions, and mortality (US EPA 2019). While the mechanisms underlying relationships with PM are incompletely understood, local and systemic inflammation and coagulation have been proposed as key pathways by which PM of all different size fractions impacts health.

### *EPA Sets National Ambient Air Quality Standards (NAAQS) to Protect Health*

One of the primary mechanisms by which the EPA can act to reduce ambient air pollution levels is by setting NAAQS for pollutants considered harmful to public health and the environment. The EPA derives its authority to set NAAQS from the Clean Air Act (US EPA 2020). The NAAQS are reviewed periodically and may be revised based on the state of the science at the time of each review.

To date, the EPA has set NAAQS for six principal pollutants, including $PM_{2.5}$ and $PM_{10}$. The current 24-hour NAAQS for $PM_{2.5}$ is 35 $\mu g/m^3$ while the annual standard is 12 $\mu g/m^3$ (US EPA 2020). The 24-hour NAAQS for $PM_{10}$ is 150 $\mu g/m^3$ (US EPA 2020).

### *Regulations Might Have Even Stronger Health Impacts if Targeted to Independent Size Fractions*

The rich scientific literature on the health impacts of $PM_{2.5}$ and $PM_{10}$ has allowed the EPA to set NAAQS for each of these pollutants. Yet the EPA would ideally prefer to regulate $PM_{2.5}$ and $PM_{10-2.5}$ since $PM_{10}$ contains all particles with diameter $\leq$10 $\mu m$, including $PM_{2.5}$. This overlapping nature of $PM_{2.5}$ and $PM_{10}$ makes it difficult to determine whether observed $PM_{10}$ health effects are due to the portion of $PM_{10}$ that is $PM_{2.5}$, or if the larger size fraction of $PM_{10-2.5}$ indeed has independent health impacts from those of $PM_{2.5}$.

$PM_{10-2.5}$ is found in the US at similar concentrations to $PM_{2.5}$ (US EPA 2019) and, like $PM_{2.5}$, also penetrates into the lungs and is highly inflammatory (Brook et al. 2002). Yet, there are many reasons to believe that $PM_{10-2.5}$ contributes additional, independent, health risks from those of $PM_{2.5}$. For example, $PM_{10-2.5}$ originates from different sources (US EPA 2019), has different composition (Masri et al. 2015), and deposits differently in the body from $PM_{2.5}$ (Schulz et al. 2000). In fact, toxicology studies have shown that

$PM_{10-2.5}$ can induce reactive oxygen species and initiate inflammatory responses in vivo and in vitro, possibly more strongly than $PM_{2.5}$ (Monn & Becker 1999; Shi et al. 2003; Pozzi et al. 2003; Becker et al. 2005; Schins et al. 2004). Studies have also shown that, like $PM_{2.5}$, $PM_{10-2.5}$ may produce adverse health effects through pulmonary oxidative stress that leads to a systemic inflammatory cascade in the lungs, blood, and arteries (Tuder et al. 2006; Seaton et al. 1995; Donaldson et al. 2001).

While the epidemiology literature on $PM_{10-2.5}$ is very small, there is suggestive but inconclusive evidence for independent health impacts of $PM_{10-2.5}$ exposure. Using central-site monitors, there is a small literature that suggests that long-term exposures to large particles between 10 and 2.5 μm or 15 and 2.5 μm are associated with larger risks of all-cause mortality (HEI 2000; Lipfert et al. 2006; McDonnell et al. 2000), coronary heart disease (Chen et al. 2005), and non-malignant respiratory disease (McDonnell et al. 2000), though these results were not typically distinguishable from no association. Two other large studies found no evidence of an association between long-term exposures to $PM_{10-2.5}$ and total mortality (HEI 2000) and nonmalignant respiratory mortality (Dimakopoulou et al. 2014). This is in contrast to a national analysis of short-term exposures to $PM_{10-2.5}$ and cause-specific mortality which found the largest effect of exposure on respiratory mortality, a result that was statistically significant in combined results across 47 cities, even adjusted for $PM_{2.5}$ (Zanobetti et al. 2009).

For non-fatal cardiovascular outcomes, there is some evidence of short-term associations with $PM_{10-2.5}$. For example, Peters et al. (2001) found positive but not statistically significant associations between 2-hour and 24-hr $PM_{10-2.5}$ exposure and myocardial infarction onset in a case-crossover study in Boston, with all exposure

measurements coming from a single site in South Boston. Using collocated $PM_{10}$ and $PM_{2.5}$ monitors to calculate $PM_{10-2.5}$ concentrations in 108 US counties, Peng et al. (2008) similarly found positive but not statistically significant associations between same-day $PM_{10-2.5}$ exposure and county-level cardiovascular hospital admission rates among Medicare enrollees after adjustment for $PM_{2.5}$. Tolbert et al. (2007) also found positive but not statistically significant associations between same-day $PM_{10-2.5}$ measured at a central monitor in Atlanta and city-wide cardiovascular related emergency department visit counts in a single-pollutant model.

Fewer studies have evaluated associations of health with long-term exposures to $PM_{10-2.5}$. Adar et al. (2015a), one of the few studies looking at subclinical disease, found suggestive but inconclusive associations between 5-year $PM_{10-2.5}$ residential exposure estimated with land-use regression and summary measures of systemic inflammation and coagulation among participants in three of the six Multi-Ethnic Study of Atherosclerosis (MESA) study areas using cross-sectional analysis. A connection with inflammation might help to explain some of the observed associations with cardiac events. Associations differed by component and the analysis suffered from low power. Adhikari et al. (2016) also evaluated long-term $PM_{10-2.5}$ exposure among the same study population and found similarly weak evidence of an association with lower heart rate variability.

***Recent Advances in Exposure Science May Allow for Better Regulation of PM***

A major challenge to epidemiologists in assessing the health risks of $PM_{10-2.5}$ has been a lack of monitors from which $PM_{10-2.5}$ exposures can be estimated. Historically, only 1% of US counties had collocated $PM_{10}$ and $PM_{2.5}$ monitors with which to estimate $PM_{10-2.5}$ (US EPA 2019). This is especially problematic for studying the long-term health

effects of $PM_{10-2.5}$ since $PM_{10-2.5}$ is substantially more spatially variable than many other pollutants. For example, the longer atmospheric lifetime for $PM_{2.5}$ compared to $PM_{10-2.5}$ (Wilson & Suh 1997) results in $PM_{2.5}$ being more homogeneously distributed than $PM_{10-2.5}$, whose concentrations are more reflective of proximity to local sources (US EPA 2019). Therefore, the use of only a few central monitors for $PM_{10-2.5}$ is largely insufficient to accurately reflect the exposures of individuals across a whole region. As a result, only a handful of investigations have examined the health implications of long-term exposures to $PM_{10-2.5}$ and these studies often suffer from power issues, likely due to biases towards the null caused by measurement error (Adar et al. 2014).

Fortunately for the state of the science, "big data" from National Aeronautics and Space Administration (NASA) satellites have created opportunities to assess $PM_{10-2.5}$ at all locations in the US. Aerosol optical depth (AOD), a measure of light extinction by aerosol scattering and absorption in the atmospheric column, is sampled continuously from space at a 1 $km^2$ resolution using Moderate Resolution Imaging Spectroradiometer (MODIS) technology on the polar orbiting and sun-synchronous NASA Terra satellite (Nordio et al. 2013; Sorek-Hamer et al. 2016; Kloog et al. 2011). The availability of these daily measurements across all locations of the world, along with advancements in spatiotemporal prediction modeling, now allow for the estimation of air pollution levels at fine-scale spatial and temporal resolution even where no monitoring stations exist (Kloog et al. 2011). This approach adds substantial information and spatial resolution that are of critical importance in long-term air pollution epidemiology studies.

Previous research has shown good predictive ability using this satellite data-based approach for $PM_{2.5}$ (cross-validation (CV) $R^2$: 0.7 to 0.9) and related associations with

health (chronic coronary heart disease mortality rate, incidence of acute myocardial infarction, and cardiovascular and respiratory related hospital admissions) in the US, Italy, and Israel (Kloog et al. 2012; Nordio et al. 2013; Kloog et al. 2011; Kloog et al. 2015; Hu 2009; Madrigano et al. 2013; McGuinn et al. 2016; Kloog et al. 2012). More recently, the same methods were used to predict $PM_{10}$ with similar performance (out-of-sample $R^2$: 0.8), even in an area with complex geographic and weather patterns (Nordio et al. 2013; Kloog et al. 2015). To date, however, no model for $PM_{10\text{-}2.5}$ has been developed using satellite information and thus this modern source of data has not yet been used by epidemiology studies to inform the EPA regulation setting process.

### *EPA Uses Source-Specific Emissions Standards and Pollution Reduction Programs to Protect Health*

Another approach the EPA takes to reduce ambient air pollution in the US is to set source-specific emissions standards and design pollution reduction programs. This has often targeted motor vehicle emissions, which typically contribute between 24%-38% to $PM_{2.5}$ concentrations and between 27%-30% to $PM_{10}$ concentrations in the US (US EPA 2017; Karagulian et al. 2015). For example, in 2014 the EPA issued a Tier 3 regulation that requires the reduction of tailpipe emissions of PM from passenger cars by 70% and from trucks by 60% (US EPA 2014).

The EPA has also designed non-binding air pollution reduction policies and programs targeted specifically at diesel engine sources since it is estimated that diesel engines are responsible for approximately 75% of all mobile source emissions (Fulper et al. 2012). For example, the voluntary diesel retrofit program encourages the installation of pollution-reducing technology on existing diesels through partnerships, retrofit technology assessment, funding and financial incentives, demonstration projects, and

outreach, marketing, and service (US EPA 2015). Provisions of the Diesel Emissions Reduction Act (DERA) of 2010 added a rebate program option, known as the National Clean Diesel Rebate Program. Under this program the EPA could offer funding to eligible applicants to reduce diesel emissions from a variety of mobile sources.

The first round of funding under the National Clean Diesel Rebate Program was the 2012 School Bus Rebate Program. School buses were targeted by the EPA because emissions from these buses can elevate concentrations of many harmful pollutants, including PM, by a factor of 2 to 10 (Adar et al. 2008; Rim et al. 2008; Sabin et al. 2005; Behrentz et al. 2005; Zhang et al. 2010; Marshall et al. 2005; Liu et al. 2010) in a sensitive population of children. While the 25 million children in the US riding buses to school (Snyder & Dillow 2011) only spend a small fraction of their day on school buses, that time has been shown to contribute a disproportionately high fraction to students' daily air pollution exposure (Behrentz et al. 2005). As a result, in 2012 the EPA awarded $1.88 million to public and private fleet owners to replace older school buses with new, cleaner school buses (US EPA 2012). The program has continued and through the 2017 program year, the EPA has awarded almost $28 million for the replacement or retrofit of older buses (US EPA 2012 and 2014-2017).

In spite of this large investment by the EPA, there has been very limited research evaluating the effectiveness of the National Clean Diesel Rebate Program, which awarded rebate funding to applicants randomly, based on the results of a lottery. Only one study, in Seattle, measured concentrations in buses that adopted cleaner fuels and technologies onto school buses as a result of EPA's voluntary diesel retrofit program. This study showed that there were 10-50% reductions in $PM_{2.5}$ concentrations on school

buses using ultralow-sulfur diesel fuel, diesel oxidation catalysts, and/or closed crankcase ventilation systems (Adar et al. 2015b). These pollution reductions also translated to improved health for the students who rode the buses, with reduced levels of exhaled nitric oxide, improved lung function measures and lower absenteeism rates. Another ecological study evaluating the impact of voluntary school bus retrofits in the Puget Sound region of Washington State used a difference-in-difference analysis approach and found that school bus retrofits induced reductions in bronchitis, asthma, and pneumonia incidence for at-risk populations (Beatty & Shimshack 2011). A final study in Georgia showed that school districts that retrofitted their school buses had larger increases in aerobic capacity on state-required physical activity tests and significant gains on standardized testing for academic achievement as compared to other districts; they also observed weak and imprecise associations with attendance (Austin et al. 2019). While these studies have shown the public health successes of school bus retrofit programs in two states, this national EPA program has yet to be evaluated.

### *EPA Action Requires Scientific Research*

The commonality between EPA's NAAQS regulations and other emissions reduction standards, policies, and programs is that they are designed to protect health and are informed by scientific research (US EPA 2019; US EPA 2014). For example, prior to actually setting a NAAQS level, the EPA undergoes a multi-year review of the scientific research to determine which pollutants to set NAAQS for and what level and form those standards should take (US EPA 2020). Similarly, when designing source-specific emissions standards or pollution reduction policies, EPA considers the potential health benefits that could result from specific air pollution reduction programs. And, for a

program such as the School Bus Rebate Program that allocates funding on an annual basis, evaluation of the effectiveness of the program is important when deciding whether to re-allocate the funding in future years.

***Summary of Dissertation Aims***

With the following three Specific Aims, this dissertation attempts to inform the science that can be used by the EPA to set a $PM_{10-2.5}$ NAAQS as well as to evaluate the effectiveness of the national EPA DERA School Bus Rebate Program:

**Specific Aim 1**

Predict daily concentrations of $PM_{10-2.5}$ at a 1 $km^2$ spatial resolution within six US urban areas using spatiotemporal prediction modeling with AOD data from the NASA Terra satellite and compare the prediction performance to that of three simpler alternative exposure prediction approaches.

**Specific Aim 2**

Use satellite-derived $PM_{10-2.5}$ exposure estimates that were developed in Specific Aim 1 along with detailed health information available in the Multi-Ethnic Study of Atherosclerosis (MESA) to quantify associations between long-term exposure to $PM_{10-2.5}$ and key subclinical markers of cardiovascular disease.

***Hypothesis 2a:***

Long-term $PM_{10-2.5}$ exposure will be positively associated with c-reactive protein (CRP) and interleukin-6 (IL-6), as markers of inflammation, and fibrinogen, factor VIII, D-dimer, and plasmin-antiplasmin complex (PAP), as markers of coagulation, over the 10 years of follow-up in MESA after adjusting for traditional risk factors as well as co-pollutants, including $PM_{2.5}$ and $NO_x$.

***Hypothesis 2b:***

Relationships with $PM_{10-2.5}$ will be stronger for older and minority participants, and for participants residing in neighborhoods of lower socioeconomic status.

**Specific Aim 3**

Quantify the impacts of EPA funding to replace older, more polluting school buses with cleaner upgrades through the EPA's DERA School Bus Rebate Program on school district absenteeism rates.

***Hypothesis 3:***

School districts awarded funding through the EPA's DERA School Bus Rebate Program lottery will see greater declines in absentee rates after receiving funding for school bus replacements than eligible school districts that apply but are not awarded funding for school bus replacement.

Chapters two through four of this dissertation describe the methods and results for each specific aim. Chapter 2 uses advanced spatiotemporal prediction modeling approaches with AOD data from the NASA Terra satellite to estimate daily and long-term average concentrations of $PM_{10-2.5}$ at a 1 $km^2$ resolution in six US urban areas (Aim 1). Chapter 3 uses these $PM_{10-2.5}$ concentration estimates to cross-sectionally estimate associations between long-term $PM_{10-2.5}$ and markers of inflammation and coagulation in the MESA cohort (Aim 2). Chapter 4 takes advantage of the EPA's randomized allocation of rebate funding for school bus replacements and retrofits to causally assess the impacts of the EPA's 2012-2017 DERA School Bus Rebate Programs on school district attendance rates (Aim 3). Chapter 5 summarizes the overall findings, strengths and limitations, and

implications of this dissertation, and concludes with a discussion of future directions for this research.

**References:**


Adar SD, Davey M, Sullivan JR, Compher M, Szpiro ALiu LJS, Predicting airborne particle levels aboard Washington State school buses. Atmospheric Environment, 2008. 42:7590-7599.

Adar, S.D., Filigrana, P.A., Clements, N., Peel, J.L., 2014. Ambient Coarse Particulate Matter and Human Health: A Systematic Review and Meta-Analysis. Curr Envir Health Rpt. 1, 258-274.

Adar SD, D'Souza J, Mendelsohn-Victor K, Jacobs Jr. DR, Cushman M, Sheppard L, et al., Markers of inflammation and coagulation after long-term exposure to coarse particulate matter: a cross-sectional analysis from the multi-ethnic study of atherosclerosis. Environmental Health Perspectives, 2015a. 123(6):541-548.

Adar, S.D., D'Souza, J., Sheppard, L., Kaufman, J.D., Hallstrand, T.S., Davey, M.E., Sullivan, J.R., Jahnke, J., Koenig, J., Larson, T.V., Liu, L.J.S., 2015b. Adopting Clean Fuels and Technologies on School Buses: Pollution and Health Impacts in Children. Am J Respir Crit Care Med. 191, 1413-1421.

Adhikari R, D'Souza J, Soliman EZ, Burke GL, Daviglus ML, Jacobs Jr. DR, et al., Long-term Coarse Particulate Matter Exposure and Heart Rate Variability in the Multi-ethnic Study of Atherosclerosis. Epidemiology, 2016. 27(3):405-413.

Austin, W., Heutel, G., Kreisman, D., 2019. School bus emissions, student health and academic performance. Econ Educ Rev. 70, 109-126.

Beatty, T.K.M., Shimshack, J.P., 2011. School buses, diesel emissions, and respiratory health. J Health Econ. 30, 987-999.

Becker S, Dailey LA, Soukup JM, Grambow SC, Devlin RBHuang Y-CT, Seasonal Variations in Air Pollution Particle-Induced Inflammatory Mediator Release and Oxidative Stress. Environmental Health Perspectives, 2005. 113:1032-1038.

Behrentz E, Sabin LD, Winer AM, Ritz DR, Pankratz DV, Colome SD, et al., Relative Importance of School Bus-Related Microenvironments to Children's Pollutant Exposure. Journal of the Air & Waste Management Association, 2005. 55(10):1418-1430.

Brauer M, The Global Burden of Disease from Air Pollution. February 2016: Presentation at the American Association for the Advancement of Science Annual Meeting. Washington, DC.

Brook RD, Brook JR, Urch B, Vincent R, Rajagopalan SSilverman F, Inhalation of Fine Particulate Air Pollution and Ozone Causes Acute Arterial Vasoconstriction in Healthy Adults. Circulation, 2002. 105(13):1534-1536.

Chen LH, Knutsen SF, Shavlik D, Beeson WL, Petersen F, Ghamsary M, et al., The Association between Fatal Coronary Heart Disease and Ambient Particulate Air Pollution: Are Females at Greater Risk? Environmental Health Perspectives, 2005. 113:1723-1729.

Dimakopoulou K, Samoli E, Beelen R, Stafoggia M, Andersen ZJ, Hoffmann B, et al., Air Pollution and Nonmalignant Respiratory Americal Journal of Respiratory and

Critical Care Medicine Mortality in 16 Cohorts within the ESCAPE Project, 2014. 189(6):684-696.

Donaldson K, Stone V, Seaton AMacNee W, Ambient Particle Inhalation and the Cardiovascular System: Potential Mechanisms. Environmental Health Perspectives, 2001. 109:523-527.

Fulper CR, Bailey CR, Baldauf RW, Cook JR, Somers JH, Quality OoTaA, et al., Factors Influencing the Contributions of Diesel and Gasoline Exhaust to PM2.5 Emission Inventories, in EPA Emission Inventory Conference. 2012.

Health Effects Institute, Special Report: Reanalysis of the Harvard Six Cities Study and the American Cancer Society Study of Particulate Air Pollution and Mortality. 2000: Health Effects Institute, Boston MA.

Hu Z, Spatial analysis of MODIS aerosol optical depth, PM2.5, and chronic coronary heart disease. International Journal of Health Geographics, 2009. 8:27-36.

Karagulian F, Belis CA, Dora CFC, Pruss-Ustun AM, Bonjour S, Adair-Rohani H, et al., Contributions to cities' ambient particulate matter (PM): A systematic review of local source contributions at global level. Atmospheric Environment, 2015. 120:475-483.

Kloog I, Koutrakis P, Coull BA, Lee HJSchwartz J, Assessing temporally and spatially resolved PM2.5 exposures for epidemiological studies using satellite aerosol optical depth measurements. Atmospheric Environment, 2011. 45(35):6267-6275.

Kloog I, Nordio F, Coull BASchwartz J, Incorporating local land use regression and satellite aerosol optical depth in a hybrid model of spatiotemporal PM2.5 exposures in the Mid-Atlantic states. Environmental Science & Technology, 2012. 46(21):11913-11921.

Kloog I, Sorek-Hamer M, Lyapustin A, Coull B, Wang Y, Just AC, et al., Estimating daily PM 2.5 and PM 10 across the complex geo-climate region of Israel using MAIAC satellite-based AOD data. Atmospheric Environment, 2015. 122:409-416.

Lim SS, Vos T, Flaxman AD, Danaei G, Shibuya K, Adair-Rohani H, et al., A comparative risk assessment of burden of disease and injury attributable to 67 risk factors and risk factor clusters in 21 regions, 1990-2010: a systematic analysis for the Global Burden of Disease Study 2010. The Lancet, 2012. 380:2224-2260.

Lipfert FW, Wyzga RE, Baty JDMiller JP, Traffic density as a surrogate measure of environmental exposures in studies of air pollution health effects: Long-term mortality in a cohort of US veterans. Atmospheric Environment, 2006. 40:154-169.

Liu LJS, Phuleria HC, Webber W, Davey M, Lawson DR, Ireson RG, et al., Quantification of self pollution from two diesel school buses using three independent methods. Atmospheric Environment, 2010. 44:3422-3431.

Madrigano J, Kloog I, Goldberg R, Coull BA, Mittleman MASchwartz J, Long-term exposure to PM2.5 and incidence of acute myocardial infarction. Environmental Health Perspectives, 2013. 121(2):192-196.

Marshall JDBehrentz E, Vehicle Self-Pollution Intake Fraction: Children's Exposure to School Bus Emissions. Environmental Science & Technology, 2005. 39:2559-2563.

Masri S, Kang C-MKoutrakis P, Composition and sources of fine and coarse particles collected during 2002-2010 in Boston, MA. Journal of the Air & Waste Management Association, 2015. 65(3):287-297.

McDonnell WF, Nishino-Ishikawa N, Petersen FF, Chen LHAbbey DE, Relationships of mortality with the fine and coarse fractions of long-term ambient PM10 concentrations in nonsmokers. Journal of Exposure Analysis and Environmental Epidemiology, 2000. 10:427-436.

McGuinn LA, Ward-Caviness CK, Neas LM, Schneider A, Diaz-Sanchez D, Cascio WE, et al., Association between satellite-based estimates of long-term PM2.5 exposure and coronary artery disease. Environmental Research, 2016. 145:9-17.

Monn CBecker S, Cytotoxicity and Induction of Proinflammatory Cytokines from Human Monocytes Exposed to Fine (PM2.5) and Coarse Particles (PM10-2.5) in Outdoor and Indoor Air. Toxicology and Applied Pharmacology, 1999. 155:245-252.

Nordio F, Kloog I, Coull BA, Chudnovsky A, Grillo P, Bertazzi PA, et al., Estimating spatio-temporal resolved PM10 aerosol mass concentrations using MODIS satellite data and land use regression over Lombardy, Italy. Atmospheric Environment, 2013. 74:227-236.

Peng RD, Chang HH, Bell ML, McDermott A, Zeger SL, Samet JM, et al., Coarse ParticulateMatter Air Pollution and Hospital Admissions for Cardiovascular and Respiratory Diseases Among Medicare Patients. JAMA, 2008. 299(18):2172-2179.

Peters A, Dockery DW, Muller JEMittleman MA, Increased Particulate Air Pollution and the Triggering of Myocardial Infarction. Circulation, 2001. 103:2810-2815.

Pope CA, 3rd, Cropper M, Coggins JCohen A, Health benefits of air pollution abatement policy: Role of the shape of the concentration-response function. J Air Waste Manag Assoc, 2015. 65(5):516-22.

Pope CA, 3rd, Invited Commentary: Particulate Matter-Mortality Exposure-Response Relations and Threshold. American Journal of Epidemiology, 2000. 152(5):407-412.

Pozzi R, De Berardis B, Paoletti LGuastadisegni C, Inflammatory mediators induced by coarse (PM2.5-10) and fine (PM2.5) urban air particles in RAQ 264.7 cells. Toxicology, 2003. 183:243-254.

Rim D, Siegel J, Spinhirne J, Webb AMcDonald-Buller E, Characteristics of cabin air quality in school buses in Central Texas. Atmospheric Environment, 2008. 42:6453-6464.

Sabin LD, Behrentz E, Winer AM, Jeong S, Ritz DR, Pankratz DV, et al., Characterizing the range of children's air pollutant exposure during school bus commutes. Journal of Exposure Analysis and Environmental Epidemiology, 2005. 15:377-387.

Schins RP, Lightbody JH, Borm PJ, Shi T, Donaldson KStone V, Inflammatory effects of coarse and fine particulate matter in relation to chemical and biological constituents. Toxicology and Applied Pharmacology, 2004. 195:1-11.

Schulz H, Brand PHeyder J, Particle-Lung Interactions, Chapter 5. 2000, Boca Raton, FL: CRC Press.

Seaton A, MacNee W, Donaldson KGodden D, Particulate air pollution and acute health effects. Lancet, 1995. 345:176-178.

Shi T, Knaapen A, Begerow J, Birmili W, Borm PARPF S, Temporal variation of hydroxyl radical generation and 8-hydroxy-2'-deoxyguanosine formation by coarse and fine particulate matter. Occupational and Environmental Medicine, 2003. 60(5):315-321.

Snyder, T.D., Dillow, S.A., 2011. Digest of Education Statistics 2010 (NCES 2011-015), Table 184. National Center for Education Statistics, Institute of Education Sciences, U.S. Department of Education. Washington, DC.

Sorek-Hamer M, Just ACKloog I, Satellite remote sensing in epidemiological studies. Current Opinion in Pediatrics, 2016. 28(2):228-234.

Tolbert PE, Klein M, Peel JL, Sarnat SESarnat JA, Multipollutant modeling issues in a study of ambient air quality and emergency department visits in Atlanta. Journal of Exposure Science and Environmental Epidemiology, 2007. 17:S29-S35.

Tuder RM, Yoshida T, Arap W, Pasqualini RPetrache I, Cellular and Molecular Mechanisms of Alveolar Destruction in Emphysema - An Evolutionary Perspective. Proceedings of the American Thoracic Society, 2006. 3:503-511.

US EPA, Policy Assessment for the Review of the National Ambient Air Quality Standards for Particulate Matter. 2020: Research Triangle Park: NCEA-RTP Office.

US EPA, 2019. Integrated science assessment for particulate matter. Research Triangle Park: NCEA-RTP Office.

US EPA, EPA's Report on the Environment (ROE). 2017: U.S. Environmental Protection Agency, Washington, DC, 2017.

US EPA, Voluntary Diesel Retrofit Program, "Making Diesel Engines Cleaner". 2015: Office of Transportation and Air Quality.

US EPA, EPA Sets Tier 3 Motor Vehicle Emission and Fuel Standards: Regulatory Announcement. 2014: Office of Transportation and Air Quality.

US EPA, 2012, 2014-2017. National Clean Diesel Rebate Program: 2012,2014-2017 School Bus Replacement Funding Opportunity Program Guides. Office of Transportation and Air Quality.WHO, Ambient air pollution: A global assessment of exposure and burden of disease.

Wilson WESuh HH, Fine Particles and Coarse Particles: Concentration Relationships Relevant to Epidemiologic Studies. Journal of the Air & Waste Management Association, 1997. 47(12):1238-1249.

Zanobetti ASchwartz J, The Effect of Fine and Coarse Particulate Air Pollution on Mortality: A National Analysis. Environmental Health Perspectives, 2009. 117:898–903.

Zhang QZhu Y, Measurements of ultrafine particles and other vehicular pollutants inside school buses in South Texas. Atmospheric Environment, 2010. 44:253-261.

