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Estimating health effects from modeled air quality time series data

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Abstract

Estimating health effects from modeled air quality time series data

By Joseph Y. Abrams

Ambient air pollution is a leading risk factor for global disease burden. Epidemiological studies can contribute to improved efforts for the measurement and mitigation of the harmful health effects of air pollution. This dissertation addressed two primary research questions:

- What are the effects of the oxidative potential of ambient particulate matter on human health?
- What are the health benefits of air pollution control policies?

Oxidative potential (OP) has been proposed as a major mechanism of particulate toxicity. To answer the first research question, we estimated health associations for the OP of water-soluble fine particulate matter ($PM_{2.5}$) measured using a dithiothreitol assay (OP^{DTT}). Daily counts of emergency department (ED) visits for several cardiorespiratory outcomes were obtained for 42 hospitals serving patients in the 5-county Atlanta metropolitan area. OP^{DTT} was measured for 196 days, and measured OP^{DTT} was positively associated with ED visits for respiratory disease, asthma, and ischemic heart disease. These associations were generally not attenuated in bipollutant models with many commonly measured pollutants.

Extending this analysis, we developed a predictive model for OP^{DTT} using concurrently measured air quality and meteorology variables. This predictive model was used to backcast daily OP^{DTT} values for 1999-2013, and we estimated health associations for these modeled OP^{DTT} values. Modeled OP^{DTT} was associated with ED visits for respiratory disease and asthma, and these associations were not attenuated in bipollutant models with $PM_{2.5}$ mass.

To answer the second research question, we used counterfactual estimates for ambient pollutant levels if several policies affecting the Atlanta area were not implemented. After creating a multipollutant health effects model, these counterfactual estimates were contrasted with measured ambient pollutant levels to estimate the health impact of these policies. Greater proportions of visits were prevented in later years as effects of policies became more fully realized. Air pollution control policies were estimated to substantially prevent ED visits for respiratory disease, asthma, cardiovascular disease, and congestive heart failure.

The findings from these studies provide support for a promising measure of particle toxicity and present results which may be useful for informing future air pollution control strategies.

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This dissertation is dedicated to little Arjoon, as a reminder that when we are surrounded by the right people, anything is possible.

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CHAPTER 1: INTRODUCTION

Important research in any scientific field aims strives to fill knowledge gaps that are critical to our understanding of patterns and processes governing the universe. These gaps may exist for many reasons, such as: lack of prior interest in a topic, lack of adequate methodology to investigate the topic, or lack of sufficient observable data to study the topic. The last of these reasons – lack of sufficient observable data – is the main impediment which has hampered progress in the research areas addressed in this dissertation. The studies presented herein implement methodologies to generate modeled air quality data which were then used to examine issues crucial to the field of air pollution epidemiology.

There are two primary research questions addressed in this dissertation. The first question asked: What are the effects of the oxidative potential (OP) of ambient particulate matter (PM) on human health? This research question assessed the health impacts of a novel method of characterizing the toxicity of ambient air pollution: the capacity of aerosols to cause oxidative damage. Two study aims were contained within this research question. Aim I assessed the association between measured particulate OP and cardiorespiratory emergency department (ED) visits over a 196 day period in the Atlanta, GA metropolitan area. This study was important for determining whether measured OP was a promising predictor of the acute health effects of PM. Aim II extended the analyses performed in Aim I by utilizing predictive modeling to estimate daily OP values over a 15-year time period in Atlanta. Associations between these modeled OP values and cardiorespiratory ED visits were assessed in order to more fully investigate the utility of OP as a measure of particulate toxicity.

The second research question asked: What are the health benefits of air pollution control policies? Aim III, which addressed this questions, involved the estimation of the number and percent of cardiorespiratory ED visits prevented through the implementation of several specific pollution control policies that regulated emissions in the Atlanta area. We utilized a counterfactual study approach, and methods were developed by collaborators at the Georgia Institute of Technology to generate modeled daily estimates of ambient pollutant levels if these policies had not been implemented. We incorporated these modeled pollutant values into our health effects models to estimate the overall health impacts of these pollution control policies.