## CHAPTER 2 :

## Estimating Long-term $PM_{10-2.5}$ Concentrations in Six US Cities Using Satellite-Based AOD Data

### Introduction:

Airborne particulate matter (PM) is physically diverse and is comprised of particles over a wide range of sizes (US EPA 2009). In the epidemiology literature, the most common sizes studied are $PM_{2.5}$ (aerodynamic diameter $\leq$ 2.5 μm) and $PM_{10}$ (aerodynamic diameter $\leq$ 10 μm). Relatively little research has focused on $PM_{10-2.5}$ (aerodynamic diameter $\leq$ 10 μm and > 2.5 μm), known as coarse particulate matter. A major challenge to epidemiologists in assessing the health risks of $PM_{10-2.5}$ has been a lack of monitors from which exposures can be estimated. Historically, only 1% of counties in the United States (US) have collocated $PM_{10}$ and $PM_{2.5}$ monitors with which to estimate $PM_{10-2.5}$ (US EPA 2009). This is especially problematic for studying the long-term health effects of $PM_{10-2.5}$ since $PM_{10-2.5}$ is more spatially variable than $PM_{2.5}$ or $PM_{10}$ due to higher gravitational settling of larger particles (US EPA 2009; US EPA 2019; Wilson & Suh 1997). Therefore, there is concern that the use of only a few central monitors for $PM_{10-2.5}$ will be insufficient to accurately reflect the exposures of individuals across a whole region, especially in urban areas, which often have considerable spatial variability in $PM_{10-2.5}$ concentrations (Lagudu et al. 2011; Pakbin et al. 2010; Sawvel et al. 2015; Thornburg et al. 2009; US EPA 2019). As a result, only a handful of

investigations have examined the health implications of long-term exposures to $PM_{10-2.5}$ and many have suffered from power issues, likely due to biases towards the null caused by measurement error (Adar et al. 2014).

Fortunately, data from National Aeronautics and Space Administration (NASA) satellites have created opportunities to assess PM concentrations at all locations across space. Aerosol optical depth (AOD) is a measure of light extinction by aerosol scattering and absorption in the atmospheric column, which is sampled continuously from space at a 1 $km^2$ resolution (Kloog et al. 2011; Nordio et al. 2013; Sorek-Hamer et al. 2016). The availability of these daily measurements, along with advancements in spatiotemporal prediction modeling, allows for the estimation of air pollution levels at fine-scale spatial and temporal resolution even where no monitoring stations exist (Kloog et al. 2011).

Previous research has shown good predictive ability using satellite data-based prediction models for $PM_{2.5}$ (cross-validation (CV) $R^2$: 0.7 to 0.9) in the US, Italy, Israel, and Switzerland (Kloog et al. 2012a; Kloog et al. 2011; Kloog et al. 2015; Hu 2009; Hu et al. 2014; Lee et al. 2016; Madrigano et al. 2013; McGuinn et al. 2016; Kloog et al. 2012b; de Hoogh et al. 2018). The same methods were used to predict $PM_{10}$ with similar performance in Italy (CV $R^2$: 0.65 to 0.79; Nordio et al. 2013; Stafoggia et al. 2017; Stafoggia et al. 2019) and Israel (CV $R^2$: 0.79 to 0.92; Kloog et al. 2015; Shtein et al. 2018). Recently, one study used the abundant number of $PM_{10}$ monitoring stations in Italy to predict both $PM_{2.5}$ and $PM_{10-2.5}$ concentrations using AOD and land-use data and found CV $R^2$ for annual averages ranging from 0.43 to 0.59 (Stafoggia et al. 2019). To date, however, no model for $PM_{10-2.5}$ has been developed in the US using satellite information and thus this modern source of data has not yet been used in epidemiology

studies. Therefore, in this study, we use AOD measured on the NASA Terra satellite to calculate daily 1 $km^2$ resolution $PM_{10-2.5}$ predictions in six US urban areas.

**Material and Methods:**

***Study domain:***

Our study domain included the six regions of the Multi-Ethnic Study of Atherosclerosis (MESA) (Bild et al. 2002). To capture sufficient monitoring stations in these regions, we focused our models on the areas within 60 km of the centroids of Chicago, Illinois; New York, New York; and St. Paul, Minnesota; and within 80 km of the centroid of Baltimore, Maryland. For Los Angeles, California our study domain was based on the irregular recruitment area of study participants and the unique topology of the region. Our area extended from just west of Santa Monica to the San Jacinto mountain range on the east, and from San Fernando on the north to Irvine on the south, excluding the Santa Ana Mountains. The Winston-Salem, North Carolina study domain was roughly the area within 60 km of the city's centroid, although we extended the domain south to include monitoring sites in Charlotte and east to Raleigh (Figure 2.1). These six metropolitan areas are very diverse in terms of climate, geographical features, proximity to large water bodies, and urbanicity.

***PM monitoring data:***

We obtained daily Federal Reference Method (FRM) monitoring data for $PM_{2.5}$ and $PM_{10}$ mass for the years 2000 through 2012 from the US Environmental Protection Agency's (EPA) Air Quality System (AQS). We restricted our datasets to one station per location and to stations with at least 30 observations throughout the study period. Since $PM_{10}$ measurements are reported to EPA at standard conditions whereas $PM_{2.5}$ is reported

at local conditions, we used temperature and pressure data (see below) to convert reported $PM_{10}$ to local conditions so that $PM_{10}$ and $PM_{2.5}$ were on the same scale prior to calculating $PM_{10-2.5}$ concentrations (US EPA 2009).

***AOD satellite data:***

AOD data is sampled continuously from space at a 1 $km^2$ resolution using Moderate Resolution Imaging Spectroradiometer (MODIS) technology on the polar orbiting and sun-synchronous NASA Terra satellite (Levy et al. 2007; Remer et al. 2005). The AOD data are retrieved by NASA using the Multi Angle Implementation of Atmospheric Correction (MAIAC) algorithm, which begins by gridding MODIS measurements of L1B data to a fixed 1x1 km grid so that the same gridcell is observed over time. The MAIAC algorithm then uses time series analysis and a combination of pixel and image-based processing to improve accuracy of cloud detection, aerosol retrievals, and atmospheric correction (Lyapustin et al. 2011a; Lyapustin et al. 2011b; Lyapustin et al. 2012). Although newer satellites are now available, we used 2000-2012 AOD data collected on the Terra satellite since it was the only satellite in operation at the beginning of our study period.

***Spatial and temporal predictors of $PM_{2.5}$ and $PM_{10}$:***

In addition to the satellite AOD observations, we also included many spatial and temporal predictors as fixed effects in our linear mixed effects hybrid prediction model. We used R statistical software version 3.6.1 (R 2019) to generate all spatial and temporal predictors for each 1x1 km gridcell as detailed below.

*Elevation:*

We estimated average gridcell elevation values using data from the USGS 3D Elevation Program (3DEP), which produces a satellite-based, seamless digital elevation model covering the conterminous US and Hawaii at a spatial resolution of 1/3 arc sec (approximately 10 meters) (USGS 2017).

*Land use:*

We calculated the percentage of 15 different land use classes for each gridcell using raster data from the USGS National Land Cover Databases (NLCD) for years 2001, 2006, and 2011 (USGS 2001; USGS 2006; USGS 2011). These data are measured at a 30-meter resolution. The 2001 NLCD measures were assigned to gridcells for days in 2000 through mid-2003; 2006 NLCD measures were assigned to gridcells for days in mid-2003 through mid-2008, and; 2011 NLCD measures were assigned to gridcells for days in mid-2008 through 2012.

*Normalized Difference Vegetation Index:*

We spatially and temporally matched monthly, 1 $km^2$ resolved vegetation data from the NASA Terra Moderate Resolution Imaging Spectroradiometer MOD13A3 version 6 Normalized Difference Vegetation Index (NDVI) (Didan 2015) to study gridcells.

*Planetary boundary layer:*

Using data from the European Centre for Medium-Range Weather Forecasts (ECMWF) ERA Interim Daily global atmospheric reanalysis model at a spatial resolution of 0.125 degrees (~14 $km^2$) and 3-hour temporal resolution (Dee et al. 2011), we estimated daily average planetary boundary layer (PBL) height by spatially and temporally matching daily averaged PBL to study gridcell centroids.

*Meteorology:*

Meteorological data for air pressure, air temperature, evaporation, precipitable water, specific humidity, u-wind, v-wind, and visibility came from the National Oceanic and Atmospheric Administration's National Centers for Environmental Prediction North American Regional Reanalysis (NARR) dataset (Mesinger et al. 2006). This modeled data has a spatial resolution of approximately 0.3 degrees (~32km) and 3-hour temporal resolution, which we averaged to the day and spatially and temporally matched to study gridcell centroids.

*Population:*

We obtained US Census block-group total population counts and block-group shapefiles for the 2000 and 2010 Decennial censuses from the IPUMS National Historical Geographic Information System (NHGIS) (Manson et al. 2018). We then calculated two block-group spatially-weighted population measures: the first applied the 2000 Census-based population count to all days in years 2000 – 2004 and the 2010 Census-based population count to all days in 2005 – 2012 while the second linearly interpolated gridcell population for each year between the 2000 and 2010 Census values.

*Roads and railways:*

We used primary and secondary road and railway feature data from the US Census TIGER/Line Shapefile online download system (US Census Bureau 2010) to calculate the density of all primary and secondary roads (combined) in each gridcell. Additionally, we calculated the distance from each gridcell centroid to the nearest primary road, secondary road, and rail track.

*Water bodies:*

Water feature data came from the USGS National Hydrography Dataset (USGS 2019) (for both waterbody and water area categories). We calculated the distance from each gridcell centroid to the nearest water feature of any size and large water body (where we defined each city's large water body as follows: Chesapeake Bay for Baltimore; Lake Michigan for Chicago; Pacific Ocean for Los Angeles; Atlantic Ocean and Long Island Sound for New York; Lake Superior for St. Paul; and Atlantic Ocean for Winston-Salem).

***Statistical methods:***

This section describes the multi-stage statistical approaches used in this study. Briefly, we used a previously developed spatiotemporal mixed effects modelling approach (Kloog et al. 2012a; Kloog et al. 2014; Kloog et al. 2015) with satellite AOD data to predict daily $PM_{2.5}$ and, separately, $PM_{10}$, at a 1 $km^2$ spatial resolution. We then used these predictions to calculate 1 $km^2$ spatially resolved daily and long-term $PM_{10-2.5}$ concentrations via subtraction across six metropolitan areas in the US. Predicting $PM_{2.5}$ and $PM_{10}$ separately, as opposed to predicting $PM_{10-2.5}$ directly, increased the amount of information used in the models since our study areas had many EPA sites that were not collocated. This choice also allowed for a more geographically diverse set of stations to inform our predictions, which will then better represent the areas where participants in future health analyses reside. All statistical modeling was done using R software version 3.5.0 (R 2018) and all maps were created using R software 3.6.1 (R 2019).

*PM predictions:*

In the first stage of our analysis, we fit calibration model (2.1), which predicts measured PM as a function of AOD for all PM observations with an available AOD value within 1.1 km. We constructed individual models for each city and pollutant ($PM_{2.5}$ and $PM_{10}$):

$$PM_{ij} = (\alpha + \mu_j) + (\beta_1 + \nu_j)AOD_{ij} + \sum_{m=1}^{10} \gamma_{1_m} X_{1_{m_{ij}}} + \sum_{m=1}^{24} \gamma_{2_m} X_{2_{m_i}} + \varepsilon_{ij} \quad (2.1)$$

Where: $PM_{ij}$ is the measured $PM_{2.5}$ or $PM_{10}$ concentration in a city at site *i* on day *j*; $\alpha$ is the fixed intercept and $\mu_j$ is the day-specific random intercept; $\beta_1$ is the fixed slope for AOD while $\nu_j$ is the day-specific random slope for AOD. $AOD_{ij}$ is the AOD value for the gridcell corresponding to site *i* on day *j*; $X_{1_{m_{ij}}}$ is the m$^{th}$ spatiotemporal predictor in the gridcell corresponding to site *i* on day *j* (i.e., vegetation, eight meteorology predictors, and PBL height) and $\gamma_{1_m}$ is the slope of the m$^{th}$ spatiotemporal predictor; $X_{2_{m_i}}$ is the m$^{th}$ spatial predictor in the gridcell corresponding to site *i* (i.e., elevation, two population measures, fifteen land use categories, road density, and proximity to: primary road, secondary road, railroad, any water body, and large water body) and $\gamma_{2_m}$ is the slope of the m$^{th}$ spatial predictor.

Since AOD data can be unreliable due to cloud contamination, snow-cover, surface brightness, and other factors, we excluded observations with an AOD uncertainty value ≤ 0 or ≥ 0.04, per MAIAC guidelines. Observations where the gridcell included ≥ 5% open water (based on the land use data) were also excluded since AOD data can be similarly unreliable near water surfaces. We additionally excluded observations where the AOD and/or the PM value was at or below the city-specific 1$^{st}$ percentile or at or above the city-specific 99$^{th}$ percentile to reduce the potential influence of outlier values on these

first stage calibration models[1]. Since many of the land use categories had little variation within the modeling domains, we excluded predictors where the value of the 25$^{th}$ percentile was equal to the 75$^{th}$ percentile[2].

Within this cleaned dataset, AOD can be missing not-at-random and can be missing for reasons that are correlated with PM levels (e.g., levels of cloud and snow coverage that are not excluded based on the AOD uncertainty value, described above). This could impact the calibration stage regression coefficients in equation 2.1 and therefore the calibration model-based predictions. To address this potential bias, we created inverse probability weights (IPW) to up-weight observed gridcell-days that share characteristics with days that have more missing AOD data. The weights were calculated by fitting the following logistic regression model (2.2) separately for each year and each city for the probability, *p*, of having a non-missing AOD value for gridcell *i* on day *j*:

$$ln\left(\frac{p}{1-p}\right) = \beta_0 + \beta_1 Elevation_i + \beta_2 PBL_{ij} + \beta_3 Temperature_{ij} + \sum_{k=4}^{14} \beta_k I(Month)_j \qquad (2.2)$$

Using weights of $\frac{1}{\hat{p}}$ derived from (2.2), we then used backward selection with the Akaike Information Criterion (AIC) to select the fixed effects used in each calibration model (2.1). This generated city- and pollutant-specific calibration models which we used to predict PM for gridcell-days with available AOD data (including the IPW weighting). Finally, to predict PM in gridcell-days without available AOD data, we fit the following generalized additive mixed model, which uses average regional measured PM and a

[1] The St. Paul $PM_{10}$ analysis used thresholds of 2.5$^{th}$ and 97.5$^{th}$ percentiles to improve the model fit.
[2] The calibration model for Chicago $PM_{2.5}$ excluded predictors where the value of the 1$^{st}$ percentile was equal to the 99$^{th}$ percentile to improve model fit.

smooth function of the gridcell centroid coordinates, to predict the AOD-based PM estimates that were calculated with the model (2.1) fit:

$$PredPM_{ij} = (\alpha + \mu_i) + (\beta_1 + v_i)MPM_{ij} + s(lat_i, lon_i)_{k(j)} + \varepsilon_{ij} \qquad (2.3)$$

$PredPM_{ij}$ is the predicted PM calculated with calibration model (2.1) for gridcell-days with available AOD data; $\alpha$ is the fixed intercept and $\mu_i$ is the gridcell-specific random intercept; $MPM_{ij}$ is the mean PM from all EPA sites within 60 km of the centroid of gridcell *i* on day *j*; $\beta_1$ is the fixed slope on MPM while $v_i$ is the gridcell-specific random slope for MPM; $s(lat_i, lon_i)_{k(j)}$ is a thin plate spline of the latitude and longitude of the centroid of gridcell *i* for the two-month period, k(*j*), in which day *j* falls (i.e., we fit a separate thin plate spline smoothing function for each two month period in the study period).

Our final $PM_{2.5}$ and $PM_{10}$ predictions were created by selecting – by day and gridcell – the 'best' available PM measure, where the daily gridcell-average EPA measured PM value was selected first, followed by the calibration-based model predictions, and then the smoothing model PM predictions. This approach results in a full-coverage prediction dataset for each city for each PM size fraction for days with and without AOD measurements. We then estimated $PM_{10\text{-}2.5}$ concentrations as the difference between $PM_{10}$ and $PM_{2.5}$ concentrations.

*Model Evaluation:*

We performed 'leave-one-station-out' (LOSO) cross-validation (CV) to assess the performance of our models. Specifically, to generate the calibration model CV predictions, we repeatedly left out one of the N total PM monitors in each city and re-fit

the AIC-chosen calibration model on only data from the N-1 remaining PM stations. We then used the model fit from the N-1 sites to predict PM at the held-out site. Conceptually, this approach assesses the performance of the calibration models vs. observed values at an unobserved location. The smoothing model CV predictions were generated by recursively fitting the smoothing model on the predicted values from the calibration model fit from the N-1 sites.

We separately evaluated the calibration CV predictions and our final CV predictions, where the latter were selected from the 'best' of either the calibration model CV or smoothing model CV predictions. Both were evaluated for all three pollutants and against all available EPA PM monitoring data throughout the study period (i.e., for PM with and without paired available AOD data, as appropriate). Since the EPA does not provide publicly available $PM_{10-2.5}$ data, we created a validation dataset of daily and long-term average $PM_{10-2.5}$ concentrations by subtracting $PM_{2.5}$ from $PM_{10}$ measured at EPA FRM monitoring stations with collocated monitors.

To evaluate our CV predictions, we regressed the spatially and temporally paired daily observed concentrations on the daily CV predicted concentrations and summarized the $R^2$, intercept, and slope; we also calculated the root mean square error (RMSE) of the predictions. To examine the ability of our models to estimate the spatial variation in PM concentrations, we regressed our CV predictions against observed concentrations averaged over the full study-period and again summarized the $R^2$, intercept, and slope, and again calculated the RMSE. To isolate and assess the temporal performance of the models, we calculated the overall $R^2$ for our CV predictions separately for each EPA monitoring site. We then generated summary statistics (i.e., mean and standard deviation)

of monitor-specific $R^2$, intercept, slope, and RMSE values, separately for each city and pollutant.

*Alternative modeling approaches:*

In secondary analyses, we evaluated three alternate approaches for estimation of $PM_{10-2.5}$: two alternatives to compare to our model's spatial performance and one to compare to our model's temporal performance. For the spatial comparisons we first conducted a nearest monitor analysis to determine whether our $PM_{10-2.5}$ prediction approach performed better spatially than a simpler method used in some of the $PM_{10-2.5}$ long-term health effects literature (Lipsett et al. 2006; Miller et al. 2007; Chen et al. 2015). We then performed inverse distance weighting (IDW) using weights of squared inverse distance as a second comparison to our spatial performance. Specifically, for both alternative approaches, we left out one collocated $PM_{2.5}$ and $PM_{10}$ site in each study area at a time and assigned it – by day – the $PM_{10-2.5}$ concentration from the collocated $PM_{2.5}$ and $PM_{10}$ EPA site that was geographically closest to the held-out site (for the nearest monitor approach) or the $PM_{10-2.5}$ prediction at the location of the held-out site from the IDW interpolation of all other collocated $PM_{2.5}$ and $PM_{10}$ EPA sites in the study area (for the IDW approach). This was done repeatedly so that each site was held out once in each analysis. We then compared the study-period average $PM_{10-2.5}$ concentrations at the held-out sites, separately, to the nearest observed $PM_{10-2.5}$ concentrations (for the nearest monitor approach) and to the IDW interpolated $PM_{10-2.5}$ concentrations (for the IDW approach) and reported spatial $Rs^2$, intercepts, slopes, and RMSE values, separately for each city and alternative approach.

We similarly determined whether our $PM_{10-2.5}$ prediction approach performed better temporally than a regional average $PM_{10-2.5}$ measurement, which is an alternative method commonly used in the $PM_{10-2.5}$ health effects time series literature (Chen et al. 2004; Lin et al. 2005; Malig et al. 2013; Peng et al. 2008; Rodopoulou et al. 2014; Stafoggia et al. 2013; US EPA 2019; Zhao et al. 2016). Specifically, for each daily measured $PM_{10-2.5}$ concentration at a given collocated $PM_{2.5}$ and $PM_{10}$ site, we calculated the daily average $PM_{10-2.5}$ value from all other collocated $PM_{2.5}$ and $PM_{10}$ sites in the study area except itself for that day. We then compared the daily $PM_{10-2.5}$ concentrations at the held-out site to the daily region-average $PM_{10-2.5}$ concentrations, separately for each held-out monitoring site and reported the mean and standard deviation of monitor-specific reported $Rs^2$, intercepts, slopes, and RMSE values, separately for each city and pollutant.

**Results:**

Figure 2.1 shows the study area for each of the six study regions, including the locations of the $PM_{2.5}$, $PM_{10}$, and collocated $PM_{2.5}$ and $PM_{10}$ EPA monitoring stations used in the analysis. Notably, each city had a higher frequency of $PM_{2.5}$ sampling (roughly one out of three days for $PM_{2.5}$ and one out of six days for $PM_{10}$) and a larger number of $PM_{2.5}$ samplers (Table 2.1). The number of PM sites used in this analysis differed by city, with New York having the most $PM_{2.5}$ samplers (N=37) and Los Angeles having the most $PM_{10}$ samplers (N=19). St. Paul had the fewest $PM_{2.5}$ (N=17) and $PM_{10}$ (N=8) samplers. The number of unique collocated $PM_{10-2.5}$ sites in each city throughout the study period ranged from 4 in St. Paul to 12 in Los Angeles (Table 2.1); however, there were no collocated sites in St. Paul in the last three years of our study period and only one collocated site in New York for the last eight years of the study

period. Based on monitoring data, we observed that the Los Angeles study region had the highest mean concentrations for both $PM_{2.5}$ (16.7 $\mu g/m^3$) and $PM_{10}$ (35.6 $\mu g/m^3$) of all 6 areas. In contrast, St. Paul had the lowest mean $PM_{2.5}$ concentration (8.6 $\mu g/m^3$) and Baltimore had the lowest mean $PM_{10}$ concentration (20.4 $\mu g/m^3$). Mean $PM_{10-2.5}$ concentrations at collocated sites throughout the study period ranged from 6.3 $\mu g/m^3$ in Winston-Salem to 20.7 $\mu g/m^3$ in Los Angeles.

In our calibration models that predicted PM based on AOD measurements, we found that AOD was consistently and strongly positively associated with $PM_{2.5}$ in all 6 areas and with $PM_{10}$ in 3 of the cities but not in the more northern cities of Chicago, St. Paul, and New York. Meteorological factors, elevation, land use development level, and daily average PBL were the predictors most commonly selected in the $PM_{2.5}$ models, while the vertical wind component, population, and humidity were the predictors most commonly selected in the $PM_{10}$ models (Table 2.A2)[3]. As shown in Table 2.2, we had strong performance for predicting long-term average $PM_{10-2.5}$ – our pollutant of primary interest – based on measured AOD. Our spatial CV $R^2$ was greater than 0.6 in four of our six cities (i.e., Baltimore, Los Angeles, New York, and St. Paul). The spatial CV $R^2$ was also good in Chicago at 0.57 but poor for Winston-Salem at 0.25. These $PM_{10-2.5}$ spatial $R^2$ were consistent with, if not better than, $PM_{2.5}$ or $PM_{10}$ alone, which ranged from 0.46 in Chicago to 0.93 in Winston-Salem for $PM_{2.5}$ and from 0.52 in Chicago to 0.95 in New York for $PM_{10}$. In contrast, we had poor predictive performance overall due to poor predictive power of $PM_{10-2.5}$ temporal variation. In fact, the model performance was much

[3] Although elevation was a selected fixed effect in the Baltimore $PM_{10}$ calibration model, given the topological characteristics of that region compared to the locations of $PM_{10}$ monitors, using elevation in the AOD-based predictions resulted in a large fraction of negative $PM_{10}$ predictions. We therefore re-performed AIC backward selection after excluding elevation as a predictor for consideration.

worse temporally for $PM_{10-2.5}$ (average temporal CV $R^2$s from 0.10 to 0.43) than for either $PM_{2.5}$ (average temporal CV $R^2$s from 0.69 to 0.83) or $PM_{10}$ (average temporal CV $R^2$s from 0.52 to 0.69) in all six cities.

Validation results of our final predictions for all three pollutants are shown in Table 2.3. As with our calibration models, our final $PM_{10-2.5}$ models had excellent spatial performance in Baltimore, Los Angeles, New York, and St. Paul, with CV $R^2$s ranging from 0.70 to 0.97. Chicago again had moderate $PM_{10-2.5}$ spatial performance (CV $R^2$: 0.51) and Winston-Salem had a low spatial CV $R^2$ of 0.31. Temporal performance remained low for our final $PM_{10-2.5}$ predictions, with mean CV $R^2$ ranging from 0.12 to 0.41. These AOD-based models all validated substantially better than both alternate spatial approaches, both of which performed poorly in all six cites (Table 2.4). In contrast, the alternate temporal approach of a city mean performed slightly better than our AOD based predictions across the study areas (based on mean CV $R^2$) although in general, the results were still poor.

Maps of our final $PM_{2.5}$, $PM_{10}$, and $PM_{10-2.5}$ predictions averaged over the study period are shown in Figure 2.2 for each area. In general, $PM_{2.5}$ predicted concentrations were highest along major roadways and in the downtown areas of all six cities, while $PM_{10}$ and $PM_{10-2.5}$ predictions exhibited similar but weaker roadway and downtown spatial patterns. Summary statistics for the final long-term average predictions, by city and pollutant, are shown in Table 2.5. Mean study area long-term average $PM_{2.5}$ ranged from 8.0 $\mu g/m^3$ in Chicago to 12.0 $\mu g/m^3$ in Winston-Salem while $PM_{10}$ ranged from 11.6 $\mu g/m^3$ in Baltimore to 37.6 $\mu g/m^3$ in New York. As with measured levels, Baltimore

had the lowest mean long-term average $PM_{10-2.5}$ predictions (2.1 $\mu g/m^3$) while New York had the highest (28.3 $\mu g/m^3$).

**Discussion:**

We used spatiotemporal mixed effects models with satellite AOD data to predict $PM_{10-2.5}$ at a $1km^2$ resolution in six metropolitan areas across the US. This extends earlier work which successfully developed and applied this approach throughout the eastern US, Italy, and Israel for $PM_{2.5}$ (Kloog et al. 2012a; Kloog et al. 2011; Kloog et al. 2015; Hu 2009; Madrigano et al. 2013; McGuinn et al. 2016; Kloog et al. 2012b) and in Italy and Israel for $PM_{10}$ (Nordio et al. 2013; Stafoggia et al. 2017; Stafoggia et al. 2019; Kloog et al. 2015; Shtein et al. 2018). Overall, our final predictions captured the long-term spatial patterns of $PM_{10-2.5}$ very well in four of our study areas (CV $R^2$ ranging from 0.7 in Los Angeles to 0.97 New York), well in one area (CV $R^2$ of 0.51 in Chicago), and modestly in one area (CV $R^2$ of 0.31 in Winston-Salem). In all six study areas, our predictions had substantially better spatial performance than both a simple nearest-monitor approach and an IDW approach. Given that urban areas often have considerable spatial variability in $PM_{10-2.5}$ concentrations (Lagudu et al. 2011; Pakbin et al. 2010; Sawvel et al. 2015; Thornburg et al. 2009; US EPA 2019), our results show the benefits of using satellite-based AOD data for long-term $PM_{10-2.5}$ epidemiological health studies.

This research adds to the literature as one of only a handful of models to predict $PM_{10-2.5}$ concentrations for use in long-term air pollution epidemiological studies. This is particularly true for the US where – to our knowledge – only two groups have generated $PM_{10-2.5}$ exposure predictions that have been used in health studies (US EPA 2019). Notably, neither has taken advantage of the additional information AOD provides when

conducting $PM_{10-2.5}$ spatiotemporal pollution prediction modeling. Previously, our group used intensive $PM_{10-2.5}$ monitoring campaigns as part of the MESA Coarse study (Zhang et al. 2014) to predict spatial patterns of $PM_{10-2.5}$ using land use regression methods in three of the six cities studied here. While our model performance using the intensive sampling data was largely better than these new AOD-models, they were not substantially or consistently so. For example, we previously had CV $R^2$s of 0.68 (RMSE: 1.16 $\mu g/m^3$) and 0.41 (RMSE: 1.09 $\mu g/m^3$) in Chicago and Winston-Salem, respectively, as compared to CV $R^2$s of 0.51 (RMSE: 3.43 $\mu g/m^3$) and 0.31 (RMSE: 1.85 $\mu g/m^3$) for our current models. In contrast, our new St. Paul models have a CV $R^2$ of 0.84 (RMSE: 2.54 $\mu g/m^3$) as compared to our earlier models of 0.51 (RMSE 2.33 $\mu g/m^3$). Given that monitoring field studies are very expensive to conduct and cannot capture the temporal variability in $PM_{10-2.5}$ concentrations, this AOD-informed approach offers important benefits over predictions derived from spatially intensive ground monitoring.

Another study of the whole conterminous US used generalized additive mixed models with geographic, meteorological, and visibility data to predict $PM_{2.5}$ and $PM_{10}$ concentrations at the monthly scale based on EPA monitoring data (Yanosky et al. 2008; Yanosky et al. 2009; Yanosky et al. 2014). Over the period from 1999-2007 they found a spatial CV $R^2$ of 0.61 for their predictions, with performance that varied across geographical regions from 0.33 in the Southcentral US to 0.64 in the Southwest. Importantly, Yanosky et al. (2014) hypothesized that the inclusion of AOD measures in spatiotemporal models might improve model predictive accuracy, especially in areas distant from air quality monitors. In fact, this did appear to be the case as our final long-term average CV predictions had much better spatial performance in Baltimore, New

York, and St. Paul (0.75 to 0.97 vs. 0.49 to 0.53), better performance in Los Angeles (0.70 vs. 0.64), and marginally better performance in Chicago (0.51 vs. 0.49). Only in Winston-Salem did their models have better predictive ability, although they also had only modest performance (0.31 vs. 0.36).

Differences in our Winston-Salem $PM_{10-2.5}$ results as compared to those in the Southeast region in Yanosky et al. (2014) highlights one of the key challenges of predicting concentrations for localized areas as we have done in this work. Unlike many other studies that have predicted PM levels across larger regions or nations, our study focused on smaller metropolitan areas. While predicting over smaller areas has the potential to increase accuracy if there is effect modification of predictors by place, it can come at the cost of lost variation in exposures. Notably, there was only a 5 $\mu g/m^3$ range in the long-term average $PM_{10-2.5}$ concentrations in Winston-Salem across the eleven collocated $PM_{10-2.5}$ sites during our study period. In contrast, our other cities had monitor level averages with ranges closer to 10 to 20 $\mu g/m^3$. This lack of variation surely contributed to our inability to model the spatial variability in $PM_{10-2.5}$ levels well.

Figure 2.1 and Figure 2.2 highlight a second limitation of studying a smaller area, which is that the models can be informed by relatively few monitoring sites and thus there is often less variation in the types of places where air quality stations are sited. For example, in the New York region all of the $PM_{10}$ monitors were sited in low elevation, urban areas that were near the coast. This resulted in the areas west of the city having many predictor values outside of the design space of the data used to fit the calibration model. This, in combination with the coefficients for these predictors, resulted in high predicted concentrations of $PM_{10}$ (and subsequently $PM_{10-2.5}$) in the area west of New

York City. A similar phenomenon is visible in Winston-Salem where the $PM_{10}$ stations are all sited in close proximity to the major highways and areas distant to the highways have very low predicted values.

Finally, we note that our models were not fit directly on $PM_{10-2.5}$ measurements, but rather on $PM_{2.5}$ and $PM_{10}$ separately. In such models, the error from two models contributes to the performance of the predictions. Although this is common for $PM_{10-2.5}$ modeling due to a lack of size-fraction specific sampling, its impact is highlighted by the strong performance of our $PM_{2.5}$ and $PM_{10}$ models (final model CV $R^2$ 0.93 and 0.77, respectively) in Winston-Salem but not $PM_{10-2.5}$ (CV $R^2$ was 0.31).

Overall, however, we had strong performance of our models to characterize the spatial variability of $PM_{10-2.5}$. In addition, our AOD-based predictions dramatically out-performed the alternative IDW and nearest monitor approaches that have been used in other epidemiology studies to date, showing the potential improvement this approach can offer to environmental epidemiological research. In contrast, the temporal performance of our $PM_{10-2.5}$ estimates was very poor, with final model mean CV $R^2$ ranging from 0.12 in Baltimore to 0.41 in Los Angeles, suggesting that this approach does not adequately capture the daily variation in $PM_{10-2.5}$ concentrations in these six areas. Importantly, though, our poor temporal performance was largely the same as results from the city mean approach (mean temporal $R^2$ ranged from 0.20 in New York to 0.59 in Los Angeles) that has been frequently deployed in epidemiological studies. This demonstrates that $PM_{10-2.5}$ has more spatiotemporal variability than the current set of EPA monitoring stations can capture, even with the addition of satellite-based information. It further raises

questions about the impacts of measurement error in the epidemiology on short-term exposures to $PM_{10-2.5}$ in the United States.

**Conclusion:**

We have demonstrated that the use of satellite AOD data is an effective method for characterizing spatial, but not temporal variations, in $PM_{10-2.5}$ concentrations in six cities in the US. Given the high costs of field sampling, this methodology is a strong option for estimating long-term $PM_{10-2.5}$ concentrations, especially in areas with sufficient numbers of air quality monitors and spatial variability in concentrations.

**Figure 2.1 Modeling domains and EPA monitor station locations for six US study areas.**

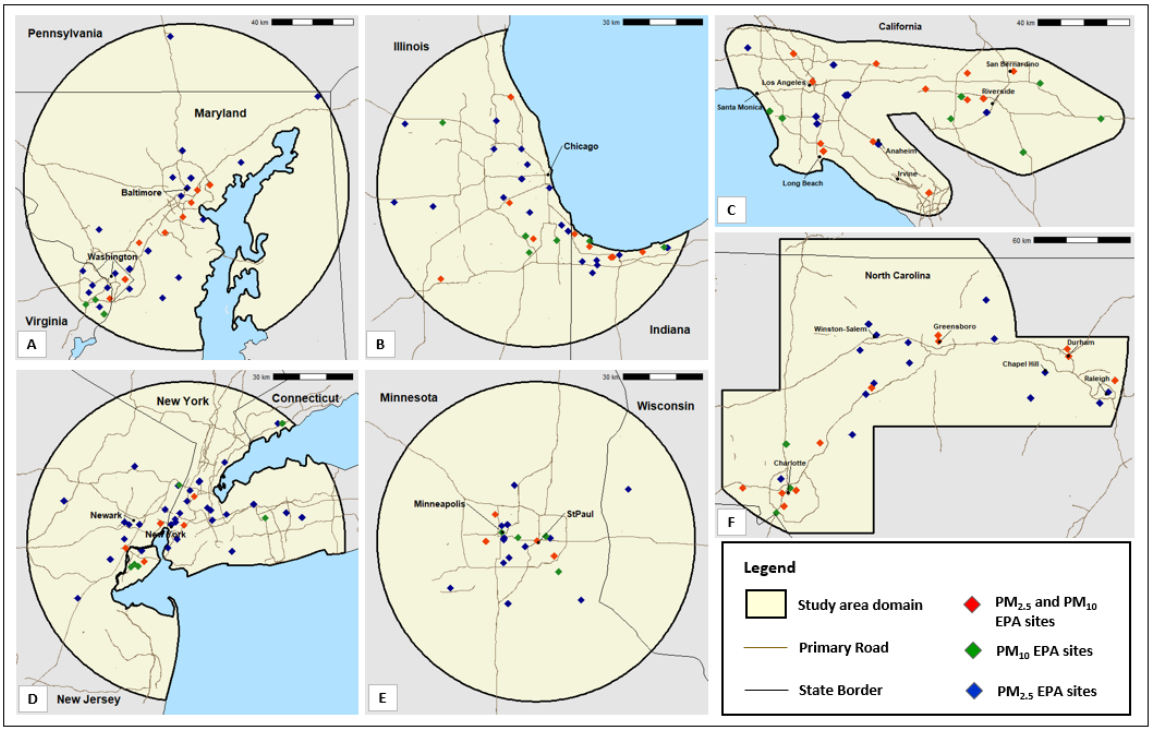


Figure 2.1 shows the study areas and EPA monitor station locations for A) Baltimore, Maryland; B) Chicago, Illinois; C) Los Angeles, California; D) New York, New York; E) St. Paul, Minnesota; and F) Winston-Salem, North Carolina.

**Figure 2.2 Maps of long-term average PM predictions (2000-2012), by pollutant and study area.**

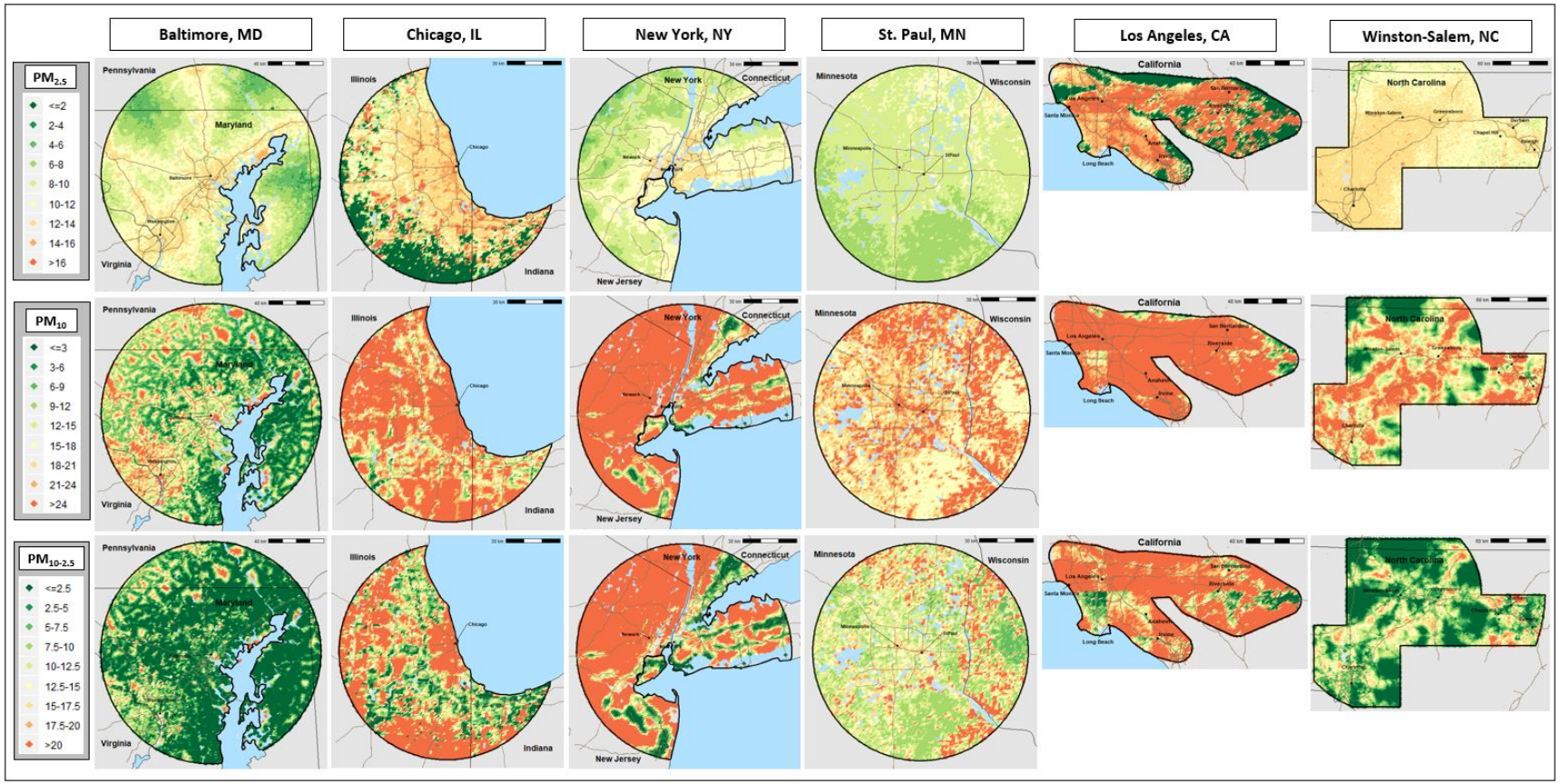

**Table 2.1 Summary statistics of daily $PM_{2.5}$, $PM_{10}$, and $PM_{10-2.5}$ concentrations ($\mu g/m^3$) used in calibration models, measured at EPA air quality monitoring stations in six US metropolitan areas for the period 2000-2012.**

| City | Pollutant | Number of Sites | Number of Observations | Mean | Median | Min | Max | IQR |
|---|---|---|---|---|---|---|---|---|
| Baltimore | $PM_{2.5}$ | 30 | 11,587 | 12.2 | 10.6 | 3.2 | 38.2 | 8.2 |
| | $PM_{10}$ | 13 | 1,382 | 20.4 | 18 | 4 | 60 | 13 |
| | $PM_{10\text{-}2.5}$ | 8 | 816 | 9.2 | 6.4 | -20.5 | 73.4 | 8.4 |
| Chicago | $PM_{2.5}$ | 28 | 8,309 | 12.9 | 11.5 | 3.2 | 37.1 | 8.7 |
| | $PM_{10}$ | 15 | 1,934 | 23.5 | 22 | 6 | 61 | 15 |
| | $PM_{10\text{-}2.5}$ | 9 | 1,035 | 10.5 | 8.5 | -13.6 | 94.0 | 9.1 |
| Los Angeles | $PM_{2.5}$ | 22 | 13,491 | 16.7 | 14 | 2.8 | 59.3 | 11 |
| | $PM_{10}$ | 19 | 4,513 | 35.6 | 33 | 7 | 95 | 22 |
| | $PM_{10\text{-}2.5}$ | 12 | 2,950 | 20.7 | 18.0 | -19.7 | 123.2 | 14.7 |
| New York | $PM_{2.5}$ | 37 | 11,340 | 11.1 | 9.1 | 2.7 | 38.5 | 8.3 |
| | $PM_{10}$ | 11 | 787 | 24.8 | 21 | 7 | 78 | 18 |
| | $PM_{10\text{-}2.5}$ | 5 | 369 | 12.4 | 9.5 | -10.4 | 70.8 | 10.0 |
| St. Paul | $PM_{2.5}$ | 17 | 3,898 | 8.6 | 7.6 | 2.2 | 26.9 | 5.3 |
| | $PM_{10}$ | 8 | 960 | 25.6 | 24 | 9 | 57 | 15 |
| | $PM_{10\text{-}2.5}$ | 4 | 394 | 17.1 | 15.2 | 1.4 | 47.9 | 11.5 |
| Winston-Salem | $PM_{2.5}$ | 27 | 15,110 | 12.7 | 11.5 | 0 | 84.5 | 8.2 |
| | $PM_{10}$ | 15 | 2,361 | 20.8 | 19 | 1 | 99 | 12 |
| | $PM_{10\text{-}2.5}$ | 11 | 1,491 | 6.3 | 5.8 | -10.9 | 49.4 | 4.5 |

**Table 2.2 Cross-validated performance of calibration models for $PM_{2.5}$, $PM_{10}$, and $PM_{10-2.5}$ predictions by study area and pollutant.**

| | | Overall | | | | Spatial | | | | Temporal[c] | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| City | Pollutant | $R^2$ | RMSE[b] | Intercept[a] | Slope[a] | $R^2$ | RMSE[b] | Intercept[a] | Slope[a] | $R^2$ | RMSE | Intercept | Slope |
| Baltimore | $PM_{2.5}$ | 0.79 | 3.45 | -0.23 (0.07) | 1.03 (0.005) | 0.65 | 0.70 | 2.73 (1.38) | 0.79 (0.11) | 0.83 (0.07) | 3.21 (0.9) | -0.43 (1.13) | 1.05 (0.07) |
| | $PM_{10}$ | 0.54 | 8.23 | -1.21 (0.58) | 1.08 (0.03) | 0.69 | 3.17 | -3.56 (5.02) | 1.19 (0.24) | 0.62 (0.14) | 7.22 (3.35) | -1.71 (4.92) | 1.07 (0.19) |
| | $PM_{10-2.5}$ | 0.16 | 9.01 | 2.86 (0.6) | 0.73 (0.06) | 0.65 | 3.18 | -1.59 (3.21) | 1.25 (0.37) | 0.1 (0.07) | 7.8 (3.83) | 4.41 (4.2) | 0.42 (0.27) |
| Chicago | $PM_{2.5}$ | 0.75 | 3.59 | -0.11 (0.09) | 1.02 (0.01) | 0.46 | 0.95 | 3.93 (1.91) | 0.7 (0.15) | 0.8 (0.11) | 3.23 (0.97) | -0.29 (1.13) | 1.03 (0.07) |
| | $PM_{10}$ | 0.48 | 8.56 | 1.54 (0.55) | 0.94 (0.02) | 0.52 | 3.40 | 8.06 (4.4) | 0.68 (0.18) | 0.53 (0.15) | 8.7 (2.01) | -3.45 (12.09) | 1.13 (0.39) |
| | $PM_{10-2.5}$ | 0.23 | 7.87 | 4.36 (0.42) | 0.68 (0.04) | 0.57 | 3.03 | 4.12 (2.63) | 0.71 (0.23) | 0.28 (0.17) | 8.14 (2.63) | 0.56 (8.82) | 0.94 (0.47) |
| Los Angeles | $PM_{2.5}$ | 0.66 | 6.86 | -0.26 (0.12) | 1.03 (0.01) | 0.56 | 2.21 | 2.13 (3.07) | 0.92 (0.18) | 0.69 (0.09) | 6.93 (2.5) | -0.27 (2.83) | 1.05 (0.17) |
| | $PM_{10}$ | 0.56 | 12.18 | -0.64 (0.5) | 1.02 (0.01) | 0.62 | 4.43 | 2.71 (6.44) | 0.94 (0.18) | 0.56 (0.12) | 12.12 (4.05) | -2.34 (10.2) | 1.05 (0.3) |
| | $PM_{10-2.5}$ | 0.43 | 9.70 | 2.99 (0.42) | 0.83 (0.02) | 0.74 | 2.70 | 3.23 (3.33) | 0.82 (0.15) | 0.43 (0.15) | 9.16 (1.97) | 0.85 (9.13) | 0.88 (0.38) |
| New York | $PM_{2.5}$ | 0.76 | 3.96 | -0.31 (0.07) | 1.04 (0.01) | 0.81 | 0.77 | -0.28 (1.01) | 1.05 (0.09) | 0.78 (0.12) | 3.97 (1.6) | -0.4 (0.85) | 1.05 (0.07) |
| | $PM_{10}$ | 0.62 | 9.61 | -1.07 (0.79) | 1.06 (0.03) | 0.95 | 1.48 | -3.28 (2.11) | 1.14 (0.09) | 0.63 (0.17) | 8.45 (2.73) | -1.03 (6.22) | 1.01 (0.23) |
| | $PM_{10-2.5}$ | 0.35 | 8.71 | 1.22 (0.92) | 0.86 (0.06) | 0.96 | 1.70 | -2.42 (1.75) | 1.1 (0.13) | 0.35 (0.19) | 7.23 (2.74) | -3.68 (16.3) | 0.91 (0.97) |
| St. Paul | $PM_{2.5}$ | 0.73 | 2.71 | -0.23 (0.1) | 1.05 (0.01) | 0.49 | 0.82 | 0.06 (2.34) | 1.03 (0.27) | 0.76 (0.15) | 2.84 (1.86) | -0.41 (0.58) | 1.08 (0.08) |
| | $PM_{10}$ | 0.50 | 9.04 | -1.53 (0.91) | 1.08 (0.03) | 0.88 | 1.55 | -2.54 (4.4) | 1.11 (0.17) | 0.52 (0.16) | 8.17 (2.78) | -1.74 (1.54) | 1.07 (0.08) |
| | $PM_{10-2.5}$ | 0.40 | 8.34 | 1.52 (1.04) | 0.89 (0.05) | 0.82 | 2.03 | 1.88 (5.4) | 0.85 (0.28) | 0.35 (0.15) | 8.27 (2.22) | 0.82 (2.69) | 0.91 (0.17) |
| Winston-Salem | $PM_{2.5}$ | 0.80 | 2.94 | -0.26 (0.06) | 1.02 (0.004) | 0.93 | 0.65 | -1.04 (0.81) | 1.08 (0.06) | 0.81 (0.07) | 2.86 (0.68) | -0.3 (0.73) | 1.02 (0.05) |
| | $PM_{10}$ | 0.67 | 5.87 | -0.32 (0.33) | 1.04 (0.02) | 0.72 | 2.02 | 0.54 (3.53) | 0.98 (0.17) | 0.69 (0.09) | 5.27 (1.45) | -0.4 (3.57) | 1.01 (0.2) |
| | $PM_{10-2.5}$ | 0.19 | 4.68 | 3.38 (0.19) | 0.46 (0.02) | 0.25 | 1.88 | 4.04 (1.36) | 0.34 (0.2) | 0.22 (0.15) | 4.46 (1.18) | 2.43 (1.85) | 0.55 (0.3) |

[a] Shown as parameter estimate ± standard error from a linear regression of observations versus predictions
[b] Root of the mean squared error
[c] Shown as the mean (standard deviation) of the statistic, across all monitor-level results from linear regressions of observations versus predictions

**Table 2.3 Cross-validated performance of final 'best' models for $PM_{2.5}$, $PM_{10}$, and $PM_{10-2.5}$ predictions by study area and pollutant.**

| | | Overall | | | | Spatial | | | | Temporal[c] | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| City | Pollutant | $R^2$ | RMSE[b] | Intercept[a] | Slope[a] | $R^2$ | RMSE[b] | Intercept[a] | Slope[a] | $R^2$ | RMSE | Intercept | Slope |
| Baltimore | $PM_{2.5}$ | 0.86 | 3.14 | -1.97 (0.03) | 1.19 (0.002) | 0.75 | 0.87 | 0.95 (1.34) | 0.96 (0.11) | 0.87 (0.04) | 3.08 (0.67) | -1.81 (1.18) | 1.18 (0.08) |
| | $PM_{10}$ | 0.57 | 7.65 | -3.19 (0.32) | 1.14 (0.01) | 0.74 | 2.34 | 0.31 (3.6) | 0.97 (0.17) | 0.64 (0.1) | 6.67 (2.52) | -4.9 (5.42) | 1.2 (0.2) |
| | $PM_{10-2.5}$ | 0.20 | 7.91 | 1.35 (0.28) | 0.72 (0.03) | 0.75 | 2.13 | -0.29 (1.86) | 0.92 (0.22) | 0.12 (0.07) | 6.65 (2.81) | 2.02 (1.66) | 0.53 (0.31) |
| Chicago | $PM_{2.5}$ | 0.79 | 4.09 | -3.28 (0.05) | 1.29 (0.004) | 0.40 | 1.11 | 6.19 (1.89) | 0.58 (0.14) | 0.83 (0.06) | 3.86 (0.66) | -3.57 (1.42) | 1.31 (0.09) |
| | $PM_{10}$ | 0.50 | 8.71 | -0.83 (0.29) | 1.02 (0.01) | 0.52 | 3.66 | 10.22 (3.54) | 0.56 (0.15) | 0.56 (0.08) | 8.6 (1.53) | -7.06 (8.15) | 1.28 (0.21) |
| | $PM_{10-2.5}$ | 0.28 | 7.70 | 2.56 (0.19) | 0.67 (0.02) | 0.51 | 3.43 | 4.65 (1.81) | 0.46 (0.17) | 0.32 (0.1) | 7.36 (1.54) | -0.52 (3.9) | 0.96 (0.14) |
| Los Angeles | $PM_{2.5}$ | 0.70 | 6.13 | -2.18 (0.07) | 1.14 (0.004) | 0.41 | 2.21 | 5.54 (3.03) | 0.69 (0.19) | 0.75 (0.07) | 6.09 (1.29) | -2.72 (3.01) | 1.2 (0.21) |
| | $PM_{10}$ | 0.50 | 16.00 | -10.55 (0.42) | 1.29 (0.01) | 0.57 | 4.41 | 6.48 (6.05) | 0.81 (0.17) | 0.56 (0.12) | 14.98 (7.95) | -15.79 (19.43) | 1.42 (0.53) |
| | $PM_{10-2.5}$ | 0.41 | 11.54 | -1.41 (0.3) | 0.98 (0.01) | 0.70 | 3.41 | 4.6 (3.06) | 0.69 (0.14) | 0.41 (0.16) | 10.83 (2.87) | -4.08 (10.59) | 1.05 (0.45) |
| New York | $PM_{2.5}$ | 0.85 | 3.43 | -1.96 (0.03) | 1.21 (0.002) | 0.66 | 1.08 | -1.54 (1.76) | 1.17 (0.15) | 0.85 (0.06) | 3.4 (0.72) | -1.9 (0.68) | 1.2 (0.08) |
| | $PM_{10}$ | 0.61 | 9.71 | -4.6 (0.47) | 1.21 (0.02) | 0.92 | 2.14 | -4.25 (2.83) | 1.2 (0.12) | 0.62 (0.12) | 8.27 (3.17) | -4.1 (7.6) | 1.15 (0.3) |
| | $PM_{10-2.5}$ | 0.34 | 8.74 | 0.43 (0.45) | 0.89 (0.03) | 0.97 | 2.10 | -4.31 (1.63) | 1.26 (0.13) | 0.24 (0.05) | 7.77 (3.59) | -0.06 (6.19) | 0.72 (0.51) |
| St. Paul | $PM_{2.5}$ | 0.83 | 3.30 | -2.95 (0.05) | 1.41 (0.01) | 0.30 | 0.95 | 3.66 (2.5) | 0.68 (0.27) | 0.83 (0.08) | 3.29 (0.82) | -3.11 (0.61) | 1.41 (0.08) |
| | $PM_{10}$ | 0.47 | 9.56 | -3.01 (0.49) | 1.11 (0.02) | 0.84 | 1.46 | 5.2 (3.63) | 0.79 (0.14) | 0.48 (0.07) | 9.1 (1.81) | -5.95 (6.76) | 1.21 (0.2) |
| | $PM_{10-2.5}$ | 0.31 | 10.01 | 1.1 (0.59) | 0.85 (0.03) | 0.84 | 2.54 | 3.3 (3.86) | 0.71 (0.22) | 0.28 (0.12) | 9.76 (2.27) | -0.96 (5.42) | 0.91 (0.25) |
| Winston-Salem | $PM_{2.5}$ | 0.89 | 2.38 | -1.78 (0.03) | 1.14 (0.002) | 0.93 | 0.58 | -1.08 (0.8) | 1.09 (0.06) | 0.89 (0.03) | 2.33 (0.39) | -1.75 (0.82) | 1.13 (0.05) |
| | $PM_{10}$ | 0.73 | 5.04 | -1.6 (0.19) | 1.09 (0.01) | 0.77 | 1.76 | 1.51 (2.89) | 0.92 (0.14) | 0.75 (0.06) | 4.64 (1.11) | -2.28 (3.05) | 1.1 (0.14) |
| | $PM_{10-2.5}$ | 0.32 | 4.02 | 2.52 (0.1) | 0.57 (0.01) | 0.31 | 1.85 | 4.01 (1.07) | 0.33 (0.16) | 0.37 (0.08) | 3.94 (0.86) | 1.34 (1.89) | 0.72 (0.19) |

[a] Shown as parameter estimate ± standard error from a linear regression of observations versus predictions
[b] Root of the mean squared error
[c] Shown as the mean (standard deviation) of the statistic, across all monitor-level results from linear regressions of observations versus prediction

**Table 2.4 Comparison of $PM_{10-2.5}$ model evaluation using AOD-based approach versus alternative approaches.**

| A | AOD-Based Approach | | | | Alternative Spatial Approach: Nearest Co-Located Site | | | | Alternative Spatial Approach: Inverse Distance Weighting | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| City | $R^2$ | RMSE[b] | Intercept[a] | Slope[a] | $R^2$ | RMSE[b] | Intercept[a] | Slope[a] | $R^2$ | RMSE[b] | Intercept[a] | Slope[a] |
| Baltimore | 0.75 | 2.13 | -0.29 (1.86) | 0.92 (0.22) | 0.03 | 4.44 | 12.66 (14.38) | -0.67 (1.66) | 0.27 | 4.78 | 21.18 (9.67) | -1.72 (1.15) |
| Chicago | 0.51 | 3.43 | 4.65 (1.81) | 0.46 (0.17) | 0.02 | 4.02 | 7.44 (3.78) | 0.15 (0.4) | 0.04 | 3.31 | 5.75 (5.89) | 0.35 (0.65) |
| Los Angeles | 0.70 | 3.41 | 4.6 (3.06) | 0.69 (0.14) | 0.23 | 4.56 | 8.49 (6.25) | 0.52 (0.3) | 0.14 | 4.22 | 6.27 (9.91) | 0.65 (0.51) |
| New York | 0.97 | 2.10 | -4.31 (1.63) | 1.26 (0.13) | 0.57 | 9.30 | 21.32 (6.11) | -1.13 (0.56) | 0.67 | 7.81 | 31.63 (9.02) | -2.23 (0.9) |
| St. Paul | 0.84 | 2.54 | 3.3 (3.86) | 0.71 (0.22) | 0.14 | 3.93 | 9.76 (10.35) | 0.37 (0.64) | 0.02 | 3.84 | 12.04 (17.15) | 0.23 (1.08) |
| Winston-Salem | 0.31 | 1.85 | 4.01 (1.07) | 0.33 (0.16) | 0.04 | 2.35 | 7.06 (1.78) | -0.15 (0.26) | 0.03 | 1.93 | 7.37 (2.43) | -0.2 (0.37) |

[a] Shown as parameter estimate ± standard error from a linear regression of observations versus predictions
[b] Root of the mean squared error

| B | AOD-Based Approach[a] | | | | Alternative Temporal Approach: Measured City Average | | | |
|---|---|---|---|---|---|---|---|---|
| City | $R^2$ | RMSE | Intercept | Slope | $R^2$ | RMSE | Intercept | Slope |
| Baltimore | 0.12 (0.07) | 6.65 (2.81) | 2.02 (1.66) | 0.53 (0.31) | 0.26 (0.19) | 7.79 (4.09) | 3.48 (3.26) | 0.43 (0.15) |
| Chicago | 0.32 (0.1) | 7.36 (1.54) | -0.52 (3.9) | 0.96 (0.14) | 0.38 (0.06) | 7.22 (1.36) | 1.73 (3.09) | 0.81 (0.15) |
| Los Angeles | 0.41 (0.16) | 10.83 (2.87) | -4.08 (10.59) | 1.05 (0.45) | 0.59 (0.16) | 10.41 (3.08) | 1.39 (5.27) | 0.95 (0.45) |
| New York | 0.24 (0.05) | 7.77 (3.59) | -0.06 (6.19) | 0.72 (0.51) | 0.2 (0.05) | 10.35 (3.82) | 4.64 (3.19) | 0.61 (0.51) |
| St. Paul | 0.28 (0.12) | 9.76 (2.27) | -0.96 (5.42) | 0.91 (0.25) | 0.38 (0.14) | 10.79 (1.53) | 4.95 (2.6) | 0.72 (0.2) |
| Winston-Salem | 0.37 (0.08) | 3.94 (0.86) | 1.34 (1.89) | 0.72 (0.19) | 0.38 (0.14) | 3.84 (1.09) | 1.61 (1.47) | 0.7 (0.22) |

[a] Shown as the mean (standard deviation) of the statistic, across all monitor-level results from linear regressions of observations versus predictions

Table 2.4 shows the $PM_{10-2.5}$ model evaluation by study area using A) our AOD-based approach (final model CV) vs. two alternative spatial approaches (nearest monitor and inverse distance weighting); B) our AOD-based approach (final model CV) vs. an alternative temporal approach (city-average).