The ability to use modeled data allowed for more extensive study of these research questions than was previously possible. In Aims I and II, we completed the most comprehensive study to date of the acute public health effects of ambient particulate OP. In Aim III, the modeling of counterfactual ambient levels of many individual pollutants for several hypothetical scenarios allowed for sophisticated multipollutant modeling that assessed the health impacts of progressively implemented, overlapping air pollution control policies. Yet the utilization of modeled air quality data is not a simple panacea: modeling efforts can suffer from biases, model misparameterizations, and random error which all degrade the quality of studies reliant on these data. These potential problems become magnified when validation of modeled data is not possible, which is the case for these current studies.

In this dissertation, we took numerous steps to properly account for these issues. We aimed to use *a priori* model parameterizations whenever possible to prevent the possibility of data fishing as well as to limit issues of multiple comparisons. When we

did consider different model formulations, we conducted additional analyses to assess the sensitivity of results to modeling choices. Finally, while other studies typically treat modeled data as fixed, we utilized Monte Carlo methods to create simulated confidence intervals which accounted for random error uncertainty in modeled values. Together, these approaches mitigated concerns about using modeled air quality datasets, and the resulting analyses utilizing these data contributed substantially to the study of the effects of air pollution on human health.

CHAPTER 2: BACKGROUND

2.1: General health effects of air pollution

The public health impacts of ambient air pollution are an important topic of research. The World Health Organization (WHO) estimates that ambient air pollution is responsible for an estimated 3.7 million deaths in 2012, primarily through increasing risk of ischemic heart disease and stroke; total air pollution was named the single largest environmental health risk.(1) In 2013, the International Agency for Research on Cancer classified outdoor air pollution as a carcinogen.(2) As of 2014, 92% of the world's population were living in places that did not meet WHO air quality guidelines.(3) Since all people are exposed to a certain degree of airborne pollutants, research aimed at controlling and mitigating the effects of air pollution is relevant for people around the world.

While there are natural sources of air pollution, the bulk of harmful ambient pollutants originates from human activities.(4) Road transport is a major source of harmful gases such as carbon monoxide (CO) and nitrogen oxides (NO_x), volatile organic compounds (VOCs), and particulate matter (PM). Biomass burning can also contribute large amounts of toxic gases and PM, while combustion of fossil fuels is a primary source of emissions of sulfur dioxide (SO_2) as well as NO_x and PM. Industrial and agricultural processes can lead to discharge of heavy metals and persistent organic pollutants into the environment. In addition, these pollutants can react in the atmosphere to form secondary pollutants such as ozone (O_3) and sulfates (SO_4). The identification and quantification of pollutant emissions can improve efforts to reduce air pollution.

There has been abundant research on the human health effects of various pollutants. Carbon monoxide, which is a product of incomplete combustion and is caused primarily by road traffic, reduces the ability of hemoglobin to bind oxygen.(5) This can result in reduced function of high oxygen-consuming organs such as the brain and heart.(4) Ambient carbon monoxide levels have also been associated with adverse pregnancy outcomes such as low birth weight and preterm birth.(6, 7) Sulfur dioxide is primarily released from power plants using coal or heavy oils, and can lead to bronchoconstriction in asthmatic patients.(8, 9) Similarly to carbon monoxide, sulfur dioxide may also be linked to preterm birth and low birth weight.(10, 11)

Nitrogen oxides are products of high temperature combustion and are emitted from gasoline and diesel vehicles as well as power plants. Both controlled and observational studies have shown that nitrogen oxides can exacerbate asthmatic symptoms.(12-14) Nitrogen dioxide has been shown to increase susceptibility to respiratory infectious diseases,(15) and nitrogen dioxide may have negative effects on lung function grown in children.(16) Furthermore, nitrogen oxides react in sunlight with hydrocarbons (also emitted by both mobile and stationary sources) to produce another pollutant with adverse respiratory effects, ozone. Ozone is a respiratory tract irritant known to cause wheezing, coughing, and shortness of breath.(17) Ozone can lead to increased symptoms of asthma even at relatively low doses.(18, 19) Long-term exposure to ozone may lead to decreased lung function in children and adolescents.(20, 21)