**Table 2.5 Summary statistics of final long-term average (2000-2012) $PM_{2.5}$, $PM_{10}$, and $PM_{10-2.5}$ predictions ($\mu g/m^3$), by study area and pollutant.**

| City | Pollutant | Mean (SD) | 25th Percentile | 75th Percentile |
|---|---|---|---|---|
| Baltimore | $PM_{2.5}$ | 9.6 (2.3) | 8.0 | 11.4 |
| | $PM_{10}$ | 11.6 (7.6) | 5.6 | 16.7 |
| | $PM_{10-2.5}$ | 2.1 (7.1) | -3.2 | 6.7 |
| Chicago | $PM_{2.5}$ | 8 (10.3) | 7.1 | 13.5 |
| | $PM_{10}$ | 26.1 (9.5) | 19.7 | 31.7 |
| | $PM_{10-2.5}$ | 18.8 (14) | 9.3 | 26.5 |
| Los Angeles | $PM_{2.5}$ | 8.7 (16.2) | 3.9 | 17.2 |
| | $PM_{10}$ | 34.9 (11.6) | 28.1 | 43.0 |
| | $PM_{10-2.5}$ | 26 (13.4) | 16.8 | 35.4 |
| New York | $PM_{2.5}$ | 9.7 (1.6) | 8.6 | 10.9 |
| | $PM_{10}$ | 37.6 (18.4) | 25.1 | 48.4 |
| | $PM_{10-2.5}$ | 28.3 (19.4) | 14.6 | 39.5 |
| St. Paul | $PM_{2.5}$ | 8.8 (1.1) | 8.0 | 9.5 |
| | $PM_{10}$ | 21.7 (5.6) | 17.6 | 24.3 |
| | $PM_{10-2.5}$ | 13.1 (4.8) | 9.6 | 15.2 |
| Winston-Salem | $PM_{2.5}$ | 12 (1.2) | 11.4 | 12.7 |
| | $PM_{10}$ | 16.6 (9.7) | 12.3 | 23.4 |
| | $PM_{10-2.5}$ | 4.9 (9.3) | 0.8 | 11.4 |

## Appendix:

**Table 2.A1 Summary statistics of all daily $PM_{2.5}$, $PM_{10}$, and $PM_{10\text{-}2.5}$ concentrations ($\mu g/m^3$) measured at EPA air quality monitoring stations in six US metropolitan areas for the period 2000-2012, independent of paired AOD data (i.e., validation dataset).[a]**

| City | Pollutant | Number of Sites | Number of Observations | Mean | Median | Min | Max | IQR |
|---|---|---|---|---|---|---|---|---|
| Baltimore | $PM_{2.5}$ | 30 | 39,165 | 13.2 | 11.3 | 0 | 94.1 | 9.2 |
| | $PM_{10}$ | 13 | 4,694 | 20.6 | 18 | 0 | 93 | 13 |
| | $PM_{10\,2.5}$ | 8 | 2,728 | 7.8 | 5.8 | -57.1 | 73.4 | 7.6 |
| Chicago | $PM_{2.5}$ | 28 | 36,159 | 14.2 | 12.4 | 0 | 68.4 | 10 |
| | $PM_{10}$ | 15 | 8,245 | 23.3 | 21 | 0 | 110 | 15 |
| | $PM_{10\,2.5}$ | 9 | 4,514 | 9.0 | 7.3 | -18.1 | 94.0 | 9.6 |
| Los Angeles | $PM_{2.5}$ | 22 | 39,844 | 16.4 | 13.6 | 0 | 132.6 | 10.5 |
| | $PM_{10}$ | 19 | 12,928 | 34.7 | 32 | 1 | 1129 | 22 |
| | $PM_{10\,2.5}$ | 12 | 8,294 | 19.0 | 16.5 | -25.3 | 491.4 | 14.1 |
| New York | $PM_{2.5}$ | 37 | 44,589 | 12.5 | 10.3 | 0 | 86.8 | 9.5 |
| | $PM_{10}$ | 11 | 3,011 | 25.0 | 21 | 0 | 164 | 17 |
| | $PM_{10\,2.5}$ | 5 | 1,476 | 11.0 | 8.2 | -33.4 | 135.7 | 10.4 |
| St. Paul | $PM_{2.5}$ | 17 | 15,639 | 10.0 | 8.4 | 0 | 69.9 | 7 |
| | $PM_{10}$ | 8 | 4,639 | 25.8 | 23 | 0 | 107 | 16 |
| | $PM_{10\,2.5}$ | 4 | 1,742 | 15.6 | 12.5 | -16.9 | 98.0 | 12.2 |
| Winston-Salem | $PM_{2.5}$ | 27 | 38,321 | 12.9 | 11.7 | 0 | 99 | 8.6 |
| | $PM_{10}$ | 15 | 5,924 | 20.3 | 19 | 0 | 99 | 12 |
| | $PM_{10\,2.5}$ | 11 | 3,762 | 6.0 | 5.5 | -22.6 | 49.4 | 4.3 |

[a] These data are, however, restricted to only EPA sites that are used in the calibration model (i.e., sites with > 30 observations throughout the study period and only one station per location).

**Table 2.A2 Calibration model coefficients of AIC-selected spatial and temporal predictors (fixed effects), by study area and pollutant.**

| | Baltimore | | Chicago | | Los Angeles | | New York | | St. Paul | | Winston-Salem | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Model Term | $PM_{2.5}$ | $PM_{10}$ | $PM_{2.5}$ | $PM_{10}$ | $PM_{2.5}$ | $PM_{10}$ | $PM_{2.5}$ | $PM_{10}$ | $PM_{2.5}$ | $PM_{10}$ | $PM_{2.5}$ | $PM_{10}$ |
| (Intercept) | 10.35 | 17.68 | 11.99 | 23.54 | 14.25 | 33.57 | 10.16 | 24.13 | 8.05 | 25.93 | 10.92 | 17.98 |
| AOD | 7.37 | 11.64 | 2.96 | | 18.05 | 14.67 | 3.27 | | 4.20 | | 7.23 | 12.10 |
| avg_elev | -0.14 | | -0.26 | 3.51 | -1.41 | -3.67 | -0.21 | 4.26 | 0.10 | | | |
| pct_Open_Water | | | -0.27 | | | | | | | | | |
| pct_Dev_Open | | 3.93 | -2.95 | | 4.05 | 3.44 | | -2.04 | | | | -3.01 |
| pct_Dev_Low | 0.64 | 2.01 | -3.55 | | 5.06 | | 0.16 | | | | | |
| pct_Dev_Medium | 0.36 | | -4.45 | | 4.85 | 0.97 | 0.23 | | 0.40 | 1.94 | 0.24 | -2.64 |
| pct_Dev_High | 0.92 | 5.31 | -2.84 | 3.01 | 8.30 | | 0.39 | | 0.26 | 2.66 | | |
| pct_Barren | | | -1.06 | | | | | | | | | |
| pct_Decid_Forest | 0.42 | | -2.69 | 0.82 | | | 0.33 | | 0.50 | 5.22 | | |
| pct_EvGrn_Forest | | | | | | | | | | | 0.10 | |
| pct_Mix_Forest | -0.28 | | | | | | | | | | -0.29 | |
| pct_Shrub_Scrub | | | -0.73 | | | | | | | | | |
| pct_Grass_Herb | | | | -0.78 | 1.68 | 3.45 | | | | | -0.17 | |
| pct_Pasture_Hay | | | 0.19 | | | | | | | | | |
| pct_Cultiv_Crop | | | -0.29 | | | | | | | | | |
| pct_Woody_Wetland | 0.11 | | -1.03 | | | | | | | | | |
| pct_Emerg_Herb_Wetland | | | -0.41 | | | | | | | | | |
| BG_Population | | | | -9.49 | | 11.82 | -2.70 | 21.87 | | | | 1.98 |
| BG_Population_Grow | | -0.87 | | 12.97 | | -12.39 | 3.12 | -21.91 | | | -0.13 | -2.45 |
| NDVI | 0.36 | -2.00 | | | 0.38 | -0.99 | -0.31 | | 0.24 | | | |
| daily_avg_pbl | -1.58 | -1.96 | -0.52 | -1.59 | -1.00 | | -1.43 | | -0.84 | | -0.76 | -1.03 |
| Evaporation | 0.17 | | -0.62 | | -0.42 | | 0.52 | | -1.15 | | | |
| Humidity | 4.18 | 3.62 | 2.83 | 1.49 | | -8.22 | 1.57 | 3.50 | 2.93 | | | -2.53 |
| PrecipitableWater | | | | | -3.47 | | 2.50 | | -1.30 | | | |
| Pressure | -0.29 | | | | -1.90 | -15.61 | | | | | 0.25 | 1.01 |
| Temperature | -2.59 | | -1.29 | | 3.41 | 9.34 | -2.37 | | | | 1.84 | 4.96 |
| Uwind | | | | | 0.60 | | 0.73 | | | | -0.35 | |
| Visibility | 0.39 | 1.63 | -0.24 | 1.04 | 0.96 | 0.92 | 0.51 | | | | 0.35 | 0.97 |
| Vwind | 0.82 | 1.08 | 1.64 | 1.68 | 0.58 | 1.65 | 1.14 | 3.49 | 1.07 | 4.19 | 0.94 | 1.77 |
| total_roads_km | 0.15 | 2.02 | 0.34 | | 0.23 | 2.20 | | | 0.27 | 1.06 | | |
| near_prim_rd_m | -0.46 | | -0.14 | | -0.36 | 1.21 | -0.26 | 3.09 | -0.16 | | -0.09 | -0.99 |
| near_sec_rd_m | 0.19 | 4.71 | 0.45 | 4.71 | -0.48 | | -0.30 | -4.56 | | | | 1.30 |
| near_railroad_m | | | | -2.14 | | | -0.09 | -4.17 | | | | -1.09 |
| near_water_m | | | | 1.95 | 0.29 | | | | | | | |
| near_big_water_m | -0.13 | 2.89 | | | | -16.08 | -0.26 | 2.41 | -0.29 | | 0.37 | |

**References:**


Adar, S.D., Filigrana, P.A., Clements, N., Peel, J.L., 2014. Ambient Coarse Particulate Matter and Human Health: A Systematic Review and Meta-Analysis. Curr Envir Health Rpt. 1, 258-274.

Bild, D.E., Bluemke, D.A., Burke, G.L., Detrano, R., Diez Roux, A.V., Folsom, A.R., et al., 2002. Multi-Ethnic Study of Atherosclerosis: Objectives and Design. Am J Epidemiol. 156, 871-881.

Chen, Y., Yang, Q., Krewski, D., Shi, Y., Burnett, R.T., McGrail, K., 2004. Influence of Relatively Low Level of Particulate Air Pollution on Hospitalization for COPD in Elderly People. Inhal Toxicol. 16, 21-25.

Chen, C.H., Chan, C.C., Chen, B.Y., Cheng, T.J., Guo, Y.L., 2015. Effects of particulate air pollution and ozone on lung function in non-asthmatic children. Environ Res. 137, 40-48.

de Hoogh, K., Héritier, H., Stafoggia, M., Künzli, N., Kloog, I., 2018. Modelling daily PM2.5 concentrations at high spatio-temporal resolution across Switzerland. Environ Pollut. 233, 1147-1154.

Dee, D.P., Uppala, S.M., Simmons, A.J., Berrisford, P., Poli, P., Kobayashi, S., Andrae, U., Balmaseda, M.A., Balsamo, G., Bauer, P., Bechtold, P., Beljaars, A.C.M., van de Berg, L., Bidlot, J., Bormann, N., Delsol, C., Dragani, R., Fuentes, M., Geer, A.J., … Vitart, F., 2011. The ERA-Interim reanalysis: configuration and performance of the data assimilation system. QJR Meteorol Soc. 137, 553-597.

Didan, K., 2015. *MYD13A3 MODIS/Aqua Vegetation Indices Monthly L3 Global 1km SIN Grid V006*, distributed by NASA EOSDIS Land Processes DAAC.

Hu, X., Waller, L.A., Lyapustin, A., Wang, Y., Al-Hamdan M.Z., Crosson, W.L., Estes Jr., M.G., Estes, S.M., Quattrochi, D.A., Puttaswamy S.J., Liu, Y., 2014. Estimating ground-level PM2.5 concentrations in the Southeastern United States using MAIAC AOD retrievals and a two-stage model. Remote Sens Environ. 140, 220-232.

Hu, Z., 2009. Spatial analysis of MODIS aerosol optical depth, PM2.5, and chronic coronary heart disease. Int J Health Geogr. 8, 27-36.

Kloog, I., Koutrakis, P., Coull, B.A., Lee, H.J., Schwartz, J., 2011. Assessing temporally and spatially resolved PM2.5 exposures for epidemiological studies using satellite aerosol optical depth measurements. Atmos Environ. 45, 6267-6275.

Kloog, I., Nordio, F., Coull, B.A., Schwartz, J., 2012a. Incorporating local land use regression and satellite aerosol optical depth in a hybrid model of spatiotemporal PM2.5 exposures in the Mid-Atlantic states. Environ Sci Technol. 46, 11913-11921.

Kloog, I., Coull, B.A., Zanobetti, A., Koutrakis, P., Schwartz, J.D., 2012b. Acute and chronic effects of particles on hospital admissions in New-England. PLoS One. 7, 2-9.

Kloog, I., Chudnovsky, A.A., Just, A.C., Nordio, F., Koutrakis, P., Coull, B.A., Lyapustin, A., Wang, Y., Schwartz, J., 2014. A new hybrid spatio-temporal model

for estimating daily multi-year PM2.5 concentrations across northeastern USA using high resolution aerosol optical depth data. Atmos Environ. 95, 581-590.

Kloog, I., Sorek-Hamer, M., Lyapustin, A., Coull, B., Wang, Y., Just, A.C., Schwartz, J., Broday, D.M., 2015. Estimating daily PM 2.5 and PM 10 across the complex geo-climate region of Israel using MAIAC satellite-based AOD data. Atmos Environ. 122, 409-416.

Lagudu, U.R.K., Raja, S., Hopke, P.K., Chalupa, D.C., Utell, M.J., Casuccio, G., Lersch, T.L., West, R.R., 2011. Heterogeneity of Coarse Particles in an Urban Area. Environ Sci Technol. 45, 3288-3296.

Lee, M., Kloog, I., Chudnovsky, A., Lyapustin, A., Wang, Y., Melly, S., Coull, B., Koutrakis, P., Schwartz, J., 2016. Spatiotemporal prediction of fine particulate matter using high-resolution satellite images in the Southeastern US 2003-2011. J Expo Sci Environ Epidemiol. 26, 377-384.

Levy, R.C., Remer, L.A., Mattoo, S., Vermote, E.F., Kaufman, Y.J., 2007. Second-generation operational algorithm: Retrieval of aerosol properties over land from inversion of Moderate Resolution Imaging Spectroradiometer spectral reflectance. J Geophys Res. 112, D13211.

Lin, M., Stieb, D.M., Chen, Y., 2005. Coarse Particulate Matter and Hospitalization for Respiratory Infections in Children Younger Than 15 Years in Toronto: A Case-Crossover Analysis. Pediatrics. 116, 235-240.

Lipsett, M.J., Tsai, F.C., Roger, L., Woo, M., Ostro, B.D., 2006. Coarse Particles and Heart Rate Variability among Older Adults with Coronary Artery Disease in the Coachella Valley, California. Environ Health Perspect. 114, 1215-1220.

Lyapustin, A., Martonchik, J., Wang, Y., Laszlo, I., Korkin, S., 2011a. Multi-Angle Implementation of Atmospheric Correction (MAIAC): 1. Radiative Transfer Basis and Look-Up Tables. J Geophys Res. 116, D03210.

Lyapustin, A., Wang, Y., Laszlo, I., Kahn, R., Korkin, S., Remer, L., Levy, R., Reid, J.S., 2011b. MultiAngle Implementation of Atmospheric Correction (MAIAC): 2. Aerosol Algorithm. J Geophys Res. 116, D03211.

Lyapustin, A.I., Wang, Y., Laszlo, I., Hilker, T., Hall, F.G., Sellers, P.J., Tucker, C.J., Korkin, S.V., 2012. Multi-Angle Implementation of Atmospheric Correction for MODIS (MAIAC). 3: Atmospheric Correction. Remote Sens Environ. 127, 385-393.

Madrigano, J., Kloog, I., Goldberg, R., Coull, B.A., Mittleman, M.A., Schwartz, J., 2013. Long-term exposure to PM2.5 and incidence of acute myocardial infarction. Environ Health Perspect. 121, 192-196.

Malig, B.J., Green, S., Basu, R., Broadwin, R., 2013. Coarse Particles and Respiratory Emergency Department Visits in California. Am J Epidemiol. 178, 58-69.

Manson, S., Schroeder, J., Van Riper, D., Ruggles, S., 2018. IPUMS National Historical Geographic Information System: Version 13.0 [Database]. Minneapolis: University of Minnesota.

McGuinn, L.A., Ward-Caviness, C.K., Neas, L.M., Schneider, A., Diaz-Sanchez, D., Cascio, W.E., Kraus, W.E., Hauser, E., Dowdy, E., Haynes, C., Chudnovsky, A.,

Koutrakis, P., Devlin, R.B., 2016. Association between satellite-based estimates of long-term PM2.5 exposure and coronary artery disease. Environ Res. 145, 9-17.

Mesinger, F., DiMego, G., Kalnay, E., Mitchell, K., Shafran, P.C., Ebisuzaki, W., Jovic, D., Woollen, J., Rogers, E., Berbery, E.H., Ek, M.B., Fan, Y., Grumbine, R., Higgins, W., Li, H., Lin, Y., Manikin, G., Parrish, D., Shi, W., 2006. North American Regional Reanalysis. Bull Amer Meteor Soc. 87, 343–360.

Miller, K.A., Siscovick, D.S., Sheppard, L., Shepherd, K., Sullivan, J.H., Anderson, G.L., Kaufman, J.D., 2007. Long-Term Exposure to Air Pollution and Incidence of Cardiovascular Events in Women. N Engl J Med. 356, 447-458.

Nordio, F., Kloog, I., Coull, B.A., Chudnovsky, A., Grillo, P., Bertazzi, P.A., Baccarelli, A.A., Schwartz, J., 2013. Estimating spatio-temporal resolved PM10 aerosol mass concentrations using MODIS satellite data and land use regression over Lombardy, Italy. Atmos Environ. 74, 227-236.

Pakbin, P., Hudda, N., Cheung, K.L., Moore, K.F., Sioutas, C., 2010. Spatial and Temporal Variability of Coarse (PM10-2.5) Particulate Matter Concentrations in the Los Angeles Area. Aerosol Sci Tech. 44, 514-525.

Peng, R.D., Chang, H.H., Bell, M.L., McDermott, A., Zeger, S.L., Samet, J.M., Dominici, F., 2008. Coarse Particulate Matter Air Pollution and Hospital Admissions for Cardiovascular and Respiratory Diseases Among Medicare Patients. JAMA. 299, 2172-2179.

R Core Team, 2018. R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria.

R Core Team, 2019. R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria.

Remer, L.A., Kaufman, Y.J., Tanré, D., Mattoo, S., Chu, D.A., Martins, J.V., Li, R.R., Ichoku, C., Levy, R.C., Kleidman, R.G., Eck, T.F., Vermote, E., Holben, B.N., 2005. The MODIS Aerosol Algorithm, Products, and Validation. J Atmos Sci. 62, 947-973.

Rodopoulou, S., Chalbot, M.C., Samoli, E., Dubois, D.W., San Filippo, B.D., Kavouras, I.G., 2014. Air pollution and hospital emergency room and admissions for cardiovascular and respiratory diseases in Doña Ana County, New Mexico. Environ Res. 129, 39-46.

Sawvel, E.J., Willis, R., West, R.R., Casuccio, G.S., Norris, G., Kumar, N., Hammond, D., Peters, T.M., 2015. Passive sampling to capture the spatial variability of coarse particles by composition in Cleveland, OH. Atmos Environ. 105, 61-69.

Shtein, A., Karnieli, A., Katra, I., Raz, R., Levy, I., Lyapustin, A., Dorman, M., Broday, D.M., Kloog, I., 2018. Estimating daily and intra-daily PM10 and PM2.5 in Israel using a spatio-temporal hybrid modeling approach. Atmos Environ. 191, 142-152.

Sorek-Hamer, M., Just, A.C., Kloog, I., 2016. Satellite remote sensing in epidemiological studies. Curr Opin Pediatr. 28, 228-234.

Stafoggia, M., Samoli, E., Alessandrini, E., Cadum, E., Ostro, B., Berti, G., Faustini, A., Jacquemin, B., Linares, C., Pascal, M., Randi, G., Ranzi, A., Stivanello, E.,

Forastiere, F., MED-PARTICLES Study Group, 2013. Short-term associations between fine and coarse particulate matter and hospitalizations in Southern Europe: results from the MED-PARTICLES project. Environ Health Perspect. 121, 1026-1033.

Stafoggia, M., Schwartz, J., Badaloni, C., Bellander, T., Alessandrini, E., Cattani, G., de' Donato, F., Gaeta, A., Leone, G., Lyapustin, A., Sorek-Hamer, M., de Hoogh, K., Di, Q., Forastiere, F., Kloog, I., 2017. Estimation of daily PM10 concentrations in Italy (2006-2012) using finely resolved satellite data, land use variables and meteorology. Environ Int. 99, 234-244.

Stafoggia, M., Bellander, T., Bucci, S., Davoli, M., de Hoogh, K., de' Donato, F., Gariazzo, C., Lyapustin, A., Michelozzi, P., Renzi, M., Scortichini, M., Shtein, A., Viegi, G., Kloog, I., Schwartz, J., 2019. Estimation of daily PM10 and PM2.5 concentrations in Italy, 2013-2015, using a spatiotemporal land-use random-forest model. Environ Int. 124, 170-179.

Thornburg, J., Rodes, C.E., Lawless, P.A., Williams, R., 2009. Spatial and temporal variability of outdoor coarse particulate matter mass concentrations measured with a new coarse particle sampler during the Detroit Exposure and Aerosol Research Study. Atmos Environ. 43, 4251-4258.

US Census Bureau, 2010 TIGER/Line Shapefiles [machine-readable data files]/ prepared by the U.S. Census Bureau, 2012.

US EPA, Integrated Science Assessment (ISA) for Particulate Matter (Final Report, Dec 2019). U.S. Environmental Protection Agency, Washington, DC, EPA/600/R-19/188, 2019.

US EPA, Integrated Science Assessment (ISA) for Particulate Matter (Final Report, Dec 2009). U.S. Environmental Protection Agency, Washington, DC, EPA/600/R-08/139F, 2009.

USGS, 2001, NLCD 2001 Land Cover Conterminous United States remote-sensing image: Sioux Falls, SD, USGS.

USGS, 2006, NLCD 2006 Land Cover Conterminous United States remote-sensing image: Sioux Falls, SD, USGS.

USGS, 2011, NLCD 2011 Land Cover Conterminous United States remote-sensing image: Sioux Falls, SD, USGS.

USGS, 2017, 1/3rd arc-second Digital Elevation Models (DEMs) - USGS National Map 3DEP Downloadable Data Collection: U.S. Geological Survey.

USGS, 2019, National Hydrography Dataset (ver. USGS National Hydrography Dataset Best Resolution (NHD) for Hydrologic Unit (HU) 4 - 2001 (published 20191002)).

Wilson, W.E., Suh, H.H., 1997. Fine Particles and Coarse Particles: Concentration Relationships Relevant to Epidemiologic Studies. J Air Waste Manag Assoc. 47, 1238-1249.

Yanosky, J.D., Paciorek, C.J., Schwartz, J., Laden, F., Puett, R., Suh, H.H., 2008. Spatio-temporal modeling of chronic PM10 exposure for the Nurses' Health Study. Atmos Environ. 42, 4047-4062.

Yanosky, J.D., Paciorek, C.J., Suh, H.H., 2009. Predicting Chronic Fine and Coarse Particulate Exposures Using Spatiotemporal Models for the Northeastern and Midwestern United States. Environ Health Perspect. 117, 522-529.

Yanosky, J.D., Paciorek, C.J., Laden, F., Hart, J.E., Puett, R.C., Liao, D., Suh, H.H., 2014. Spatio-temporal modeling of particulate air pollution in the conterminous United States using geographic and meteorological predictors. Environ Health. 13, 63-77.

Zhang, K., Larson, T.V., Gassett, A., Szpiro, A.A., Daviglus, M., Burke, G.L., Kaufman, J.D., Adar, S.D., 2014. Characterizing Spatial Patterns of Airborne Coarse Particulate (PM10-2.5) Mass and Chemical Components in Three Cities: The Multi-Ethnic Study of Atherosclerosis. Environ Health Perspect. 122, 823-830.

Zhao, Y., Wang, S., Lang, L., Huang, C., Ma, W., Lin, H., 2017. Ambient fine and coarse particulate matter pollution and respiratory morbidity in Dongguan, China. Environ Pollut. 222, 126-131.