Particulate matter is a term describing solid or liquid particles suspended in the air that can vary in size, composition, chemical reactivity, and origin. Size is a determinant of the ability of PM to penetrate into the respiratory system. Larger particles are often

trapped by mucus in the nose and throat, mitigating effects on human health. Particles smaller than 10 micrometers (PM_{10}) can reach the lungs and bronchi, while particles smaller than 2.5 micrometers ($PM_{2.5}$) can penetrate into bronchioles and alveoli. $PM_{2.5}$ has been associated with hospital admissions for a number of respiratory outcomes (e.g. asthma, chronic obstructive pulmonary disorder, respiratory disease) and cardiovascular outcomes (e.g. myocardial infarction, coronary heart disease, stroke).(22-25) PM has been linked to lung cancer (26, 27) and has been shown to be a major determinant of cardiovascular, respiratory, and all-cause mortality.(28-30) Since PM is a heterogeneous mixture, there is no single biological pathway through which it causes adverse health effects. Greater understanding of the characteristics, components, and sources of particulate matter most directly linked to negative outcomes is critical for informing efforts to contain and mitigate the effects of PM air pollution.

Inhalation of particulate matter is associated with the release of cytokines, activated immune cells, and other mediators of inflammation in the upper and lower airways.(31, 32) This respiratory inflammation can lead to exacerbation of asthma symptoms, chronic bronchitis, and decreased gas exchange. These proinflammatory mediators, along with ultrafine particulate matter (UFP, generally categorized as particulate matter under 0.1 micrometers), can be released into the bloodstream. The resulting elevated levels of white blood cells, platelets, and myeloperoxidase are linked to vasoconstriction, atherosclerosis, and endothelial dysfunction, all major risk factors for future cardiac outcomes.(33, 34) These inflammatory pathways are hypothesized to be driven or mediated by oxidative stress caused by the *in vivo* generation of reactive oxygen species.(35, 36) Pathways through which PM causes health effects may not

always involve oxidative stress: notably, there is ample support for the hypothesis that exposure to PM can interact with lung neurons or receptors to interfere with autonomic nervous system function.(37, 38) However, oxidative stress is believed to be a major mechanism through which PM causes cardiorespiratory distress, and thus the oxidative potential (OP) of PM is a promising potential measure of particulate toxicity.

2.2: Types of air pollution epidemiologic studies

Air pollution has long been recognized as a potential health hazard: as early as classical Rome, urban air pollution was described as harmful to human health.(39) With the Industrial Revolution came heavy urbanization and increased burning of coal and oil, exposing more people to hazardous levels of air pollution. However, before the 20th century, the lack of methods to properly identify and quantify components of air pollution presented a challenge to epidemiologic research. Early public health advocates used a version of a crossover study design: for example, in the 19th century, Londoners noted an increase in mortality during periods with heavy smog.(40) Other early studies included research on lung cancer in certain occupations (e.g. coal gasworkers, nickel refinery workers) where workers endured extremely high levels of air pollution.(41)

Modern air pollution research can involve a variety of different study types. Experimental studies (using *in vitro* cultures, animal models, or human subjects) can directly test for the effects of certain pollutants. However, these studies are often costly and labor-intensive, and may involve a small sample size. Analysis of biomarkers in

experimental human studies can allow for the study of subclinical effects, but this may be insufficient for proving causation between pollution and clinical disease.

Observational cohort studies can identify long-term effects of air pollution, but require the recruitment and follow-up for a sufficiently large cohort, including longitudinal estimates of pollutant exposure. Since cohort studies generally measure cumulative pollutant exposure over an extended period of time, they are useful for estimating the chronic effects of air pollution. Furthermore, these analyses are subject to confounding by a variety of sociodemographic variables.

Case-crossover studies and time series analyses, by observing the same population (roughly) over different exposure periods, control for individual-level confounding but must address confounding by temporally-dependent variables. These studies measure differences in health outcomes at finer temporal scales over the course of the study period; therefore, they are useful for estimating the acute effects of air pollution. While both methods have certain advantages, time series analyses can result in greater precision of risk estimates.(42)

Numerous previous studies have used time series analyses to measure short-term associations between pollutants and emergency department (ED) visits in the Atlanta metropolitan area. Early studies established an association between several pollutants (such as NO_2, CO, O_3, and $PM_{2.5}$) and assorted cardiovascular and respiratory outcomes.(43, 44) Subsequent analyses quantified health effects of ambient air pollutants on children and other susceptible groups.(45-47) Efforts were made to characterize and address potential methodological issues arising in time-series studies such as measurement error (48) and spatial variability. (49, 50) Some analyses utilized

alternative exposures such as pollen counts (51) or alternative outcomes such as hospital admissions.(52) Recent studies have explored novel methods such as joint pollutant effects (53) or Bayesian ensemble-based source apportionment.(54) All these studies contributed tremendously to the epidemiologic literature, not only for the quantification of the acute effects of ambient air pollution, but also on time series analytic methodology. Crucially, these studies helped to develop optimal confounder control in order to minimize bias stemming from effects of meteorology, seasonality, long-term trends, and other time-varying factors on both air pollution and ED visitation patterns.