# CHAPTER 3 :

# Cross-Sectional Associations between Long-Term Satellite AOD Predicted $PM_{10-2.5}$ and Markers of Inflammation and Coagulation in the Multi-Ethnic Study of Atherosclerosis (MESA) Population

## Introduction:

Air pollution has been ranked as one of the top ten risk factors for morbidity and mortality in the world, largely due to its impacts on cardiovascular disease (Lim et al. 2012). Even at the current low levels of air pollution observed in the United States (US), it is estimated that nearly 80,000 lives are lost prematurely each year in the US due to the cardiovascular impacts of these exposures (Brauer et al. 2016). The mechanisms underlying these relationships are incompletely understood, though inflammation and coagulation have been proposed as some of the key pathways by which particulate matter (PM) air pollution can impact health (Brook et al. 2010; US EPA 2019; van Eeden et al. 2004). Together, these responses can initiate chronic cardiovascular disease processes such as atherosclerosis (Kaufman et al. 2016) and other adverse cardiac events such as myocardial infarctions and strokes (Brook et al. 2010; van Eeden et al. 2004).

Importantly, inflammation and coagulation are considered plausible biological mechanisms for the observed associations between cardiovascular health effects and PM of all sizes. However, to date, most research on the impacts of PM has focused on the smaller size fraction of $PM_{2.5}$ (aerodynamic diameter $\leq 2.5$ μm) (Hajat et al. 2015;

Viehmann et al. 2015; Hennig et al. 2014; Ostro et al. 2014; Lanki et al. 2015; Dabass et al. 2016; Bind et al. 2012), with only a few studies evaluating the long-term inflammation and coagulation from larger particles such as $PM_{10-2.5}$ (aerodynamic diameter ≤ 10 μm and > 2.5 μm) (Adar et al. 2015; Lanki et al. 2015; Forbes et al. 2009). This gap is noteworthy since the US EPA has determined that there is suggestive evidence of an association between long-term $PM_{10-2.5}$ and adverse cardiovascular events but notes that there are gaps in the proposed pathways that might link these (US EPA 2019).

A major challenge that has contributed to the small body of literature on the long-term inflammatory and coagulation impacts of $PM_{10-2.5}$ is the limited measurement data available to estimate $PM_{10-2.5}$ exposure for use in epidemiologic studies (Adar et al. 2014). One of only two studies of this relationship used data from the Multi-Ethnic Study of Atherosclerosis (MESA) to investigate associations with $PM_{10-2.5}$ (Adar et al. 2015). That study used detailed estimates of exposure predicted using measurements from a spatially intensive field substudy (Zhang et al. 2014). Those predictions were, however, only available for three of the six MESA sites and as a result that research was largely underpowered to find associations.

In the present study, we aimed to extend and validate the work of Adar et al. (2015) by using new $PM_{10-2.5}$ estimates which we generated using spatiotemporal models with satellite measures for all six MESA sites. Specifically, we used our $PM_{10-2.5}$ predictions in the full MESA cohort to assess the impacts of $PM_{10-2.5}$ with two markers of inflammation (interleukin-6 (IL-6) and C-reactive protein (CRP)) and four markers of coagulation (fibrinogen, factor VIII, D-dimer, and plasmin-antiplasmin complex (PAP)). This work increases statistical power and allowed us to study these relationships within

the largest and most geographically diverse US population to date and without the need for intensive $PM_{10-2.5}$ sampling.

**Methods:**

***Study population:***

We conducted this analysis using data from participants of MESA. Briefly, MESA recruited 6,814 White, Black, Hispanic, and Chinese women and men between July 2000 and September 2002 who were aged 45 to 84 years and who were free from clinical cardiovascular disease (Bild et al. 2002). Participants were recruited from Baltimore, Maryland; Chicago, Illinois; Forsyth County, North Carolina; Los Angeles County, California; northern Manhattan, New York; and St. Paul, Minnesota.

***Inflammation and coagulation biomarkers:***

Fasting blood samples were collected from all participants at baseline (2000-2002) and analyzed at the University of Vermont Laboratory for Clinical Biochemistry Research (Bild et al. 2002; Cushman et al. 1995). Our analysis considered six biomarkers, which were determined *a priori* based on previous research showing links with air pollution and their hypothesized roles in inflammatory and coagulation processes (Adar et al. 2015; Lanki et al. 2015; Hajat et al. 2015; US EPA 2009; US EPA 2019): IL-6, CRP, fibrinogen, factor VIII, D-dimer, and PAP. IL-6 was measured using ultrasensitive enzyme-linked immunosorbent assay (ELISA) (Quantikine HS Human IL-6 Immunoassay; R&D Systems, Minneapolis, MN) with a lower detection limit of < 0.094 pg/mL [coefficient of variation (CV): 6.3%]. CRP and fibrinogen were measured using the BNII nephelometer (N High Sensitivity CRP, N Antiserum to Human Fibrinogen; Dade Behring, Inc. Deerfield, IL). CRP intra-assay CVs ranged from 2.3 to 4.4% and

interassay CVs ranged from 2.1 to 5.7%. Fibrinogen intra-assay and interassay CVs were 2.7 and 2.6%, respectively. D-dimer was measured using an immuno-turbidimetric method on the Sta-R analyzer (Liatest D-DI; Diagnostica Stago, Parsippany, NJ) [analytical CV: 8%]. Factor VIII coagulant activity was determined as the clot time in factor VIIIc deficient plasma in the presence of activators utilizing the Sta-R analyzer (STA-Deficient VIII; Diagnostica Stago, Parsippany, NJ) [CV: 10%]. PAP was measured by a two-site enzyme-linked immunosorbent assay (ELISA) that utilizes two monoclonal antibodies (Holvoet et al. 1986).

***Air pollution:***

$PM_{10-2.5}$ concentration predictions are described in Chapter 2 of this dissertation. Briefly, we used measurements of Aerosol Optical Depth (AOD) from the National Aeronautics and Space Administration's (NASA) Terra satellite along with land-use regression and spatial smoothing to estimate long-term $PM_{10-2.5}$ within the six areas where MESA participants resided. In this multi-staged approach we first calibrated AOD (1 $km^2$ resolution) with daily EPA measurements of $PM_{10}$ and $PM_{2.5}$ using an area-specific mixed-modelling approach with land-use regression. Spatial and temporal predictors included elevation, land use, vegetation, planetary boundary layer, population, distance to roads, rails, large water bodies, and meteorological terms (air pressure, air temperature, evaporation, precipitable water, specific humidity, u-wind, and v-wind). We then used spatial smoothing in generalized additive mixed-models to predict daily $PM_{10}$ and $PM_{2.5}$ when AOD was missing. Finally, we estimated $PM_{10-2.5}$ by taking the difference of spatially matched $PM_{10}$ and $PM_{2.5}$ daily predictions. Our long-term $PM_{10-2.5}$ predictions were well correlated with measured levels estimated from collocated $PM_{2.5}$

and $PM_{10}$ sites, with spatial cross validated (CV) $R^2$ ranging from 0.31 in Winston-Salem, North Carolina to 0.97 in New York, and mean and median spatial CV $R^2$ across all six sites of 0.68 and 0.72, respectively.

Our exposure of interest in this work is long-term $PM_{10-2.5}$ levels (i.e., 5-year and 1-year $PM_{10-2.5}$ averages). However, the inflammation and coagulation biomarkers were measured in blood samples taken at the MESA baseline examination (2000-2002), which did not perfectly align with the satellite data used to generate our $PM_{10-2.5}$ predictions (AOD was first collected on the Terra satellite in late February 2000). Given this temporal misalignment, we elected to use $PM_{10-2.5}$ predictions for the mid-year of the baseline examination period (i.e., 2001) to reflect spatial contrasts during our exposure periods of interest. Our primary exposure therefore paired participants' 5-year residential address histories prior to their baseline exam with 2001 predictions, which assumes the spatial contrasts in $PM_{10-2.5}$ levels did not change over time. This assumption is supported by recent work (Colmer et al. 2020), which found that spatial contrasts in $PM_{2.5}$ levels across all US census tracts have remained consistent over 36 years and is similar to the exposure assignment approach used by others (Adar et al. 2015; Lanki et al. 2015). In sensitivity analyses we also estimated 1-year average $PM_{10-2.5}$ concentrations for each participant, again using 2001 air pollution predictions paired with 1-year prior to baseline exam residential address history. Participants located in grid-cells with >5% open water were linked to their closest neighboring grid-cell since we did not have $PM_{10-2.5}$ predicted concentrations for grid-cells with >5% open water.

***Covariates:***

Our analyses used additional data collected via technician administered questionnaire at the baseline exam, including the personal characteristics of age, sex, race/ethnicity, education, income, employment status, home ownership status, and marital status. Technicians also recorded information on participant medication use and health behaviors, including alcohol consumption, passive and active exposure to cigarette smoke, and weekly physical activity level. Hypertension and diabetes disease status were assessed at baseline, with hypertension defined by a measured systolic blood pressure > 140 mm Hg, diastolic blood pressure > 90 mm Hg, or use of anti-hypertensive medications (JNC VI 1997), and with diabetes defined by measured fasting serum glucose levels and medication use consistent with the 2003 American Diabetes Association guidelines (Genuth et al. 2003). Height and weight (which were used to calculate body mass index (BMI)), high-density lipoprotein (HDL), and creatinine were additionally measured during the baseline clinical examination.

To evaluate area-level confounding, we also created a neighborhood socioeconomic score (NSES) developed using principal components analysis (PCA) with sixteen census tract-level variables related to income, wealth, education, and employment, and linked to each participant's baseline address (Hajat et al. 2013). Similarly, we used predictions of the co-pollutants, $PM_{2.5}$ and $NO_X$ from the Multi-Ethnic Study of Atherosclerosis and Air Pollution (MESA Air) spatiotemporal model, which was available after 1999 (Kaufman et al. 2012; Szpiro et al. 2010). We also obtained meteorological data (temperature and relative humidity) from the National Oceanic and Atmospheric Administration's (NOAA) National Climatic Data Center and Normalized Difference Vegetation Index (NDVI) values collected on the NASA Terra satellite.

***Statistical analyses:***

We performed multivariable linear regression to estimate the cross-sectional associations between long-term $PM_{10-2.5}$ exposure and our two inflammation (IL-6 and CRP) and four coagulation (fibrinogen, factor VIII, D-dimer, and PAP) outcomes. Prior to modeling all markers were log transformed due to non-linearity. We conducted these analyses in staged fashions to understand the influence of the various confounders on our association of interest. Our first model adjusted for age (continuous), sex (binary), and race/ethnicity (non-Hispanic White, non-Hispanic Black, Hispanic, Chinese). Our second model additionally adjusted for characteristics about person and place likely to reflect confounding by SES or place including education (high school or less, some college, technical school certificate or associates/bachelors degree, graduate degree), current employment status (binary), current marital status (binary), home ownership status (binary), study site, NSES (continuous) by site, meteorology (temperature and relative humidity on the day of the baseline exam), and vegetation levels (the $25^{th}$ and $75^{th}$ percentiles of monthly 2001 levels within approximately 1km of a participant's baseline address). We also adjusted for the lifestyle factors of alcohol consumption (never, former, current), active and passive smoke exposure (never smoker/no passive smoke, never smoker/passive smoke, former smoker/no passive smoke, former smoker/passive smoke, current smoker), and level of physical activity (tertiles). We did not adjust for individual income because it was missing in a large portion of the cohort and sensitivity analyses demonstrated that our models as specified did not change with additional adjustment. Our third and *a priori* defined primary model also adjusted for $PM_{2.5}$ and $NO_X$ concentrations.

We reported all associations per 10 $\mu g/m^3$ along with their 95% confidence intervals (CIs).

In sensitivity analyses, we included further adjustment for health outcomes that may confound or mediate the association of interest (i.e., diabetes and hypertension status, BMI, HDL, creatinine, use of non-steroidal anti-inflammatory agents, use of oral steroids, current aspirin use, and use of oral anti-inflammatory asthma medication). We also assessed whether results differed by duration of residential stability by limiting our analysis of the primary models to only participants who had resided at their baseline exam residence for at least 5, and, separately, 10 years before their baseline exam. Similarly, to test the sensitivity of our results to our selected exposure averaging time, we looked at all primary model associations using one-year $PM_{10-2.5}$ averages rather than five-year averages. Finally, we evaluated the potential for effect modification by sex, race/ethnicity, study site, diabetes status, age (>70 vs. <= 70 years), and NSES (above vs. below the median), by including interaction terms of each potential modifier with $PM_{10-2.5}$ exposure in our primary model.

Participant addresses were linked to $PM_{10-2.5}$ grid-cell concentrations using R statistical software version 3.6.1 (R 2019) while all statistical modeling was performed using SAS software version 9.4 (SAS Institute Inc. Cary, NC).

**Results:**

Table 3.1 shows summary statistics for the exposures, outcomes, and covariates used in our analyses. Values are presented for the whole cohort as well as within quartiles of $PM_{10-2.5}$. Across all participants, the mean age was 62 years and 53% of the participants were female. Overall, 38% of participants were non-Hispanic White, 28%

were non-Hispanic Black, 22% were Hispanic, and 12% were Chinese. These race/ethnicity frequencies differed – by design – across the six cities (results not shown) and by quartiles of exposure, with the lowest quartile having much higher fractions of non-Hispanic White and non-Hispanic Black participants (44% and 52%, respectively) and much lower fractions of Chinese and Hispanic participants (1% and 3%, respectively) than the overall cohort. Participants in the highest exposure quartile had much lower mean NSES than the overall cohort while mean NSES among participants in each of the lowest three quartiles of exposure was greater than in the overall cohort. Vegetation levels were highest in the lowest exposure quartile and the levels decreased monotonically with increasing $PM_{10-2.5}$ exposure. Participants in the highest quartile of exposure also appeared to be generally healthier with the lowest fraction of current smokers (11%), highest fraction of participants reporting an ideal level of physical activity (63%), lowest prevalence of hypertension (39%), and the lowest average BMI (27 $km/m^2$).

Mean levels of $PM_{10-2.5}$ were 16.5 $\mu g/m^3$ overall though there were notable differences across study site. For example, nearly all participants in the lowest quartile of exposure resided in Baltimore (47%) and Winston-Salem (45%) while the highest exposure quartile was made up almost exclusively of participants in Chicago (47%), Los Angeles (35%), and New York (18%). Three of the biomarkers (IL-6, D-Dimer, and PAP) showed very little variation in mean levels across quartiles of $PM_{10-2.5}$ exposure. In contrast, mean levels of CRP decreased uniformly across the four exposure quartiles while mean levels of factor VIII decreased, although not monotonically, with increasing

exposure; mean levels of fibrinogen increased across the first three exposure quartiles, but were lowest in the highest quartile of exposure.

Using our primary model specification, which adjusted for demographic and socioeconomic factors, vegetation, meteorology, health behaviors (i.e., alcohol, smoking, and physical activity), co-pollutants, and study site, we found, counter to hypothesized, that higher levels of $PM_{10-2.5}$ were associated with lower levels of the inflammation and coagulation biomarkers (Table 3.2). The largest association with inflammation was for CRP which showed a 4.6% decrease in CRP per 10 $\mu g/m^3$ $PM_{10-2.5}$ (95% CI: -8.0, -1.0). For coagulation, the strongest association was for factor VIII which showed a 1.6% decrease per 10 $\mu g/m^3$ $PM_{10-2.5}$ (95% CI: -2.9, -0.3). Results from sensitivity analyses (Table 3.A1) that considered residential stability and used one rather than five-year average exposure were largely unchanged from our primary model results. Adjustment for characteristics of chronic health, however, eliminated almost all associations (Table 3.2). In analyses of potential effect modification by sex, age, study site, race/ethnicity, and NSES, we found some evidence of consistent heterogeneity of effects for three of the biomarkers (IL-6, fibrinogen, and PAP) with NSES and noted some differences for the IL-6 outcome with sex and age (Figure 3.1). In general the associations in St. Paul were also the largest in magnitude, and negative (with the exception of PAP), although very imprecise.

**Discussion:**

In this cross-sectional analysis we found no evidence that long-term exposures to $PM_{10-2.5}$ are associated with greater levels of inflammation and coagulation in the full MESA cohort. In fact, our findings indicated the presence of greater inflammation and

coagulation with lower $PM_{10-2.5}$ levels, which is counter to what we had hypothesized. These findings were, however largely eliminated by further adjustment for chronic health conditions, which could either suggest residual confounding or mediation of the associations by these conditions. Our results indicate that the biological mechanisms by which $PM_{10-2.5}$ might impact health are still being elucidated and that more evidence is needed to determine if $PM_{10-2.5}$ is detrimental to health.

Although our observed associations between long-term $PM_{10-2.5}$ concentrations and markers of inflammation and coagulation in participants of the MESA cohort indicated that $PM_{10-2.5}$ exposure was associated with less inflammation, biologically there is evidence that $PM_{10-2.5}$ exposures may initiate an inflammatory pathway. For example, an *in vitro* study that measured the $PM_{2.5}$ and $PM_{10-2.5}$ impacts on inflammatory mediators found that both size fractions induced IL-6 production and, importantly, that IL-6 production was more elevated in mouse macrophages after activation with $PM_{10-2.5}$ than $PM_{2.5}$ (Pozzi et al. 2003). Becker et al. (2005) similarly observed that $PM_{10-2.5}$ induced more IL-6 production than smaller PM size fractions in an *in vitro* study with human alveolar macrophages. Levels of fibrinogen – a marker of coagulation – in the blood of rats also increased in an *in vivo* study after exposure to urban $PM_{10-2.5}$ and $PM_{2.5}$, again with stronger effects in rats exposed to $PM_{10-2.5}$ than $PM_{2.5}$ (Gerlofs-Nijland et al. 2007). Collectively these toxicology studies suggest that inflammation might play a key role in the process by which $PM_{10-2.5}$ impacts health.

In contrast, the findings of the few epidemiological studies that have evaluated the impact of $PM_{10-2.5}$ on inflammation markers are less consistent and largely imprecise. For example, one of the only two other studies to look at cross-sectional relationships

between long-term $PM_{10-2.5}$ and CRP found a 6.1% increase (95% CI: -1.4, 14.1) in CRP for a 10 μg/m$^3$ increase in $PM_{10-2.5}$ within six European cohorts (Lanki et al. 2015). The other study found a 3.1% – although largely null – decrease in CRP for a 10 μg/m$^3$ increase in $PM_{10-2.5}$ within three of the six sites in MESA (Adar et al. 2015). The magnitude of this result within three of the six cities in MESA was similar to what we observed in the present study within all six cities (3.1% vs. 4.6% decrease per 10 μg/m$^3$ increase in $PM_{10-2.5}$), although the previous result was less precise than what we observed in this work. The only longitudinal analysis of the inflammation impacts of $PM_{10-2.5}$ found a 10.6% increase (95% CI: -0.2, 22.9) in high-sensitivity CRP for a 10 μg/m$^3$ increase in $PM_{10-2.5}$ within a cohort of midlife women in six US study sites (Davis et al. 2020). Another earlier study that looked at associations of CRP with larger $PM_{10}$ (aerodynamic diameter ≤ 10 μm) particles in an English cohort observed a 1.4% increase (95% CI: -9.6 to 13.8) in CRP per 10 μg/m$^3$ increase in $PM_{10}$ (Forbes et al. 2009). While none of those relationships were distinguishable from a null association, the larger body of research on long-term exposures to smaller particles, $PM_{2.5}$, and CRP has shown evidence of positive associations (Viehmann et al. 2015; Hennig et al. 2014; Ostro et al. 2014), although only within longitudinal studies; cross-sectional studies of the $PM_{2.5}$ and CRP relationship have found positive, although largely null relationships (Lanki et al. 2015; Dabass et al. 2016). Notably, one additional longitudinal study which, like ours, was also conducted within the full MESA cohort, found little support for an association between $PM_{2.5}$ and CRP (2% increase in CRP per 10 μg/m$^3$ increase in $PM_{2.5}$, 95% CI: −7.8%, 12.4%) (Hajat et al. 2015).

In terms of coagulation, the only marker that was examined in all three earlier studies looking at long-term $PM_{10-2.5}$ exposure was fibrinogen and all three found inverse, although nearly null, associations with $PM_{10-2.5}$ (Lanki et al. 2015; Adar et al. 2015; Davis et al. 2020). Specifically, Lanki et al. (2015) observed a 0.2% decrease (95% CI: -2.4, 1.8) in fibrinogen for a 10 $\mu g/m^3$ increase in $PM_{10-2.5}$, while Adar et al. (2015) observed a 2.8% decrease (95% CI: -7.5, 2.2) in fibrinogen for a 10 $\mu g/m^3$ increase in $PM_{10-2.5}$. In longitudinal analyses, Davis et al. (2020) found that a 10 $\mu g/m^3$ increase in $PM_{10-2.5}$ was associated with a 0.2% decrease in fibrinogen (95% CI: -2.5, 2.0). Results looking at the impacts of $PM_{2.5}$ on fibrinogen have been mixed and similarly imprecise (Hajat et al. 2015; Viehmann et al. 2015; Lanki et al. 2015; Dabass et al. 2016; Bind et al. 2012). Within this work, we saw the strongest coagulation results for factor VIII (1.6% decrease (95% CI: -2.9, -0.3) for a 10 $\mu g/m^3$ increase in $PM_{10-2.5}$), which was also studied in Adar et al. (2015) and Davis et al. (2020). Similar to our results but counter to what we had hypothesized, both of these studies also found that increased levels of $PM_{10-2.5}$ were associated with reductions in fibrinogen, although unlike ours, both had very imprecise estimates of association.

It is notable that the associations we observed in our – *a priori* determined – primary model specification were largely eliminated after adjustment for chronic health conditions and medication use. This may suggest that the inverse association we found in our primary analysis suffered from residual confounding by these health and medication factors. Alternatively, these health and medication factors could be consequences of $PM_{10-2.5}$ exposure, thereby making them intermediates on the pathway between $PM_{10-2.5}$ exposure and inflammation. Given the cross-sectional nature of this analysis, however,

we are unable to distinguish between these two possibilities. The cross-sectional aspect of this study is one clear limitation of this work. Interestingly, previous cross-sectional studies on the inflammatory impacts of PM have also not provided strong evidence for a positive association whereas longitudinal analyses have (US EPA 2019). While blood samples were taken from MESA participants at later exams, the baseline exam is the only one at which all participants have measures for all six biomarkers used in our analysis.

One possible explanation for the inverse associations that we observed between $PM_{10-2.5}$ and inflammation and coagulation biomarkers is that there is selection bias. In general, the MESA cohort is older and healthy since participants were age 45 to 84 and free of cardiovascular disease at baseline. If selection into the study also tracked with $PM_{10-2.5}$ exposure such that people with higher levels of exposure were more likely to be selected, then you could observe a blunting of an association that could result in counter to hypothesized results.

A second explanation for the inverse associations that we observed and the few differences between our results and others is that the chemical components of $PM_{10-2.5}$ in the MESA study areas are different from those found in the locations of other research studies that have found positive associations between PM and inflammation markers. This hypothesis is supported by the work in Adar et al. (2015), which found different associations with different $PM_{10-2.5}$ particle components within the three MESA study sites in their analysis. Specifically, endotoxin – a component of $PM_{10-2.5}$ that is found in bacterial cell membranes – was the $PM_{10-2.5}$ component most strongly associated with inflammation and, importantly, it was inversely associated with $PM_{10-2.5}$ mass. In contrast, copper – which originates from traffic – was the component most strongly

associated with increased markers of coagulation. Notably, these individual component results were much stronger and more precise than results with overall $PM_{10-2.5}$ mass, and they were positive, with increased levels of each component associated with increased levels of the biomarker. Unlike Adar et al. (2015), however, we did not have information on particle components of $PM_{10-2.5}$ with which to assess similar component-specific associations. As an alternative, we adjusted for vegetation since endotoxin can be higher in areas with more vegetation (Menetrez et al. 2009). Similarly we adjusted for $NO_x$ as an alternate measure of traffic. These adjustments suggest that this might not be the underlying explanation for our counter-to-hypothesized observed associations. Our results were also relatively consistent across these six study sites, which have varying levels of urbanicity. This combination of variation in urbanicity and geographical diversity present in our study may suggest that our observed associations do not depend on particular pollution sources. Nonetheless, it is a limitation of using satellite-based exposure predictions that are calibrated to regulatory monitoring data that we are unable to directly investigate component-specific effects.

In spite of this particular limitation, our use of finely resolved satellite-based $PM_{10-2.5}$ predicted concentrations to estimate exposure is a major strength of this work as it allowed us to estimate exposures at a 1 $km^2$ resolution across all of the MESA cities even where there are no ground-level measurements. This enabled us to include all participants from the MESA study in our analysis, more than doubling the study population of our earlier work. As a result, this study of $PM_{10-2.5}$, inflammation, and coagulation is the largest and most geographically diverse of its kind in the US population to date. This advancement of using satellite-based models is not uncommon

for $PM_{2.5}$ (Kloog et al. 2012; Kloog et al. 2015) and yet to date, few epidemiological studies on the health effects of $PM_{10-2.5}$ exposure have taken advantage of these type of predictions to estimate exposure. For example, one of the only three other studies to look at inflammation and long-term $PM_{10-2.5}$ exposure relied on data from a participant's nearest EPA $PM_{10}$ and $PM_{2.5}$ monitors within 20km to assign exposure (Davis et al. 2020). While this is not an uncommon approach used to assign air pollution exposure, it greatly limits the amount of exposure variation available in a health analyses and can lead to exposure misclassification since it doesn't capture all of the spatial variation in air pollution levels across an area.

One other weakness of the satellite-based models, in addition to lacking information on species, was the lack of predictions before 2000. This resulted in a temporal mismatch between our $PM_{10-2.5}$ exposure estimates and the exposure time of interest before the baseline exam given that we used 2001 $PM_{10-2.5}$ concentrations to represent exposure from approximately 1996-2002 (depending on a participant's date of baseline exam). However, our analysis using 1-year average exposures which were much more temporally aligned with the exposure period of interest (i.e., the time before the baseline exam) did not show any differences compared to our base analysis, indicating that the temporal mismatch of our exposure likely did not meaningfully impact our results. Notably, we did include residential address histories for all participants to capture the spatial dimension of participants' exposure. A final limitation of our work is that our results may not be generalizable to the whole population given that we conducted this study within MESA, which included only participants aged 45 and older at the time of recruitment.

**Conclusion:**

In this cross-sectional assessment we did not find evidence that long-term $PM_{10-2.5}$ exposure results in increased inflammation or coagulation, as we had hypothesized. Rather we found some evidence that increased levels of $PM_{10-2.5}$ were associated with lower levels of inflammation and coagulation, counter to our hypotheses. While these findings may be partially explained by confounding, it may be that more research is needed to determine if these pathway(s) are as important in humans as they have been shown to be in toxicology studies.