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CHAPTER 3: RESEARCH QUESTION I

3.1: Oxidative potential

Oxidative potential (OP) of particulate matter describes the extent to which particles contain or can generate free radicals *in vivo*, often endogenously through the mitochondrial electron transport chain. Free radicals, especially reactive oxygen species (ROS) such as superoxide (O_2^-) and hydrogen peroxide (H_2O_2), coordinate with antioxidant systems to maintain oxidative homeostasis.(1) In addition, they may play important roles in physiological processes such as the amplification of immune responses to environmental pathogens, the regulation of cell adhesion, and the induction of apoptosis.(2) However, exposure to environmental toxins, including reactive chemical species in ambient particulate matter, can result in elevated levels of ROS and subsequent oxidative stress which lead to systemic inflammation and acute adverse health outcomes.(3) In addition, oxidative damage can degrade vital biologic components such as polyunsaturated fatty acids, nucleic acids, and proteins. Due to the wide-ranging destructive capacity of oxidative stress, particulate OP been implicated in a variety of chronic diseases such as rheumatoid arthritis, metabolic disorders, and assorted neurodegenerative diseases.(4) The degradation of certain enzymes and nucleic acids may additionally accelerate the aging process.(5)

Particulate matter can contain a variety of different classes of species which may lead to higher OP. These include transition metals (e.g. copper, iron), quinones, polycyclic aromatic hydrocarbons, and elemental carbon. Different types of assays have been developed to attempt to measure the OP of ambient PM. The electron spin resistance (ESR) assay measures the capacity of PM to convert hydrogen peroxide to

hydroxyl radicals.(6) Assays for ascorbic acid (AA) and glutathione (GSSG), two antioxidants, measure their level of depletion.(7) The dithiothreitol (DTT) assay mimics the *in vivo* generation of superoxide radicals by nicotinamide adenine dinucleotide (NADH) and nicotinamide adenine dinucleotide phosphate (NADPH).(8, 9) Cellular assays, such as those using rat alveolar macrophage (NR8383) cells, can directly measure the oxidation of intracellular probes.(10) Table 1.1 displays a sample of studies which measure the oxidative potential of ambient PM. For this study, a semi-automated DTT system was used for the large-scale measurement of the OP of water-soluble particulate matter. This measurement of OP will be further described in Chapter 5.1.

Table 3.1: A sample of studies measuring oxidative potential of ambient particulate matter. Number of samples is estimated when not explicitly described in paper. Measures of oxidative potential derived from different PM fractions (i.e. different sizes of PM) are counted as separate samples, while dilutions taken from the same PM fraction are not.

Study	Method	Samples
Akhtar (2010) (11)	dithiothreitol (DTT)	6
Boogaard (2012) (12)	electron spin resonance (ESR)	At least 105
Briede (2005) (13)	electron spin resonance (ESR)	At least 22
Charrier (2012) (14)	dithiothreitol (DTT)	60
Charrier (2015) (15)	dithiothreitol (DTT)	19
Cho (2005) (16)	dithiothreitol (DTT)	32
Chung (2006) (17)	dithiothreitol (DTT)	11
Daher (2014) (18)	macrophage assay w/dichlorodihydrofluorescein diacetate (DCFH-DA) probe	~80
De Vizcaya-Ruiz (2006) (19)	dithiothreitol (DTT)	40
Godri (2011) (7)	ascorbic acid (AA), glutathione (GSSG)	14