**Table 3.1 Summary statistics [mean ± SD, percent, or geometric mean (GSD)] for the complete MESA population ("All") and by quartile of $PM_{10-2.5}$ 5-year average exposure.**

| Characteristic | All | Quartile 1 | Quartile 2 | Quartile 3 | Quartile 4 |
|---|---|---|---|---|---|
| n | 6,814 | 1,643 | 1,667 | 1,680 | 1,678 |
| Age (years) | 62 ± 10 | 63 ± 10 | 61 ± 10 | 62 ± 11 | 63 ± 10 |
| Female (%) | 53 | 54 | 52 | 52 | 54 |
| Race/ethnicity (%) | | | | | |
| White | 38 | 44 | 47 | 29 | 35 |
| Chinese | 12 | 1 | 6 | 20 | 20 |
| Black | 28 | 52 | 20 | 20 | 19 |
| Hispanic | 22 | 3 | 27 | 32 | 26 |
| NSES | -0.29 ± 1.36 | -0.08 ± 1 | 0.11 ± 0.88 | -0.14 ± 1.41 | -1.04 ± 1.69 |
| Income (%) | | | | | |
| < $30,000 | 37 | 32 | 35 | 44 | 37 |
| $30,000-$50,000 | 23 | 24 | 26 | 22 | 19 |
| $50,000-$75,000 | 17 | 20 | 19 | 16 | 14 |
| > $75,000 | 23 | 24 | 20 | 18 | 29 |
| Employed (%) | 48 | 43 | 51 | 50 | 48 |
| Married (%) | 61 | 59 | 64 | 60 | 60 |
| Home Owner (%) | 67 | 83 | 73 | 50 | 65 |
| Education level (%) | | | | | |
| High school or less | 36 | 32 | 38 | 42 | 33 |
| High school and some college | 16 | 19 | 16 | 15 | 16 |
| College | 29 | 30 | 33 | 27 | 28 |
| Advanced degree | 18 | 19 | 14 | 16 | 23 |
| Smoking status (%) | | | | | |
| Never | 50 | 45 | 49 | 54 | 53 |
| Former | 37 | 41 | 37 | 33 | 36 |
| Current | 13 | 14 | 13 | 14 | 11 |
| Alcohol status (%) | | | | | |
| Never | 21 | 18 | 18 | 24 | 22 |
| Former | 24 | 29 | 26 | 23 | 19 |
| Current | 55 | 54 | 56 | 53 | 60 |
| Physical Activity Level (%) | | | | | |
| Poor | 23 | 24 | 23 | 24 | 20 |
| Intermediate | 18 | 18 | 18 | 18 | 17 |
| Ideal | 59 | 58 | 58 | 58 | 63 |
| NDVI | | | | | |
| 25th Percentile | 0.28 ± 0.1 | 0.37 ± 0.09 | 0.3 ± 0.1 | 0.23 ± 0.08 | 0.22 ± 0.08 |
| 75th Percentile | 0.46 ± 0.16 | 0.58 ± 0.14 | 0.54 ± 0.14 | 0.39 ± 0.13 | 0.34 ± 0.1 |
| Temperature (°C) | 12.8 ± 9.2 | 13.7 ± 8.5 | 11.1 ± 10 | 12.9 ± 9.4 | 13.4 ± 8.7 |
| Relative Humidity (%) | 68.5 ± 15.1 | 66.6 ± 15.4 | 67.2 ± 14.9 | 68.4 ± 15.2 | 71.6 ± 14.2 |
| Diabetes (%) | 13 | 14 | 11 | 13 | 12 |
| Hypertension (%) | 45 | 54 | 45 | 42 | 39 |
| BMI ($kg/m^2$) | 28 ± 5 | 29 ± 6 | 29 ± 5 | 28 ± 6 | 27 ± 5 |
| Study Site (%) | | | | | |
| Baltimore | 16 | 47 | 17 | 1 | 0.1 |
| Chicago | 17 | 2 | 5 | 15 | 47 |
| Los Angeles | 19 | 5 | 6 | 30 | 35 |
| New York | 16 | 0.4 | 12 | 32 | 18 |
| St. Paul | 16 | 0 | 42 | 21 | 0.3 |
| Winston-Salem | 16 | 45 | 18 | 1 | 0 |
| Pollutants | | | | | |
| $PM_{2.5}$ ($\mu g/m^3$) | 16.5 ± 3.4 | 15.7 ± 1.8 | 14.4 ± 2.8 | 17.3 ± 3.9 | 18.6 ± 3.1 |
| $NO_X$ ($\mu g/m^3$) | 49.8 ± 27 | 36.5 ± 19.4 | 36.5 ± 23.9 | 63.2 ± 28.6 | 61.8 ± 21.6 |
| $PM_{10-2.5}$ ($\mu g/m^3$) | 15.5 ± 13 | 1.7 ± 3.2 | 10.5 ± 2.3 | 16.7 ± 2.2 | 33 ± 11.6 |
| Inflammation markers | | | | | |
| IL-6 (pg/mL) | 1.2 (1.9) | 1.3 (1.9) | 1.3 (1.9) | 1.2 (1.9) | 1.2 (1.9) |
| CRP (mg/L) | 1.9 (3.2) | 2.2 (3.2) | 2.1 (3.1) | 1.8 (3.3) | 1.6 (3.2) |
| Coagulation markers | | | | | |
| Fibrinogen antigen (mg/dL) | 339.3 (1.2) | 338 (1.2) | 340.8 (1.2) | 343.5 (1.2) | 334.5 (1.2) |
| Factor VIII (%) | 150.8 (1.5) | 155.6 (1.5) | 148.9 (1.5) | 151.5 (1.5) | 147.6 (1.5) |
| D-Dimer ($\mu g/mL$) | 0.2 (2.5) | 0.2 (2.6) | 0.2 (2.5) | 0.2 (2.5) | 0.2 (2.6) |
| PAP (nM) | 4.4 (1.5) | 4.5 (1.5) | 4.4 (1.5) | 4.4 (1.5) | 4.4 (1.5) |

**Table 3.2 Percent change (95% CI) in inflammation and coagulation markers per 10 µg/m$^3$ of $PM_{10-2.5}$, by outcome measure and model.**

| Outcome Measure | Model 1[a] | Model 2[b] | Primary Model[c] | Extended Model[d] |
|---|---|---|---|---|
| Inflammation | | | | |
| IL-6 | -2.9 (-4.1, -1.7) | -2.2 (-4.2, -0.2) | -3.1 (-5.0, -1.0) | -1.4 (-3.2, 0.6) |
| CRP | -5.0 (-7.0, -3.0) | -3.5 (-6.9, -0.1) | -4.6 (-8.0, -1.0) | -2.2 (-5.5, 1.2) |
| Coagulation | | | | |
| Fibrinogen | -0.3 (-0.6, 0.1) | -0.7 (-1.4, -0.1) | -0.7 (-1.3, 0.0) | -0.3 (-0.9, 0.4) |
| Factor VIII | -0.8 (-1.6, 0.0) | -1.5 (-2.8, -0.2) | -1.6 (-2.9, -0.3) | -1.4 (-2.8, -0.1) |
| D-Dimer | -1.1 (-2.8, 0.6) | -2.3 (-4.9, 0.5) | -0.8 (-3.5, 2.0) | 0.5 (-2.4, 3.4) |
| PAP | 1.2 (0.5, 1.9) | -0.1 (-1.2, 1.1) | 0.2 (-1.0, 1.4) | -0.4 (-1.5, 0.8) |

[a] Adjusted for: age, sex, race/ethnicity.
[b] Further adjusted for: education, current employment, current marital status, home ownership, site, NSES*site, temperature, relative humidity, NDVI, alcohol consumption, active and passive smoke exposure, and physical activity level.
[c] Primary model further adjusted for: $PM_{2.5}$ and $NO_X$.
[d] Extended model further adjusted for: diabetes and hypertension status, BMI, HDL, creatinine, use of non-steroidal anti-inflammatory agents, use of oral steroids, current aspirin use, and use of oral anti-inflammatory asthma medication.

**Figure 3.1 Effect modification of the percent change in markers of inflammation and coagulation per 10 µg/m$^3$ of $PM_{10-2.5}$ by sex, age, site, race/ethnicity, and NSES.**

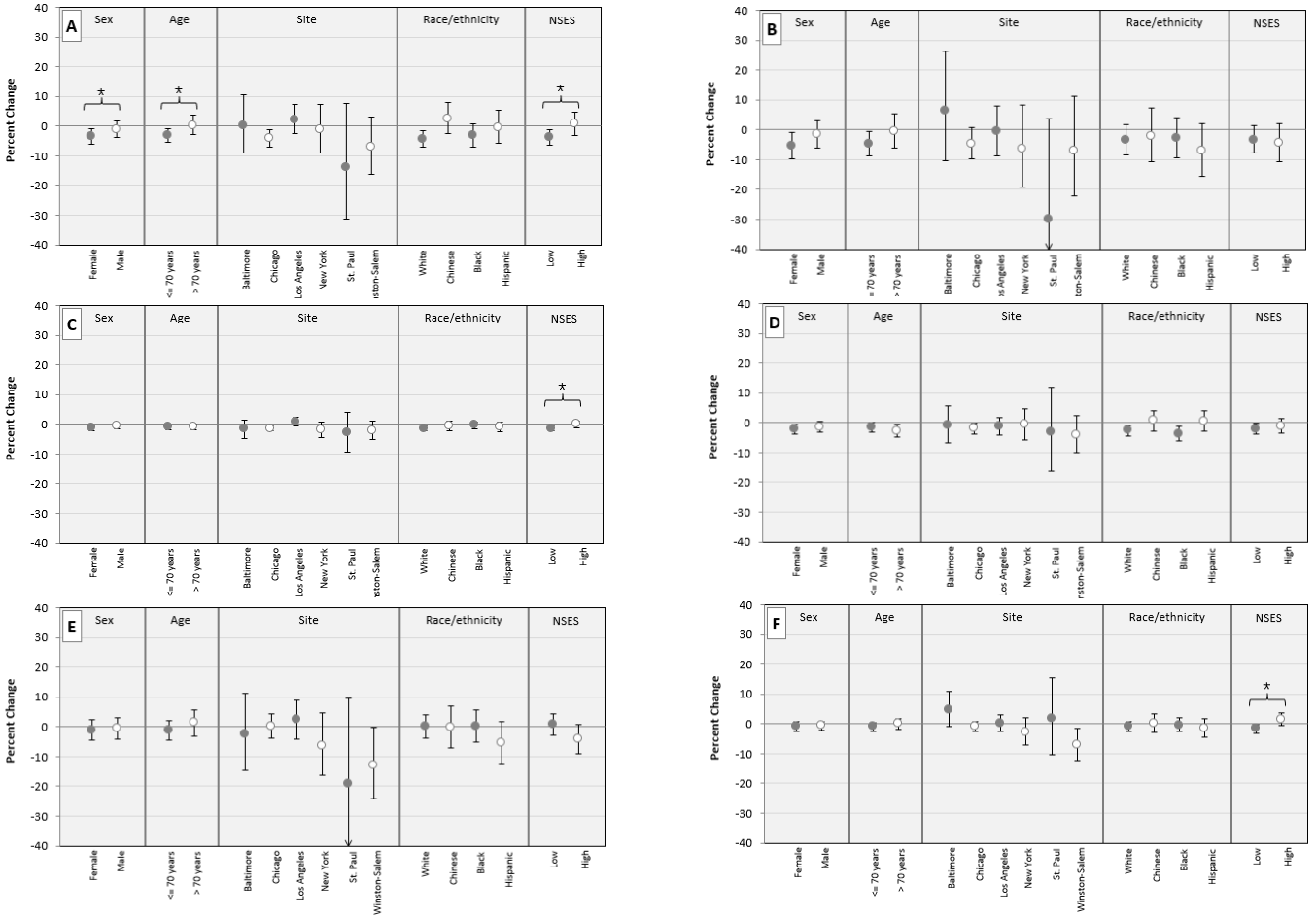


Figure 3.1 shows associations of $PM_{10-2.5}$ with interleukin-6 (A), C-reactive protein (B), fibrinogen (C), factor VIII (D), D-dimer (E), and plasmin-antiplasmin complex (F) by sex, age, site, race/ethnicity, and NSES. Abbreviations: NSES, neighborhood socioeconomic status. Associations are for the percent change per 10 µg/m$^3$. Asterisk (*) indicates significant interactions.

## Appendix:

**Table 3.A1 Percent change (95% CI) in inflammation and coagulation markers per 10 µg/m$^3$ of $PM_{10-2.5}$ in primary and sensitivity analyses, by outcome measure.**

| Outcome Measure | Primary Model[a] | Residential Stability 5+ years[b] | Residential Stability 10+ years[c] | 1 year $PM_{10-2.5}$ Exposure Averaging Time[d] |
|---|---|---|---|---|
| Inflammation | | | | |
| IL-6 | -3.1 (-5.0, -1.0) | -3.1 (-5.2, -0.8) | -3.4 (-5.9, -1.0) | -3.1 (-5.0, -1.1) |
| CRP | -4.6 (-8.0, -1.0) | -5.1 (-8.7, -1.3) | -4.5 (-8.6, -0.1) | -4.4 (-7.7, -1.0) |
| Coagulation | | | | |
| Fibrinogen | -0.7 (-1.3, 0.0) | -0.8 (-1.5, -0.1) | -0.7 (-1.5, 0.1) | -0.8 (-1.4, -0.2) |
| Factor VIII | -1.6 (-2.9, -0.3) | -2.0 (-3.3, -0.5) | -1.4 (-3.0, 0.2) | -1.9 (-3.1, -0.6) |
| D-Dimer | -0.8 (-3.5, 2.0) | -1.1 (-4.0, 1.9) | -0.4 (-3.8, 3.0) | -1.5 (-4.1, 1.2) |
| PAP | 0.2 (-1.0, 1.4) | 0.5 (-0.8, 1.8) | 0.8 (-0.6, 2.3) | 0.1 (-1.1, 1.2) |

[a] Adjusted for: age, sex, race/ethnicity, education, current employment, current marital status, home ownership, site, NSES*site, temperature, relative humidity, NDVI, alcohol consumption, active and passive smoke exposure, physical activity level, $PM_{2.5}$, and $NO_X$.
[b] Primary model restricted to participants who resided at their baseline exam address for 5 or more years prior to baseline exam.
[c] Primary model restricted to participants who resided at their baseline exam address for 10 or more years prior to baseline exam.
[d] Primary model using 1-year average $PM_{10-2.5}$ before baseline exam as the main exposure.

**References:**


Adar, S.D., Filigrana, P.A., Clements, N., Peel, J.L., 2014. Ambient Coarse Particulate Matter and Human Health: A Systematic Review and Meta-Analysis. Curr Envir Health Rpt. 1, 258-274.

Adar, S.D., D'Souza, J., Mendelsohn-Victor, K., Jacobs Jr., D.R., Cushman, M., Sheppard, L., Thorne, P.S., Burke, G.L., Daviglus M.L., Szpiro, A.A., Diez Roux, A.V., Kaufman, J.D., Larson, T.V., 2015. Markers of Inflammation and Coagulation after Long-Term Exposure to Coarse Particulate Matter: A Cross-Sectional Analysis from the Multi-Ethnic Study of Atherosclerosis. Environ Health Perspect. 123, 541-548.

Becker, S., Dailey, L.A., Soukup, J.M., Grambow, S.C., Devlin, R.B., Huang, Y-C.T., 2005. Seasonal Variations in Air Pollution Particle-Induced Inflammatory Mediator Release and Oxidative Stress. Environ Health Perspect. 113, 1032-1038.

Bild, D.E., Bluemke, D.A., Burke, G.L., Detrano, R., Diez Roux, A.V., Folsom, A.R., Greenland, P., Jacobs Jr., D.R., Kronmal, R., Liu, K., Nelson, J.C., O'Leary, D., Saad, M.F., Shea, S., Szklo, M., Tracy, R.P., 2002. Multi-Ethnic Study of Atherosclerosis: Objectives and Design. Am J Epidemiol. 156, 871-881.

Bind, M.A., Baccarelli, A., Zanobetti, A., Tarantini, L., Suh, H., Vokonas, P., Schwartz, J., 2012. Air pollution and markers of coagulation, inflammation, and endothelial function: Associations and epigene-environment interactions in an elderly cohort. Epidemiology. 23, 332-340.

Brauer, M., February 2016. The Global Burden of Disease from Air Pollution. Presentation at the American Association for the Advancement of Science Annual Meeting. Washington, DC.

Brook, R.D., Rajagopalan, S., Pope, C.A. III, Brook, J.R., Bhatnagar, A., Diez-Roux, A.V., et al., 2010. Particulate matter air pollution and cardiovascular disease: an update to the scientific statement from the American Heart Association. Circulation 121, 2331–2378.

Colmer, J., Hardman, I., Shimshack, J., Voorheis, J., 2020. Disparities in PM2.5 air pollution in the United States. Science. 269, 575-578.

Cushman, M., Cornell, E.S., Howard, P.R., Bovill, E.G., Tracy, R.P., 1995. Laboratory methods and quality assurance in the Cardiovascular Health Study. Clin Chem. 41, 264-270.

Dabass, A., Talbott, E.O., Venkat, A., Rager, J., Marsh, G.M., Sharma, R.K., Holguin, F., 2016. Association of exposure to particulate matter (PM2.5) air pollution and biomarkers of cardiovascular disease risk in adult NHANES participants (2001-2008). Int J Hyg Environ Health. 219, 301-310.

Davis, E., Malig, B., Broadwin, R., Ebisu, K., Basu, R., Gold, E.B., Qi, L., Derby, C.A., Park, S.K., Wu, X., 2020. Association between coarse particulate matter and inflammatory and hemostatic markers in a cohort of midlife women. Environ Health. 19, 111.

Forbes, L.J., Patel, M.D., Rudnicka, A.R., Cook, D.G., Bush, T., Stedman, J.R., et al. 2009. Chronic exposure to outdoor air pollution and markers of systemic inflammation. Epidemiology. 20, 245–253.

Genuth, S., Alberti, K.G.M.M., Bennett, P., Buse, J., DeFronzo, R., Kahn, R., 2003. Follow-up report on the diagnosis of diabetes mellitus. Diabetes Care. 26, 3160-3167.

Gerlofs-Nijland, M.E., Dormans, J.A.M.A., Bloemen, H.J.T., Leseman, D.L.A.C., Boere, A.J.F., Kelly, F.J., Mudway, I.S., Jimenez, A.A., Donaldson, K., Guastadisegni, C., Janssen, N.A.H., Brunekreef, B., Sandström, T., van Bree, L., Cassee, F.R., 2007. Toxicity of Coarse and Fine Particulate Matter from Sites with Contrasting Traffic Profiles. Inhal Toxicol. 19, 1055-1069.

Hajat, A., Diez-Roux, A.V., Adar, S.D., Auchincloss, A.H., Lovasi, G.S., O'Neill, M.S., Sheppard, L., Kaufman, J.D., 2013. Air Pollution and Individual and Neighborhood Socioeconomic Status: Evidence from the Multi-Ethnic Study of Atherosclerosis (MESA). Environ Health Perspect. 121, 1325-1333.

Hajat, A., Allison, M., Diez-Roux, A.V., Jenny, N.S., Jorgensen, N.W., Szpiro, A.A., Vedal, S., Kaufman, J.D., 2015. Long-term exposure to air pollution and markers of inflammation, coagulation, and endothelial activation: a repeat-measures analysis in the multi-ethnic study of atherosclerosis (MESA). Epidemiology. 26, 310-320.

Hennig, F., Fuks, K., Moebus, S., Weinmayr, G., Memmesheimer, M., Jakobs, H., Bröcker-Preuss, M., Führer-Sakel, D., Möhlenkamp, S., Erbel, R., Jöckel, KH., Hoffmann, B., 2014. Association between source-specific particulate matter air pollution and hs-CRP: local traffic and industrial emissions. Environ Health Perspect. 122, 703-710.

Holvoet, P., DeBoer, A., Vernstreken, M., Collen, D., 1986. An enzyme-linked immunosorbent assay (ELISA) for the measurement of plasmin-alpha-2-antiplasmin complex in human plasma - application to the detection of in vivo activation of the fibrinolytic system. Thromb Haemost. 56, 124-127.

Jenny, N.S., Brown, E.R., Detrano, R., Folsom, A.R., Saad, M.F., Shea, S., Szklo, M., Herrington, D.M., Jacobs Jr., D.R., 2010. Associations of inflammatory markers with coronary artery calcification: Results from the Multi-Ethnic Study of Atherosclerosis. Atherosclerosis. 209, 226-229.

Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure, 1997. The sixth report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. Arch Intern Med. 157, 2413-2446.

Kaufman, J.D., Adar, S.D., Allen, R.W., Barr, R.G., Budoff, M.J., Burke, G.L., Casillas, A.M., Cohen, M.A., Curl, C.L., Daviglus, M.L., Diez Roux, A.V., Jacobs Jr., D.R., Kronmal, R.A., Larson, T.V., Liu, S.LJ., Lumley, T., Navas-Acien, A., O'Leary, D.H., Rotter, J.I., Sampson, P.D., Sheppard, L., Siscovick, D.S., Stein, J.H., Szpiro, A.A., Tracy, R.P., 2012. Prospective Study of Particulate Air Pollution Exposures, Subclinical Atherosclerosis, and Clinical Cardiovascular

Disease The Multi-Ethnic Study of Atherosclerosis and Air Pollution (MESA Air). Am J Epidemiol. 176, 825-837.

Kaufman, J.D., Adar, S.D., Barr, R.G., Budoff, M., Burke, G.L., Curl, C.L., et al., 2016. Association between air pollution and coronary artery calcification within six metropolitan areas in the USA (the Multi-Ethnic Study of Atherosclerosis and Air Pollution): a longitudinal cohort study. Lancet. 388, 696-704.

Lanki, T., Hampel, R., Tiittanen, P., Andrich, S., Beelen, R., Brunekreef, B., Dratva, J., De Faire, U., Fuks, K.B., Hoffman, B., Imboden, M., Jousilahti, P., Koenig, W., Mahabadi, A.A., Künzli, N., Pedersen, NL., Penell, J., Pershagen, G., Probst-Hensch, N.M., Schaffner, E., Schindler, C., Sugiri, D., Swart, WJ., Tsai, M.Y., Turunen, A.W., Weinmayr, G., Wolf, K., Yli-Tuomi, T., Peters, A., 2015. Air pollution from road traffic and systemic inflammation in adults: A cross-sectional analysis in the european escape project. Environ Health Perspect. 123, 785-791.

Lim, S.S., Vos, T., Flaxman, A.D., Danaei, G., Shibuya, K., Adair-Rohani, H., et al., 2012. A comparative risk assessment of burden of disease and injury attributable to 67 risk factors and risk factor clusters in 21 regions, 1990-2010: a systematic analysis for the Global Burden of Disease Study 2010. Lancet. 380, 2224-2260.

Menetrez, M.Y., Foarde, K.K., Esch, R.K., Schwartz, T.D., Dean, T.R., Hays, M.D., Cho, S.H., Betancourt, D.A., Moore, S.A., 2009. An evaluation of indoor and outdoor biological particulate matter. Atmos Environ. 43, 5476-5483.

Ostro, B., Malig, B., Broadwin, R., Basu, R., Gold, E.B., Bromberger, J.T., Derby, C., Feinstein, S., Greendale, G.A., Jackson, E.A., Kravitz, H.M., Matthews, K.A., Sternfeld, B., Tomey, K., Green, R.R., Green, R., 2014. Chronic PM2.5 exposure and inflammation: Determining sensitive subgroups in mid-life women. Environ Res. 132, 168-175.

Pollitt, R.A., Kaufman, J.S., Rose, K.M., Diez-Roux, A.V., Zeng, D., Heiss, G., 2008. Cumulative life course and adult socioeconomic status and markers of inflammation in adulthood. J Epidemiol Community Health. 62, 484-491.

Pozzi, R., De Berardis, B., Paoletti, L., Guastadisegni, C., 2003. Inflammatory mediators induced by coarse (PM2.5-10) and fine (PM2.5) urban air particles in RAQ 264.7 cells. Toxicology. 183, 243-254.

R Core Team, 2019. R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria.

Szpiro, A.A., Sampson, P.D., Sheppard, L., Lumley, T., Adar, S.D., Kaufman, J., 2010. Predicting Intra-Urban Variation in Air Pollution Concentrations with Complex Spatio-Temporal Dependencies. Environmetrics. 21, 606-631.

US EPA, 2009. Integrated science assessment for particulate matter. Research Triangle Park: NCEA-RTP Office.

US EPA, 2019. Integrated science assessment for particulate matter. Research Triangle Park: NCEA-RTP Office.

van Eeden, S.F., Yeung, A., Quinlam, K., Hogg, J.C., 2005. Systemic Response to Ambient Particulate Matter: relevance to chronic obstructive pulmonary disease. Proc Am Thorac Soc. 2, 61-67.

Viehmann, A., Hertel, S., Fuks, K., Eisele, L., Moebus, S., Möhlenkamp, S., Nonnemacher, M., Jakobs, H., Erbel, R., Jöckel, K.H., Hoffmann, B., 2015. Long-term residential exposure to urban air pollution, and repeated measures of systemic blood markers of inflammation and coagulation. Occup Environ Med. 72, 656-663.

Zhang ,K., Larson, T.V., Gassett, A.J., Szpiro, A.A., Daviglus, M., Burke, G.L., Kaufman, J.D., Adar, S.D., 2014. Characterizing Spatial Patterns of Airborne Coarse Particulate (PM10-2.5) Mass and Chemical Components in Three Cities: The Multi-Ethnic Study of Atherosclerosis. Environ Health Perspect. 122, 823-830.

# CHAPTER 4 :

# Assessing National Attendance Benefits of the EPA's Diesel Emissions Reduction Act (DERA) School Bus Rebate Program: A Randomized Controlled Trial Design

## Introduction:

Approximately 25 million children ride buses to school each day in the United States (US) (Snyder & Dillow 2011). While school buses remain the safest means to transport children to school from a traffic accident perspective (TRB 2002), the use of older school buses often means students experience high exposures to diesel exhaust during their commutes since exhaust can enter school buses indirectly via leaky cabins or directly through open windows or doors. With exposures to pollutants inside school buses reaching levels as high as ten times the levels found in ambient air (Adar et al. 2008), even relatively short commutes on dirty school buses can contribute a disproportionately high fraction to students' daily air pollution exposures (Behrentz et al. 2005). This is of great concern given that exposures to traffic-related pollutants are known to result in adverse health effects including inflammation, poor lung function, and increased risk of asthma attacks (HEI 2010), which can lead to missed days of school for students (Silverstein et al. 2001; Akinbami et al. 2011).

Importantly, however, not all school buses generate the same exposures to diesel exhaust. The EPA finds that buses equipped with diesel particulate matter filters, for example, have 60 to 90% lower emissions of particulate matter compared to non-

retrofitted vehicles (US EPA 2003). Similarly, testing of in-cabin air in Washington (Adar et al. 2015) and Alabama (Hammond et al. 2007) school buses has shown that clean air technologies, such as diesel oxidation catalysts (DOCs) that reduce toxic emissions from the tailpipe and closed crankcase ventilation systems (CCVs) that minimize emissions from the engine block, can result in 50 to 60% reductions in particle concentrations inside of bus cabins relative to older, non-retrofitted buses. While this work suggests that school districts should replace older school buses with newer buses that incorporate these technologies, new buses are very costly at approximately $100,000 to $300,000 per bus (Noel & McCormack 2014). As a result, the average school bus is on the road for 16 years before being decommissioned (McMahon 2017) and most children ride school buses with older technologies that are highly polluting.

To help hasten the transition of school districts to cleaner vehicles, the US Environmental Protection Agency (EPA) set aside funding to help public and private fleet owners replace or retrofit old, highly polluting school buses under the National Clean Diesel Rebate Program, which was authorized by the Diesel Emissions Reduction Act (DERA) of 2010 (US EPA 2012). Using a random lottery approach to allocate funds, this EPA program (referred to here as the DERA School Bus Rebate Program) has awarded over $56 million dollars to replace or retrofit school buses since the program began in 2012, and the program continues to distribute funds (US EPA 2012; US EPA 2014; US EPA 2015; US EPA 2016; US EPA 2017; US EPA 2018; US EPA 2019; US EPA 2020). Although there are three published studies that have shown the public health and school attendance successes of school bus retrofit programs in two states (Adar et al. 2015;

Beatty & Shimshack 2011; Austin et al. 2019), the effectiveness of the EPA's national DERA School Bus Rebate Program has yet to be evaluated.

In this study, we take advantage of the randomized allocation of funding for school bus replacements and retrofits to causally assess the impacts of the EPA's DERA School Bus Rebate Program on student attendance at the national level. In secondary analyses we evaluate the potential for heterogeneity of effects by quartiles of estimated ridership on applicant buses as well as by the difference in model year for the replacement buses relative to the older buses, since EPA emissions standards have strengthened over time.

## Material and Methods:

### *Program to be evaluated:*

Starting in 2012, the EPA's DERA School Bus Rebate Program provided funding to replace diesel-powered school buses with older engines with new diesel, alternate fuel, battery, hybrid, or electric school buses (US EPA 2012; US EPA 2014; US EPA 2015; US EPA 2016; US EPA 2017). In 2015-2017 funding was added for retrofits of school buses with DOCs and CCVs (US EPA 2015; US EPA 2016; US EPA 2017). Additional funding was added in 2016 and 2017 for EPA-verified fuel operated heaters onboard buses to reduce idling for heat (US EPA 2016; US EPA 2017) (Table 4.1).

The EPA's eligibility criteria allowed school districts and private bus transportation companies who serviced school districts to apply for funding. Each applicant could apply for funding for up to 5 or 10 buses, depending on program year, and could enter up to two applications depending on fleet size and program year. There were also specific age requirements for the engines eligible to be replaced in each

funding cycle and for the type and age of eligible replacement engines (see Table 4.1 and Table 4.A1 for details).

The deadline for each of the rebate programs was the end of the calendar year, at which point the EPA entered all eligible applicants into a lottery and randomly selected applicants for funding using a random number generator. The number of buses requested by an applicant played no factor in the selection process. Rather, the EPA selected applications for funding until all available funds were exhausted. However, in recent program years, some EPA Regional offices had additional funding for school bus replacements. In these cases, regional offices awarded funding to additional applicants based on the randomized rank of applicants who did not receive funding from the EPA national program (Table 4.A2). No restrictions were placed on the number of years that an applicant could enter the lottery.

The EPA notified all applicants in the spring (i.e., at the end of the school year) if they were selected for funds. Winners then purchased their replacement buses or installed retrofits in the summer following the lottery and used their new buses for the first time in the fall (i.e., at the start of the next school year). For example, all 2012 applicants that won the lottery replaced their buses in the summer of 2013 and began using the new buses at the start of the 2013-2014 school year, which we refer to throughout this analysis as the 'after' lottery year. For 2012 applicants, the 2012-2013 school year would then be the 'before' year. The same convention holds for all years of the EPA funding lottery. All awardees are required to submit proof of new bus purchases and of scrappage of their old buses.

***EPA funding applicant data:***

We obtained data on all applicants for each lottery program year from the EPA under a Freedom of Information Act (FOIA) request. The data for all applicants included: lottery selection status, applicant name and district served (in the case where the applicant was a private bus transportation company), address, the number of buses requested to be replaced, and the amount of funding requested. For districts that were awarded funding, we additionally received information on the number of buses/engines replaced or retrofitted, the amount of funding received, the fuel type for replaced buses, and the type of upgrade purchased. We also received data on the annual miles traveled and engine model year of the replaced (i.e., baseline) buses, although this information was most often averaged across all replaced buses in a district.

***School district information:***

School district descriptive information for each entrant's baseline school year came from the US Department of Education's (ED) yearly Local Education Agency (School District) Universe Survey Data. These publicly available data include the number of students (total, and by grade and race/ethnicity), number of schools, and urbanicity (i.e., city, suburb, town, rural) of each district. The geographical size (i.e., land area of each school district) was provided in the National Center for Education Statistics School District Geographic Relationship files for the school years of 2013-2014, 2015-2016, and 2017-2018. As a proxy for district socioeconomic status, we used data on the number of students in a school who were eligible for the free and/or reduced price lunch program during the baseline school year from the US ED yearly Public Elementary/Secondary School Universe Survey Data, which we aggregated to the district level.

***School district attendance data:***

We collected 2012-2013 through 2018-2019 school year annual attendance rates for school districts that applied for funding from each state's Department of Education, either from public websites or through individual data requests with a state. Annual attendance rates reflect the average number of students present at all schools in a district across all days of a school year divided by the number of students serviced by that district. We linked annual attendance rate data for both the school year before and after the purchase of new buses to EPA entrants by name to have the most proximate data to an entrant's lottery selection status inform the analysis and to reduce the influence of trends.

***Data exclusions:***

We restricted our analyses to entrants that served individual school districts since they can be linked to school attendance records. For similar reasons, we excluded entrants from Puerto Rico and Hawaii since these areas report on the aggregate level and cannot be linked to individual district data, DOE descriptive information, or attendance data. Finally, we excluded entrants that represented private schools, non-traditional (e.g., special education and technology centers), and tribal schools since attendance data was not consistently available across states. Finally, in order to prevent outliers from impacting our findings we restricted our analysis to entrants with changes in attendance rates of 5 percentage points or less across the before and after lottery school years. This cutoff was consistent with the literature for reasonable levels and seemed to be consistent with errors (Guryan et al. 2020; Rogers & Feller 2018; Adar et al. 2015).

***Statistical design and analysis:***

We first compared means (for continuous variables) and proportions (for categorical variables) of baseline measured characteristics of the winning and losing districts in our analytical dataset to check for balance among the funding applicants by selection status. Then, to evaluate the impact of the EPA's DERA School Bus Rebate Program on attendance, we used the classical intent-to-treat (ITT) analyses for randomized controlled trials since the EPA awarded funding randomly to applicants.

Our primary analysis used model (4.1), where $Attendance_{it+1}$ is the continuous attendance rate for each applicant school district i in the school year after the year t lottery (i.e., the 2012, or 2014-2017 lotteries) at which time the new buses were in use. $Winner_{it}$ is an indicator equal to 1 if school district i was selected to receive funding in lottery year t and 0 if not. To account for any time-invariant differences that occurred by chance between winning and losing districts, we adjusted for $Attendance_{it}$, which is the attendance rate for school district i in the school year of lottery t prior to when the new buses were in use. This adjustment supports causal conclusions with the greatest efficiency by focusing on within-area differences between the pre- and post-randomization levels (Vickers 2001; Vickers & Altman 2001). We also adjusted for applicants who submitted more than one application within a lottery year using the indicator $MultiEntrant_{it}$ since the later lottery years allowed districts with large fleets to submit up to two applications. Given that some EPA regions provided funding to additional districts for the purchase of clean buses in the later lottery years, we included fixed effects for the EPA regions ($Region_i$). To maximize power, we combined data from all lottery years but included fixed effects for lottery year ($Time_{it}$) to adjust for any potential confounding over time that may have occurred since the percentages of lottery

winners changed by year. Since school districts are not limited to entering the lottery in only one year, we estimated associations and 95% confidence intervals using general estimating equations (GEE) with robust standard errors clustered at the state level to account for any potential correlation in the data. $\beta_1$ is the model outcome of interest, the ITT effect.

$$Attendance_{it+1} = \beta_0 + \beta_1 Winner_{it} + \beta_2 Attendance_{it} + \beta_3 MultiEntrant_{it} + \beta Region_i + \beta Time_{it} + \varepsilon_{it} \quad (4.1)$$

Our primary analysis used overall district attendance rates since rates were not available for only school-bus riders. This level of aggregation likely dilutes the treatment effect even though school bus emissions may impact non-riders when buses idle in close proximity to where students play, study, or wait for other transportation. Therefore, we evaluated effect modification of our main association by estimated fractions of children who are likely to ride the buses requested for replacement (i.e. the fraction that would be impacted by the treatment). Since there are no databases of school bus ridership rates at the district level, we estimated this fraction by multiplying the number of buses requested for replacement (1 to 10) by 72, which is the capacity for a standard school bus,[4] and dividing by the total student enrollment for a district at baseline. We evaluated quartiles of this fraction as interaction terms in our model. In secondary analyses we also examined this fraction as a continuous exposure of interest, although in this specification the fraction would be set to 0 for losing entrants. Since bus usage can vary from 1 route per day per bus to 3 or more (e.g., if a bus transported students to an elementary school and then separately to a middle school and/or high school), we additionally considered

[4] https://www.trackschoolbus.com/blog/how-many-seats-are-there-in-a-school-bus/

alternative specifications of the percent of impacted students by varying the number of bus routes per funded bus for entrants in suburbs and cities to two or three.

We further compared the difference in attendance based on the median age difference in the model year of the replacement and original bus using an indicator for winners whose difference in the model year of the replacement and original buses was greater than the median (i.e., >15 years) and a separate indicator for winners whose difference in the model year of the replacement and original buses was at the median or lower (i.e., ≤15 years). We also tested for effect modification by urbanicity since students in rural districts are more likely to ride the school bus more than 30 minutes in each direction (Howley et al. 2001). Effect modification for urbanicity was conducted using an interaction term with the lottery selection status indicator in (4.1). Finally, we tested the sensitivity of our primary results to alternatively modeling the difference in attendance rates before and after the lottery rather than controlling for the prior year's attendance rate to ensure that our findings were robust to our analytic choices.

**Results:**

Across all five lottery years, there were a total of 3,153 entrants to the DERA School Bus Rebate Program. District-level attendance data were not available for Hawaii (N=8), Puerto Rico (N=9), Pennsylvania (N=71), and Washington (N=86) for any years of the analysis. Data were similarly missing for Alabama (N=18), Arizona (N=11), and Montana (N=14) in the 2015-2016 through 2018-2019 school years; New Jersey (N=44) from 2012-2013 and 2013-2014; and North Dakota (N=16) between 2012 and 2013. We further excluded 31 private bus transportation company entrants whose buses are used across multiple school districts and 13 school district consortium entrants who represent

multiple school districts as well as 5 private, 22 non-traditional (e.g., special education and technology centers), and 5 tribal schools whose attendance data was not comparable to other schools. Additionally, we excluded 18 districts with improbable changes in attendance over a one year period. Ultimately, we were able to evaluate associations using attendance data from 87% of the EPA applicants.

Of the 2,731 entrants in our final analytical sample, 2,360 were not selected for funding and 371 were selected for funding (Table 4.2). When comparing the districts in terms of size, demographic make-up, and a proxy for socioeconomic status (i.e., free or reduced price lunch eligibility) at baseline, we found no statistical differences between the winning and losing districts. That said, the districts not selected for funding were slightly larger geographically (284 square miles versus 247 square miles for selected districts), included more schools (15 schools versus 13 schools for selected districts), had more students (9,355 versus 8,369 for selected districts), and had slightly higher rates of students eligible for free or reduced price lunch (48% versus 46% for selected districts) than districts selected for funding. Importantly, however, the baseline attendance rate was very similar between the two sets of applicants, at 94.9% for the losing districts and 94.8% for the winning districts.

In our primary analysis, we found that districts that were selected for the DERA School Bus Rebate funding had a 0.053 percentage point (pp) higher attendance rate in the year after the lottery (95% CI: -0.023, 0.128) as compared to districts that were not selected for funding (Table 4.3). For an average size district of 10,000 students, this translates to approximately 5 additional students attending school each day in districts that won funding in the lottery as compared to non-winning districts. We also observed

evidence of greater impacts of winning the lottery with increasing levels of ridership on the buses requested for replacement. Effect modification results by quartiles of expected ridership on buses (Q1: 0.05 – 3.8%; Q2: 3.8 – 8.3%; Q3: 8.3 – 16.2%; Q4: 16.3 – 100%) requested for replacement showed a near dose-response relationship with attendance, with impacts reaching as high as a 0.12 pp (95% CI: -0.068, 0.307) improvement in attendance after winning the lottery in the highest estimated ridership group. This is consistent with our secondary analysis, which showed that a 1 pp increase in the fraction of students impacted by the new buses was associated with a 0.004 pp (95% CI: -0.0005, 0.009) increase in the district's attendance rate (Table 4.3). Results were nearly identical for the alternative specifications of our individual-level estimate, which used different assumptions of the number of routes driven by replaced buses according to a district's urbanicity level (results not shown).

In other analyses, we observed that changes in attendance were largely driven by the replacement of older buses. Applicants that replaced buses more than 15 years old had a statistically significant 0.095 pp improvement in attendance (95% CI: 0.005, 0.184) as compared to districts who were not selected for funding. The results were nearly null for the set of applicants that replaced buses less than 15 years old (-0.016 pp; 95% CI: -0.15, 0.118) (Table 4.3). Similarly, results by urbanicity classification showed the strongest impacts in districts located in areas designated as towns (0.128 pp; 95% CI: -0.025, 0.28), and near null results in rural (0.015 pp; 95% CI: -0.108, 0.138) and city (0.014 pp; 95% CI: -0.406, 0.434) designated districts.

When we tested the sensitivity of our primary analysis to using the change in attendance rate as the dependent variable rather than the attendance rate after the lottery,

adjusted for attendance before the lottery, we found a slightly larger funding effect of 0.068 pp (95% CI: -0.022, 0.159).

**Discussion:**

In this national analysis of the impacts of the US EPA's DERA School Bus Rebate Program, we found suggestive evidence that receiving rebate funds to replace or retrofit older, more polluting school buses with newer, cleaner buses was associated with an increase in school district attendance rates. Districts that were selected for school bus rebate funding had a 0.053 pp higher attendance rate in the year after the lottery (95% CI: -0.023, 0.128) as compared to districts that were not selected for funding. In districts that won funding, this translates to approximately 5 additional students attending school each day in an average size district of 10,000 students. The attendance effects were strongest when larger proportions of students were impacted by the program and when the oldest, most polluting buses were replaced, with applicants who replaced buses more than 15 years old having a 0.095 pp improvement in attendance (95% CI: 0.005, 0.184) compared to districts who were not selected for funding

Our findings are noteworthy given that nearly 8 million students (16%) missed more than 15 days of school in the 2015-2016 school year (Chang et al. 2018) and that school attendance has repeatedly been associated with student achievement (Aucejo & Romano 2016; Gershenson et al. 2015; Gottfried 2010; Gottfried 2011; Gottfried 2014; Humm Patnode et al. 2018). Excessive school absenteeism has also been linked to substance use, grade retention, and school dropout (Henry & Huizinga 2007; Kearney 2008; Rocque et al. 2016), the latter of which can have economic and health consequences in adulthood (Cutler & Lleras-Muney 2008). This work suggests that the

DERA School Bus Rebate Program has had an important impact on children's health in our nation. Importantly, the impacts of this program are likely to continue since approximately 25 million children ride buses to school each day in the US (Snyder & Dillow 2011) and the average US school bus fleet decommissions buses after 16 years (McMahon 2017). Given our findings of greater improvements in absenteeism with replacement of older buses, this program is furthermore likely to be of the greatest significance in lower income areas since school districts likely have fewer resources available to replace or retrofit older buses in the absence of programs such as this one.

This work has direct relevance to public policy as it is the first to evaluate the effectiveness of the national EPA DERA School Bus Rebate Program. Although the program was designed to reduce diesel emissions from school buses given the known health impacts of diesel exhaust, its effectiveness has yet to be evaluated. This study is also unique in that it leveraged the randomized allotment of clean bus funding to school districts to estimate the causal impact on school districts of switching to cleaner school buses. While the existing literature has found similar results to ours and has provided some evidence for causality of these associations, none of the technologies studied by previous research were randomly assigned. This raises the possibility that the school districts that adopted cleaner buses or times when cleaner school buses were used are fundamentally different from districts or times without cleaner buses due to some other characteristics that are important to health and student attendance. Our design, however, reduces concerns of confounding by measured or unmeasured school district-related characteristics.

Interestingly, our results are consistent with what has been seen in the one cohort study that has evaluated the impacts of bus retrofits on the health and school attendance of individual riders. That intensive examination of 275 students demonstrated that when children were riding newer, cleaner buses they were less likely to experience inflammation in their lungs and miss school than when they were riding older, dirtier school buses (Adar et al. 2015). They also found that individual students experienced a 5 to 15% reduction in the risk of absenteeism after switching to buses with cleaner technologies (Adar et al. 2015).

Our findings are also consistent with two additional observational studies that have evaluated the benefits of cleaner school buses on the state level using ecological designs. Beatty & Shimshack (2011) evaluated the impact of voluntary school bus retrofits using a difference-in-difference analysis approach of community hospitalization records in Washington State. While they did not study the impact of the retrofits on attendance, they reported that school bus retrofits were associated with reduced community-wide hospitalizations for bronchitis, asthma, and pneumonia in at-risk populations, all of which can lead to missed days of school. A second study showed that children in Georgia school districts that retrofitted their school buses had larger increases in aerobic capacity on state-required physical activity tests and significant gains on standardized testing for academic achievement as compared to other districts (Austin et al. 2019). They also estimated a 0.15 pp increase in school district attendance if all buses in a fleet fully adopted clean air technologies, though their findings were not distinguishable from no association. This translates to a 0.03 pp increase in attendance for

a district that retrofitted 19% of its fleet, which was the average percent of buses in a fleet that were retrofitted in their study.

One other, non-published, study has looked at national level impacts of clean school buses based on a different and separate, EPA competitive grant program, which also funds school bus retrofits and replacements (Austin 2019). In contrast to the Rebate program studied here, selection for that funding is not awarded randomly and among other evaluation criteria, applicants from areas with poor air quality are given preference. In that work, the author reported very small improvements in county level air quality and similar gains on standardized testing for academic achievement as reported in Austin et al. (2019). Attendance was not studied.

In spite of the notable improvements in attendance observed in this work, our results are for the school district level and thus include both bus riders and non-bus riders. As a result, our findings likely underestimate the true impacts to students who were directly affected by the change to new, cleaner buses. To partially address this, we attempted to estimate the impacts of the EPA's DERA School Bus Rebate Program based on the fraction of individuals riding the replaced buses and found that every 1 pp increase in the fraction of students riding the new buses was associated with a 0.004 pp (95% CI: -0.0005, 0.009) increase in the district's attendance rate. We also evaluated effect modification of our results by bus ridership. The near dose-response relationship we observed across quartiles of estimated bus ridership levels on the buses requested for replacement suggests, logically, that the larger the fraction of students that switch to riding a cleaner school bus, the greater the attendance improvement. The districts with the highest levels of estimated bus ridership on the buses requested for replacement had

an order of magnitude greater increase in attendance compared to districts in the lowest quartile of estimated bus ridership (0.12 pp (95% CI: -0.068, 0.307) vs. 0.01 pp (95% CI: -0.114, 0.135)). For an average size district of 10,000 students, this translates to approximately 12 additional students attending school each day in districts with high rates of ridership on new clean buses compared to only 1 additional student attending school each day in districts with low rates of ridership on new clean buses.

Like our findings regarding the rates of bus ridership, our effect modification results by the improvement in model years also provide support for our findings and strengthen our conclusions. We found that applicants who replaced buses more than 15 years old had a 0.095 pp improvement in attendance (95% CI: 0.005, 0.184) compared to districts who were not selected for funding, while the set of applicants that replaced buses less than 15 years old had a negligible impact (-0.016; 95% CI: -0.15, 0.118) (Table 4.3). Model years of the replaced buses ranged from 1986 to 2001 (average of 1996) for districts who replaced buses more than 15 years old and from 1997 to 2006 (average of 2002) for districts who replaced buses less than 15 years old. For context, US EPA exhaust emissions standards for PM from buses had an approximate six-fold improvement for 1991-1997 model year buses compared to 1990 and older model year buses, with smaller improvements beginning in 1998 and 2004 (US EPA 2016b). Our results are therefore unsurprising given that only entrants with the largest model year improvement replaced buses of model year 1997 and older, which had the weakest emissions standards. These findings suggest that as emissions standards strengthen and the dirtiest buses are retired from use, the overall attendance impacts of this program would decline if there is not further improvement in clean bus technologies.

As with all studies, our work has some limitations. The first of which is the relatively small number of entrants who were ultimately awarded funding, which reduced power for this analysis. We had previously intended to include an additional year of the EPA program in our analysis (i.e., the 2018 lottery). However, the 'after' year for that lottery was the 2019-2020 school year which included the global COVID-19 pandemic. Given the impacts of the pandemic on public schooling, we concluded that including this year of attendance data in our analysis would be too disruptive to our results and therefore excluded it. Similarly, there was some unavailability of attendance data for some states in some years of the analysis that decreased our analytical sample size by approximately 10 percent. While this likely reduced our study's power, it should not bias the results given the randomized nature of lottery selection status. Another limitation is that there were 29 districts who were selected for funding but ultimately did not purchase a clean bus. Per conversations with EPA, that occurred when an applicant was not able to acquire the matching funds needed to purchase a clean replacement bus. Consistent with our decision to use an intention-to-treat rather than an as-treated approach, these applicants were treated as lottery funding winners in our analysis. Similarly, districts that were not selected for funding ultimately could have replaced or retrofitted buses outside of this program, yet they were treated as having lost the lottery in our analysis. These specifications retain the benefits of randomization but have the result that we have estimated a lower bound for the true association between being selected to receive rebate funding for clean buses and school district attendance rates.

**Conclusion:**

Overall, we find suggestive evidence that the EPA's DERA School Bus Rebate Program has improved student attendance, especially in the districts that removed the oldest buses and those with high levels of bus ridership on the impacted buses. Given the importance of attendance to student educational success, our results suggest that this program is both successful at increasing the pace at which older, highly polluting buses are removed from use and that those actions have positive impacts on student attendance levels.

**Table 4.1 Summary of the EPA DERA School Bus Rebate Program, by year.**

| Lottery Year | Diesel Bus Engines to be Replaced | Replacement Bus Engines | Number of Applications Allowed | Number of Buses Eligible per Application | Rebate Amount per Bus | Number of Lottery Winners | Number of Lottery Losers | Total Funding Awarded |
|---|---|---|---|---|---|---|---|---|
| 2012 | 1994-2003 | 2012 or later | 1 | 5 | $20K - $30K | 36 | 973 | $1.88 million |
| 2014 | ≤ 2006 | 2014 or later | 1 | 5 | $15K - $25K | 73 | 474 | $3.94 million |
| 2015 | ≤ 2006 | 2015 or later | 1 (if fleet <=100 buses)<br>2 (if fleet >100 buses) | 10 | $15K - $25K | 86 | 451 | $6.04 million |
| 2016 | ≤ 2006 | 2016 or later | 1 (if fleet <=100 buses)<br>2 (if fleet >100 buses) | 10 | $15K - $25K | 92 | 422 | $7.24 million |
| 2017 | ≤ 2006 | 2017 or later | 1 (if fleet <=100 buses)<br>2 (if fleet >100 buses) | 10 | $15K - $20K | 143 | 403 | $8.20 million |
| | | | | | Total: | 430 | 2,723 | $27.29 million |

**Table 4.2 Characteristics of school district entrants[a] at baseline, by lottery status.**

| Charasteristic | 'Losers' (N=2,360) | 'Winners' (N=371) | p-value |
|---|---|---|---|
| Schools in District | 15 (40) | 13 (29) | 0.26 |
| Students in District | 9,355 (29,018) | 8,369 (22,591) | 0.45 |
| District Students, White (%) | 73.1 (25.6) | 74 (24) | 0.53 |
| District Students Eligible for Free Lunch (%) | 40.6 (20.2) | 38.9 (19.2) | 0.13 |
| District Students Eligible for Reduced Price Lunch (%) | 7.9 (4.4) | 7.7 (3.7) | 0.40 |
| District Students Eligible for Free or Reduced Price Lunch (%) | 48.2 (20.4) | 46.3 (19.6) | 0.10 |
| Buses requested for Replacement/Retrofit | 3.6 (2.7) | 3.7 (3.1) | 0.60 |
| Funding Requested for Replacement/Retrofit ($) | 77,401 (58,280) | 73,491 (61,940) | 0.23 |
| District Attendance Rate (%) | 94.93 (1.37) | 94.82 (1.34) | 0.16 |
| District Land Area (square miles) | 284 (695) | 247 (456) | 0.18 |
| District Urbanicity - no. (%) | | | |
| Rural | 1,016 (43.1) | 169 (45.6) | 0.35 |
| Town | 528 (22.4) | 71 (19.1) | |
| Suburb | 585 (24.8) | 100 (27) | |
| City | 231 (9.8) | 31 (8.4) | |

[a] For entrants ultimately included in the analytical sample.

**Table 4.3 Impact of clean buses on attendance overall and by ridership and difference in the replaced and replacement bus model years.**

| Model | Parameter Estimate | 95% CI | *p*-Value |
|---|---|---|---|
| District-Level Impact[a] | 0.053 | -0.023, 0.128 | 0.17 |
| Percent Ridership on Buses Requested for Replacement[b] | | | |
| Quartile 1: (0.05% - 3.8%) | 0.016 | -0.112, 0.144 | 0.82 |
| Quartile 2: (3.8% - 8.3%) | 0.014 | -0.085, 0.113 | |
| Quartile 3: (8.3% - 16.2%) | 0.049 | -0.098, 0.197 | |
| Quartile 4: (16.3% - 100%) | 0.120 | -0.068, 0.307 | |
| Individual-Level Impact[c] | 0.004 | -0.0005, 0.009 | 0.08 |
| Years of Improvement in Bus Model Year | | | |
| <= 15 years | -0.016 | -0.15, 0.118 | 0.82 |
| > 15 years | 0.095 | 0.005, 0.184 | 0.04 |

[a] Dependent variable is the attendance rate in the year after the lottery. Model is adjusted for attendance rate in the year before the lottery, as well as EPA Region, lottery year, and an indicator for having more than one application in a given lottery year.
[b] p-value for Bus Ridership on Requested Buses is from the interaction term.
[c] Dependent variable is the attendance rate in the year after the lottery. Independent variable of interest is the estimated percent of students who ride the replaced buses, assuming all replaced buses drive 1 route.

## Appendix:

### Table 4.A1 EPA DERA School Bus Rebate Program details, by year.

| Lottery Year | Program Details | Funding by Vehicle Class | Retrofit Details |
|---|---|---|---|
| 2012 | Replacements only. New buses powered by a certified 2012 or newer model year engine, or operate solely on electricity. Eligible replacement school buses may operate on conventional diesel (ULSD), battery or hybrid drivetrains, or alternative fuels | Class 3-5: $20K<br>Class 6-7: $25K<br>Class 8: $30K | |
| 2014 | Replacements only. New buses powered by a certified 2014 or newer model year engine, or operate solely on electricity. Eligible replacement school buses may operate on conventional diesel (ULSD), battery or hybrid drive trains, or alternative fuels | Class 3-5: $15K<br>Class 6-7: $20K<br>Class 8: $25K | |
| 2015 | Replacements and Retrofits. New buses powered by a certified 2015 or newer model year engine, or operate solely on electricity. Eligible replacement school buses may operate on conventional diesel (ULSD), battery or hybrid drive trains, or alternative fuels | Class 3-5: $15K<br>Class 6-7: $20K<br>Class 8: $25K | Retrofits: up to $3K for DOC+CCV (per bus) |
| 2016 | Replacements and Retrofits. New buses powered by a certified 2016 or newer model year engine, or operate solely on electricity. Eligible replacement school buses may operate on conventional diesel (ULSD), gasoline, battery or hybrid drivetrains, or alternative fuels | Class 3-5: $15K<br>Class 6-7: $20K<br>Class 8: $25K | Retrofits: up to $4K for DOC+CCV, $6K for DOC+CCV+FOH (all per bus) |
| 2017 | Replacements and Retrofits. New buses powered by a certified 2017 or newer model year engine, or operate solely on electricity. Eligible replacement school buses may operate on conventional diesel (ULSD), gasoline, battery or hybrid drivetrains, or alternative fuels. | Class 3-5: $15K<br>Class 6-8: $20K | Retrofits: up to $3K for DOC, $4Kfor DOC+CCV, $5K for DOC+FOH, $6K for DOC+CCV+FOH (all per bus) |

**Table 4.A2 Number of entrants receiving EPA DERA School Bus Rebate Program funding, by source of funding and year.[a]**

| | Lottery Year | | | | | |
|---|---|---|---|---|---|---|
| Awarding Entity | 2012 | 2014 | 2015 | 2016 | 2017 | Total |
| EPA Headquarters | 28 (100%) | 53 (75%) | 44 (62%) | 58 (71%) | 92 (67%) | 275 |
| EPA Region 1 | 0 (0%) | 3 (4%) | 9 (13%) | 3 (4%) | 4 (3%) | 19 |
| EPA Region 2 | 0 (0%) | 0 (0%) | 10 (14%) | 11 (13%) | 6 (4%) | 27 |
| EPA Region 3 | 0 (0%) | 0 (0%) | 0 (0%) | 1 (1%) | 0 (0%) | 1 |
| EPA Region 4 | 0 (0%) | 0 (0%) | 0 (0%) | 6 (7%) | 11 (8%) | 17 |
| EPA Region 5 | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) | 10 (7%) | 10 |
| EPA Region 6 | 0 (0%) | 2 (3%) | 6 (8%) | 1 (1%) | 0 (0%) | 9 |
| EPA Region 7 | 0 (0%) | 13 (18%) | 1 (1%) | 2 (2%) | 14 (10%) | 30 |
| EPA Region 8 | 0 (0%) | 0 (0%) | 1 (1%) | 0 (0%) | 0 (0%) | 1 |
| EPA Region 9 | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) | 0 |
| EPA Region 10 | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) | 0 |
| Total: | 28 | 71 | 71 | 82 | 137 | 389 |

[a] This table only summarizes the entrants who were ultimately awarded funding (i.e., it does not include the entrants (N=41) who were selected to receive funding but ultimately did not).

**References:**


Adar, S.D., Davey, M., Sullivan, J.R., Compher, M., Szpiro, A., Liu, L.J.S., 2008. Predicting airborne particle levels aboard Washington State school buses. Atmos Environ. 42, 7590-7599.

Adar, S.D., D'Souza, J., Sheppard, L., Kaufman, J.D., Hallstrand, T.S., Davey, M.E., Sullivan, J.R., Jahnke, J., Koenig, J., Larson, T.V., Liu, L.J.S., 2015. Adopting Clean Fuels and Technologies on School Buses: Pollution and Health Impacts in Children. Am J Respir Crit Care Med. 191, 1413-1421.

Akinbami, L.J., Moorman, J.E., Liu, X., 2011. Asthma prevalence, health care use, and mortality: United States, 2005-2009. National health statistics reports; no 32. Hyattsville, MD: National Center for Health Statistics.

Aucejo, E.M., Romano, T.F., 2016. Assessing the effect of school days and absences on test score performance. Econ Educ Rev. 55, 70-87.

Austin, W., Heutel, G., Kreisman, D., 2019. School bus emissions, student health and academic performance. Econ Educ Rev. 70, 109-126.

Austin, W., 2019. School Bus Diesel Retrofits, Air Quality, and Academic Performance: National Evidence Using Satellite Data. Unpublished. Available at: http://wes-austin.com/files/Bus_Retrofits_National_102119.pdf.

Beatty, T.K.M., Shimshack, J.P., 2011. School buses, diesel emissions, and respiratory health. J Health Econ. 30, 987-999.

Behrentz, E., Sabin, L.D., Winer, A.M., Fitz, D.R., Pankratz, D.V., Colome, S.D., Fruin, S.A., 2005. Relative Importance of School Bus-Related Microenvironments to Children's Pollutant Exposure. J Air Waste Manag Assoc. 55, 1418-1430.

CDC, 2008. 2008 National Health Interview Survey (NHIS) Data. Current Asthma Population Estimates (Table 3-1).

Chang, H.N., Bauer, L., Byrnes, V., 2018. Data maters: Using chronic absence to accelerate action for student success. Attendance Works and Everyone Graduates Center.

Currie, J., Hanushek, E.A., Kahn, E.M., Neidell, M., Rivkin, S.G., 2009. Does Pollution Increase School Absences? Rev Econ Stat. 91, 682-694.

Cutler, D., Lleras-Muney, A., 2008. Education and Health: Evaluating Theories and Evidence. Making Americans Healthier: Social and Economic Policy as Health Policy, edited by J House, R Schoeni, G Kaplan, and H Pollack. New York: Russell Sage Foundation.

Deaton, A., Cartwright, N., 2018. Understanding and misunderstanding randomized controlled trials. Soc Sci Med. 210, 2-21.

Gershenson, S., Jacknowitz, A., Brannegan, A., 2017. Are Student Absences Worth the Worry in U.S. Primary Schools? Educ Finance Policy. 12, 137-165.

Gottfried, M.A., 2010. Evaluating the Relationship Between Student Attendance and Achievement in Urban Elementary and Middle Schools: An Instrumental Variables Approach. Am Educ Res J. 47, 434-465.

Gottfried, M.A., 2011. The Detrimental Effects of Missing School: Evidence from Urban Siblings. Am J Educ. 117, 147-182.

Gottfried, M.A., 2014. Chronic absenteeism and its effects on students' academic and socioemotional outcomes. J. Educ. Stud. Placed Risk. 19, 53-75.

Guryan, J., Christenson, S., Cureton, A., Lai, I., Ludwig, J., Schwarz, C., Shirey, E., Turner, M.C., 2020. The Effect of Mentoring on School Attendance and Academic Outcomes: A Randomized Evaluation of the Check & Connect Program. NBER Working Paper No. 27661.

HEI Panel on the Health Effects of Traffic-Related Air Pollution, 2010. Traffic-Related Air Pollution: A Critical Review of the Literature on Emissions, Exposure, and Health Effects.

Hammond, D.M., Lalor, M.M., Jones, S.L., 2007. In-Vehicle Measurement of Particle Number Concentrations on School Buses Equipped with Diesel Retrofits. Water Air Soil Pollut. 179, 217-225.

Henry, K.L., Huizinga, D.H., 2007. Truancy's Effect on the Onset of Drug Use among Urban Adolescents Placed at Risk. J Adolesc Health. 40, 358.e9-358.e17.

Howley, A.A., Howley, A.A., Shamblen, S., 2001. Riding the School Bus: A Comparison of the Rural and Suburban Experience in Five States. J Res Rural Educ. 17, 41-63.

Humm Patnode, A., Gibbons, K., Edmunds, R. R., 2018. Attendance and Chronic Absenteeism: Literature Review. Saint Paul, MN: University of Minnesota, College of Education and Human Development, Center for Applied Research and Educational Improvement.

Kearney, C.A., 2008. School absenteeism and school refusal behavior in youth: A contemporary review. Clin Psychol Rev. 28, 451-471.

McMahon, T., March 2017. Maintenance Survey. School Bus Fleet. 32-37.

Nichols, J.D., 2003. Prediction Indicators for Students Failing the State of Indiana High School Graduation Exam. Prev Sch Fail. 47, 112-120.

Noel, L., McCormack, R., 2014. A cost benefit analysis of a V2G-capable electric school bus compared to a traditional diesel school bus. Appl Energy. 126, 246-255.

Ransom, M.R., Pope III, A., 1992. Elementary School Absences and $PM_{10}$ Pollution in Utah Valley. Environ Res. 58, 204-219.

Rocque, M., Jennings, W.G., Piquero, A.R., Ozkan, T., Farrington, D.P., 2017. The Importance of School Attendance: Findings From the Cambridge Study in Delinquent Development on the Life-Course Effects of Truancy. Crime Delinquency. 63, 592-612.

Rogers, T., Feller, A., 2018. Reducing Student Absences at Scale by Targeting Parents' Misbeliefs. Nat Hum Behav. 2, 335-342.

Silverstein, M.D., Mair, J.E., Katusic, S.K., Wollan, P.C., O'connell, E.J., Yunginger, J.W., 2001. School attendance and school performance: a population-based study of children with asthma. J Pediatr. 139, 278-283.

Snyder, T.D., Dillow, S.A., 2011. Digest of Education Statistics 2010 (NCES 2011-015), Table 184. National Center for Education Statistics, Institute of Education Sciences, U.S. Department of Education. Washington, DC.

Transportation Research Board, 2002. TRB Special Report 269: The relative risks of school travel: a national perspective and guidance for local community risk assessment.

US ED, 2009. State Regulation of Private Schools. Office of Innovation and Improvement, Washington DC.

US EPA, 2003. Technical Highlights: Questions and Answers on Using a Diesel Particulate Matter Filter in Heavy-Duty Trucks and Buses. EPA420-F-03-017. EPA Office of Transportation and Air Quality.

US EPA, 2012, 2014-2020. National Clean Diesel Rebate Program: 2012,2014-2020 School Bus Replacement Funding Opportunity Program Guides. Office of Transportation and Air Quality.

Vickers, A.J., 2001. The use of percentage change from baseline as an outcome in a controlled trial is statistically inefficient: a simulation study. BMC Med Res Methodol. 1, 6-9.

Vickers, A.J., Altman, D.G., 2001. Statistics Notes: Analysing controlled trials with baseline and follow up measurements. Br Med J. 323, 1123-1124.

# CHAPTER 5 :

# Discussion

## Summary and Implications of Main Findings:

The collective aim of this dissertation was to contribute to the science needed by the EPA to support effective air pollution regulations, policies, and programs designed to reduce exposures and protect health. From an exposure assessment perspective, it provides evidence that the use of satellite data paired with advanced spatiotemporal prediction modeling techniques can successfully generate long-term average spatially resolved $PM_{10-2.5}$ exposure estimates, even where no monitoring stations exist. From an environmental epidemiologic standpoint, it highlights the strengths and limitations of using these satellite-based $PM_{10-2.5}$ predictions to study the health impacts of $PM_{10-2.5}$ exposure to inform the science used to set air pollution regulations. Additionally, from a policy perspective, it provides evidence that a source-specific emissions reduction program, such as the EPA's DERA School Bus Rebate Program, can have measurable impacts based on the suggestive evidence we saw of the program's role in improving school district attendance levels.

In Chapter 2, we newly used AOD measured on the NASA Terra satellite to calculate daily 1 $km^2$ spatially resolved $PM_{10-2.5}$ predictions in six US urban areas. To do this, we used advanced spatiotemporal multi-stage statistical modeling approaches which have previously been used to predict daily $PM_{2.5}$ and, separately, $PM_{10}$, at the same

spatial resolution (Kloog et al. 2015; Madrigano et al. 2013; McGuinn et al. 2016; Nordio et al. 2013; Stafoggia et al. 2017; Stafoggia et al. 2019; Shtein et al. 2018). However, this approach had not previously been used to predict $PM_{10-2.5}$, which has proven more difficult to study epidemiologically given the limited availability of $PM_{10-2.5}$ measurements, especially in the US (Adar et al. 2014). Overall, our final predictions were able to capture the long-term spatial patterns of $PM_{10-2.5}$ very well in four of our study areas, well in one area, and modestly in one area. In all six study areas, our predictions had substantially better spatial performance than both a simple nearest-monitor approach and an inverse distance weighting approach, which are both alternative methods used in the environmental epidemiology literature to assign air pollution exposure. Given that urban areas, especially, often have considerable spatial variability in $PM_{10-2.5}$ concentrations, our results show the potential benefits of using spatiotemporal modeling methods with satellite-based AOD data to predict long-term $PM_{10-2.5}$ levels for use in epidemiological health studies.

Our work in Chapter 2 add to the literature as one of only a handful of exposure models to predict $PM_{10-2.5}$ concentrations for use in long-term air pollution epidemiological studies. This is particularly true for the US where – to our knowledge – only two groups have generated $PM_{10-2.5}$ exposure predictions that have been used in health studies (US EPA, 2019). Notably, neither has taken advantage of the additional information AOD provides when conducting $PM_{10-2.5}$ spatiotemporal pollution prediction modeling. In the first, members of the MESA Coarse study used intensive $PM_{10-2.5}$ monitoring campaigns to predict spatial patterns of $PM_{10-2.5}$ using land use regression methods in three of the six cities studied here (Zhang et al. 2014). While model

performance using the intensive sampling data was largely better than these new AOD-models, they were not substantially or consistently so. Given that monitoring field studies are very expensive to conduct and cannot capture the temporal variability in $PM_{10-2.5}$ concentrations, our AOD-informed approach offers important benefits over predictions derived from spatially intensive ground monitoring. In the second study to have predicted $PM_{10-2.5}$ exposure in the US, researchers used generalized additive mixed models with geographic, meteorological, and visibility data to predict $PM_{2.5}$ and $PM_{10}$ concentrations for the whole conterminous US at the monthly scale based on EPA monitoring data (Yanosky et al. 2008; Yanosky et al. 2009; Yanosky et al. 2014). While they had good overall performance, their results varied across geographical regions. Importantly, Yanosky et al. (2014) hypothesized that the inclusion of AOD measures in spatiotemporal models might improve model predictive accuracy, especially in areas distant from air quality monitors.

The poor prediction performance we observed in one of our study areas highlights a key challenge of predicting concentrations for localized areas as we have done. Unlike many other studies that have predicted PM levels across larger regions or nations, our study focused on smaller metropolitan areas. While predicting over smaller areas has the potential to increase accuracy if there is effect modification of predictors by place, it can come at the cost of lost variation in exposures. This lack of variation in measured $PM_{10-2.5}$ in our city with poor prediction performance surely contributed to our inability to model the spatial variability in $PM_{10-2.5}$ levels well.

In Chapter 3, we used the $PM_{10-2.5}$ exposure predictions generated in Chapter 2 to study cross-sectional associations between long-term average $PM_{10-2.5}$ exposure and six

biomarkers for inflammation and coagulation within the full MESA cohort. We found, counter to hypothesis, that higher levels of $PM_{10-2.5}$ were associated with lower levels of the inflammation and coagulation biomarkers. We hypothesized that these findings could be due to the specific $PM_{10-2.5}$ components that made up $PM_{10-2.5}$ in our study areas since an earlier study that was able to measure associations with individual components of $PM_{10-2.5}$ mass found varying results by particle component. For example, in Adar et al. (2015), endotoxin – which is found in bacterial cell membranes – was most strongly associated with inflammation and, importantly, was inversely associated with $PM_{10-2.5}$ mass. In contrast, copper – which originates from traffic – was most strongly associated with coagulation (Adar et al. 2015). This might suggest that differences in the relationship between $PM_{10-2.5}$ and inflammation could be due to aspects of nature; however, adjustment for vegetation did not verify this line of reasoning. Given the $PM_{10-2.5}$ component-specific differences that have been observed between $PM_{10-2.5}$ exposure and inflammation and coagulation markers, it is therefore unsurprising that our associations of $PM_{10-2.5}$ *mass* with inflammation and coagulation markers would differ from previous work, since the component make-up of $PM_{10-2.5}$ can differ by location.

This work expands the limited literature that has evaluated the long-term inflammation and coagulation impacts of larger particles such as $PM_{10-2.5}$, although the results were ultimately confusing and/or inconclusive. Importantly, inflammation and coagulation are considered plausible biological mechanisms for the observed associations between adverse health effects and PM of all sizes yet only a few studies evaluating the long-term inflammation and coagulation impacts from larger particles such as $PM_{10-2.5}$. This gap is noteworthy since the US EPA has determined that there is suggestive

evidence of an association between long-term $PM_{10-2.5}$ and adverse cardiovascular events but notes that there are gaps in the proposed pathways that might link these.

The US EPA has many programs and policies in place that aim to reduce emissions from diesel engines, given the large contribution diesel engine emissions make to total US PM emissions and the known health impacts from the inhalation of diesel engine exhaust. In Chapter 4 we evaluated the attendance impacts of one of these such programs: the EPA's DERA School Bus Rebate Program, which was designed to hasten the transition of the fleet to newer, cleaner vehicles. To do so, we took advantage of the EPA's randomized allocation of rebate funding for school bus replacements and retrofits to causally assess the impacts of the EPA's 2012-2017 DERA School Bus Rebate Programs on school district attendance rates. Using classical intent-to-treat analyses for randomized controlled trials to evaluate the school district attendance impacts of being selected for clean bus rebate funding, we found suggestive evidence that the EPA's DERA School Bus Rebate Program improved student attendance, especially in districts that removed the oldest buses and those with high levels of ridership on the applicant buses.

An important contribution Chapter 4 is that it leveraged the randomized allotment of clean bus funding to school districts to estimate the causal impact on school districts of switching to cleaner school buses. This design reduces concerns of confounding by measured or unmeasured school district-related characteristics. Interestingly, our results are consistent with what has been seen in the few observational studies on this topic, including one cohort study, which is the only study to date that has evaluated the impacts of bus retrofits on the health and school attendance of individual riders. Given the

importance of attendance to student educational success, our results suggest that this EPA program is both successful at increasing the pace at which older, highly polluting buses are removed from use and that those actions have positive impacts on student attendance levels. Given the many competing priorities for federal funding, our findings on the attendance impacts of the EPA's DERA School Bus Rebate Program can help inform decision makers when deciding whether to continue funding this voluntary emissions reduction program.

Collectively, the results of this dissertation contribute to the science needed by the EPA to support effective air pollution regulations and policies designed to reduce exposures and protect health.

**Strengths and Limitations:**

The work shown in this dissertation has many strengths. First and foremost, we newly used advanced spatiotemporal multi-stage statistical modeling approaches along with AOD data to predict $PM_{10-2.5}$ concentrations in six US urban areas. One of the primary reasons for the paucity of epidemiologic research on the health effects of $PM_{10-2.5}$ exposure is the limited availability of measurement data with which to estimate $PM_{10-2.5}$ exposure. By successfully showing the ability of this approach to predict long-term $PM_{10-2.5}$ concentrations in areas with a sufficient amount of and variability in measured data with which to build an exposure model, we have provided a proof of concept for other researchers to use similar approaches to estimate $PM_{10-2.5}$ concentrations for use in air pollution epidemiology studies. This is important given the limited, and often inconclusive, nature of the $PM_{10-2.5}$ health literature.

Another strength was our ability to evaluate the inflammation and coagulation impacts of $PM_{10-2.5}$ exposure within a large, prospective cohort study. This work extends the only other paper on $PM_{10-2.5}$ and inflammation in the United States by using our satellite-based exposure estimates to investigate the full MESA cohort, which was not previously possible given the lack of $PM_{10-2.5}$ estimates for all six cities. Also, by conducting Aim 2 within the MESA cohort, we were able to take advantage of the rich data available for the participants for confounder adjustment and evaluation of effect modification including individual-level exposure predictions for the co-pollutants of $PM_{2.5}$ and $NO_x$.

In Aim 3, we importantly were able to leverage the randomized method by which clean bus funding was allocated in order to estimate the causal impact of the EPA's DERA School Bus Rebate Program on attendance, thereby reducing concerns of confounding by measured or unmeasured school district-related characteristics. While the existing literature has found similar results and has provided some evidence for causality of these associations, none of the technologies studied by previous research were randomly assigned. Our use of a randomized design limits the possibility that the school districts that adopted cleaner buses or times when cleaner school buses were used are fundamentally different from districts or times without cleaner buses due to some other characteristics that are important to health and student attendance.

In spite of the many strengths of this dissertation, there are some limitations. In terms of Aim 1, unlike many other studies that have predicted PM levels across larger regions or nations, our study focused on smaller metropolitan areas. While predicting over smaller areas has the potential to increase accuracy if there is effect modification of

predictors by place, it can come at the cost of lost variation in exposures. In Aim 1, for example, the study area where we had the worst $PM_{10-2.5}$ predictive performance was the study area with a very small range in measured long-term average $PM_{10-2.5}$ levels; this surely contributed to our inability to model the spatial variability in $PM_{10-2.5}$ levels in that area well.

A limitation of our work in Aim 2 is that the satellite AOD data was first collected beginning in 2000. The consequence of this to our work is that there is a temporal mismatch in Aim 2 between our $PM_{10-2.5}$ exposure estimates and the exposure time of interest before the baseline exam given that we used 2001 $PM_{10-2.5}$ concentrations to represent exposure from approximately 1996-2002 (depending on the date of a participant's baseline exam). Another limitation is that our analysis in Aim 2 was cross-sectional, which is especially noteworthy given that previous cross-sectional studies on the inflammatory impacts of PM have not provided evidence for an association while longitudinal analyses have. Also, although conducting our Aim 2 analysis within the MESA cohort enabled us to use the rich set of covariate data that has been collected on MESA participants, using the MESA cohort means our results may not be generalizable to the whole population since MESA included only participants aged 45 and older at the time of recruitment.

A limitation in Aim 3 is the relatively small number of entrants who were ultimately awarded clean bus replacement rebate funding from the EPA, which reduced power for this analysis. We had previously intended to include an additional year of the EPA program in our analysis (i.e., the 2018 lottery). However, the 'after' year for that lottery was the 2019-2020 school year which included the global COVID-19 pandemic.

Given the impacts of the pandemic on public schooling, we concluded that including this year of attendance data in our analysis would be too disruptive to our results and therefore excluded it. Similarly, there was some unavailability of attendance data for some states in some years of the analysis that decreased our analytical sample size by approximately 10 percent. While this likely reduced our study's power, it should not bias the results given the randomized nature of lottery selection status.

**Future Directions:**

For each of my aims there are several directions to pursue for future research. In terms of Aim 1, future work might focus on replicating this spatiotemporal modeling approach with AOD data to other locations – specifically to areas with a sufficient amount of and variability in measured $PM_{10}$ and $PM_{2.5}$ data. Another line of inquiry that could be examined relates to our finding that the locations of many EPA monitoring sites can differ in terms of geography, land use, urbanicity, and demography from the locations where some populations reside. This can become an important consideration if the predictions at the locations of interest necessarily rely on extrapolating beyond the domain space of the variables that are used to build the model. In the spirit of the primary goal of this dissertation – to contribute to the science needed by the EPA to support effective air pollution regulations and policies designed to reduce exposures and protect health – we plan as a next step to compare and contrast the locations of monitoring sites to the areas where different populations live in terms of factors such as geography, land use, urbanicity, and demography. This could inform the EPA as to whether the current national monitoring network is sufficiently representative of the areas where the population lives. It could also inform other researchers conducting prediction modeling in

terms of things like variable selection if, for example, there are some factors that have smaller differences between monitor and population locations than others, then the former could be treated preferentially in prediction modeling variable selection.

Future directions related to our work in Aim 2 include conducting longitudinal analyses for the two biomarkers (CRP and fibrinogen) that we studied which have repeated measures among some participants in subsequent MESA exams. There are also other cardiovascular health measures for MESA participants, including two markers of atherosclerosis: carotid artery intima-media thickness (IMT) and coronary artery calcium (CAC) scores, which could be studied using our $PM_{10-2.5}$ predictions. Both IMT and CAC are considered possible downstream consequences of chronic systemic inflammation, therefore determining what association they have with $PM_{10-2.5}$ exposure could potentially inform our understanding of our results in Aim 2.

In future work related to Aim 3, we intend to evaluate the association between being selected for clean bus rebate funding from the EPA's School Bus Rebate Program and other outcomes. For example, we hypothesize that adoption of cleaner school buses will be associated with greater educational achievement. This is a natural extension of our findings in Aim 3 since the general educational literature has repeatedly demonstrated higher educational achievement with better attendance rates (Gottfried 2010; Lamdin 1996; Roby 2003). In addition, two other studies that have looked at the impact of clean bus funding have found associations with student achievement on standardized tests. We are currently planning to conduct this analysis using standardized math and English/Language Arts (ELA) scores, which are available in the Stanford Education Data Archive (SEDA). We additionally intend to evaluate the impact of the EPA's School Bus

Rebate Program on health, given the known health effects of diesel engine exhaust. Specifically, will investigate differences in emergency department visits for respiratory causes among Medicaid beneficiaries aged 5-18 between districts that were awarded funding vs. those that were not. We plan to use emergency department visits as our health measure of concern given that a previous study documented fewer emergency department visits by children for bronchitis, asthma, pneumonia, and pleurisy among Washington State school districts that retrofitted their school buses as compared to those that did not (Beatty & Shimshack, 2011).

**Conclusion:**

This dissertation showed that using satellite-based AOD data within an advanced spatiotemporal prediction modeling approach can successfully generate long-term average $PM_{10-2.5}$ concentrations, even in locations without monitoring data. The success of this approach depends necessarily on having a sufficient amount of and variability in available measurement data with which to build the model. However, in cases where those conditions are met, this approach can successfully expand the locations at which researchers can study the health impacts of $PM_{10-2.5}$ exposure. This is an important finding given that one of the main inhibitors to studying the health impacts of $PM_{10-2.5}$ exposure is the limited amount of measured data available for assigning $PM_{10-2.5}$ exposure levels to study participants. While our use of these newly estimated $PM_{10-2.5}$ predictions in Aim 2 did not yield conclusive or expected results in terms of the inflammation and coagulation impacts of $PM_{10-2.5}$ exposure, our results were largely consistent with previous research on this topic, which further confirms that our exposure prediction approach can be successful in generating $PM_{10-2.5}$ exposure estimates. In Aim 3, we find

suggestive evidence that the EPA's DERA School Bus Rebate Program has improved student attendance, especially in the districts that removed the oldest buses and those with high levels of bus ridership on the impacted buses. Given the importance of attendance to student educational success, our results suggest that this program is both successful at increasing the pace at which older, highly polluting buses are removed from use and that those actions have positive impacts on student attendance levels.

**References:**


Adar, S.D., Filigrana, P.A., Clements, N., Peel, J.L., 2014. Ambient Coarse Particulate Matter and Human Health: A Systematic Review and Meta-Analysis. Curr Envir Health Rpt. 1, 258-274.

Adar SD, D'Souza J, Mendelsohn-Victor K, Jacobs Jr. DR, Cushman M, Sheppard L, et al., Markers of inflammation and coagulation after long-term exposure to coarse particulate matter: a cross-sectional analysis from the multi-ethnic study of atherosclerosis. Environmental Health Perspectives, 2015a. 123(6):541-548.

Beatty, T.K.M., Shimshack, J.P., 2011. School buses, diesel emissions, and respiratory health. J Health Econ. 30, 987-999.

Gottfried, M.A., 2010. Evaluating the Relationship Between Student Attendance and Achievement in Urban Elementary and Middle Schools: An Instrumental Variables Approach. Am Educ Res J. 47, 434-465.

Kloog I, Sorek-Hamer M, Lyapustin A, Coull B, Wang Y, Just AC, et al., Estimating daily PM 2.5 and PM 10 across the complex geo-climate region of Israel using MAIAC satellite-based AOD data. Atmospheric Environment, 2015. 122:409-416.

Lamdin, DJ. Evidence of Student Attendance as an Independent Variable in Education Production Functions. J Educ Res. 1996. 89(3): 155-162.

Madrigano J, Kloog I, Goldberg R, Coull BA, Mittleman MASchwartz J, Long-term exposure to PM2.5 and incidence of acute myocardial infarction. Environmental Health Perspectives, 2013. 121(2):192-196.

McGuinn LA, Ward-Caviness CK, Neas LM, Schneider A, Diaz-Sanchez D, Cascio WE, et al., Association between satellite-based estimates of long-term PM2.5 exposure and coronary artery disease. Environmental Research, 2016. 145:9-17.

Nordio F, Kloog I, Coull BA, Chudnovsky A, Grillo P, Bertazzi PA, et al., Estimating spatio-temporal resolved PM10 aerosol mass concentrations using MODIS satellite data and land use regression over Lombardy, Italy. Atmospheric Environment, 2013. 74:227-236.

Roby DE. Research on School Attendance and Student Achievement: A Study of Ohio Schools. Educ Res Quart. 2003. 28(1): 4-15.

Shtein, A., Karnieli, A., Katra, I., Raz, R., Levy, I., Lyapustin, A., Dorman, M., Broday, D.M., Kloog, I., 2018. Estimating daily and intra-daily PM10 and PM2.5 in Israel using a spatio-temporal hybrid modeling approach. Atmos Environ. 191, 142-152.

Stafoggia, M., Schwartz, J., Badaloni, C., Bellander, T., Alessandrini, E., Cattani, G., de' Donato, F., Gaeta, A., Leone, G., Lyapustin, A., Sorek-Hamer, M., de Hoogh, K., Di, Q., Forastiere, F., Kloog, I., 2017. Estimation of daily PM10 concentrations in Italy (2006-2012) using finely resolved satellite data, land use variables and meteorology. Environ Int. 99, 234-244.

Stafoggia, M., Bellander, T., Bucci, S., Davoli, M., de Hoogh, K., de' Donato, F., Gariazzo, C., Lyapustin, A., Michelozzi, P., Renzi, M., Scortichini, M., Shtein, A., Viegi, G., Kloog, I., Schwartz, J., 2019. Estimation of daily PM10 and PM2.5 concentrations in Italy, 2013-2015, using a spatiotemporal land-use random-forest model. Environ Int. 124, 170-179.

US EPA, 2019. Integrated science assessment for particulate matter. Research Triangle Park: NCEA-RTP Office.

Yanosky, J.D., Paciorek, C.J., Schwartz, J., Laden, F., Puett, R., Suh, H.H., 2008. Spatio-temporal modeling of chronic PM10 exposure for the Nurses' Health Study. Atmos Environ. 42, 4047-4062.

Yanosky, J.D., Paciorek, C.J., Suh, H.H., 2009. Predicting Chronic Fine and Coarse Particulate Exposures Using Spatiotemporal Models for the Northeastern and Midwestern United States. Environ Health Perspect. 117, 522-529.

Yanosky, J.D., Paciorek, C.J., Laden, F., Hart, J.E., Puett, R.C., Liao, D., Suh, H.H., 2014. Spatio-temporal modeling of particulate air pollution in the conterminous United States using geographic and meteorological predictors. Environ Health. 13, 63-77.

Zhang ,K., Larson, T.V., Gassett, A.J., Szpiro, A.A., Daviglus, M., Burke, G.L., Kaufman, J.D., Adar, S.D., 2014. Characterizing Spatial Patterns of Airborne Coarse Particulate (PM10-2.5) Mass and Chemical Components in Three Cities: The Multi-Ethnic Study of Atherosclerosis. Environ Health Perspect. 122, 823-830.