Janssen (2014) (20)	dithiothreitol (DTT), electron spin resonance (ESR), ascorbic acid (AA)	30
Jeng (2010) (21)	dithiothreitol (DTT)	32
Landreman (2008) (22)	macrophage assay w/dichlorodihydrofluorescein diacetate (DCFH-DA) probe	50
Li (2003) (23)	dithiothreitol (DTT), glutathione (GSSG)	15
Nawrot (2009) (24)	electron spin resonance (ESR)	716
Shen (2012) (25)	ascorbic acid (AA)	11
Shi (2003) (6)	electron spin resonance (ESR)	6
Salonen (2004) (26)	electron spin resonance (ESR)	3 (pooled)
Shuster-Meiseles (2016) (27)	macrophage assay w/dichlorodihydrofluorescein diacetate (DCFH-DA) probe	18
Shi (2006) (28)	electron spin resonance (ESR)	81
Shirmohammadi (2015) (29)	macrophage assay w/dichlorodihydrofluorescein diacetate (DCFH-DA) probe	~120
Steenhof (2011) (30)	dithiothreitol (DTT)	20
Valavanidis (2000) (31)	electron spin resonance (ESR)	30
Velali (2016) (32)	dithiothreitol (DTT)	20
Verma (2009) (33)	macrophage assay w/dichlorodihydrofluorescein diacetate (DCFH-DA) probe, dithiothreitol (DTT)	5
Wessels (2010) (34)	electron spin resonance (ESR)	80
Yang (2014) (35)	dithiothreitol (DTT), electron spin resonance (ESR), ascorbic acid (AA)	15

Exposure to high levels of diesel exhaust and other sources of particulate matter have been repeatedly shown to cause measureable amounts of oxidative stress.(36, 37) Furthermore, exposure to ambient air can result in acute oxidative stress and inflammatory responses in peripheral blood as well as airway tissues.(38) Exposure to

pollutant mixtures with high OP have been linked to the exacerbation of a variety of respiratory conditions (including chronic obstructive pulmonary disorder, asthma, chronic bronchitis, and emphysema) and circulatory outcomes (including myocardial infarction, stroke, ischemic heart disease, and coronary heart disease).(39-45) In addition, diesel exhaust particles from ambient air pollution can travel to other body organs, such as the liver and kidneys.(46) Acute oxidative stress can lead to outcomes such as acute renal failure and exacerbation of non-alcoholic liver disease, suggesting that particulate OP could theoretically lead to clinical outcomes outside the respiratory or circulatory systems.(47, 48)

These studies strengthen the evidence for OP to be a major determinant of the toxicity of $PM_{2.5}$. However, studies on the harmful effects of OP are usually small experimental or observational studies which simply contrast health outcomes in people exposed to different concentrations of PM or other pollutants. Since these pollutants may involve other mechanisms of toxicity, it is unclear whether the observed harms are truly attributable to OP. Two studies attempted to address this issue by exposing volunteers to PM mixtures of similar concentration but different composition. In each of these studies, exposure to the mixture high in metals with considerable OP such as zinc, copper, and iron produced significantly higher inflammatory responses.(49, 50)

3.2: Knowledge gap addressed by current studies

While these studies are suggestive of a causal link between ambient particulate OP and adverse health outcomes, more research would be vital for validating such

results. Since many of these methods for measuring OP are labor-intensive, measurements have typically been over relatively short time periods. Because of this, until this current study there had not been a large-scale, observational study of the effect of ambient particulate OP on human health. This study has multiple benefits, such as, 1) verifying a major mechanism of harm for $PM_{2.5}$, 2) determining health outcomes for people exposed to real-world ambient levels of OP, not just experimental doses; and 3) quantifying health effects at the population level. The study we conducted was the first study to use a long-term observational epidemiologic analysis to assess population-level effects of daily oxidative potential in ambient PM, and therefore filled this critical research gap.

Study Aim I utilized a semi-automated measurement system which enabled greater number of daily OP measurements. This allowed for time series analyses using Poisson generalized linear regression to estimate associations between OP and cardiorespiratory ED visits. The regression controlled for temporal confounding using covariates from prior studies that analyzed the association between pollutants and ED visits using the same Atlanta ED data.(51-62) This study was the first to assess population-level associations of measured OP in ambient PM.

Study Aim II expanded upon this study through the construction of a predictive model for OP. The coefficients from this model were incorporated with long term air quality and meteorology data to construct daily time series of OP for a substantially longer time period. These modeled OP data were then used in regression analyses to assess their association with cardiorespiratory ED visits. Sensitivity analyses testing the effects of modeling choices as well as uncertainty analyses accounting for random

modeling error were performed in order to properly account for potential pitfalls from relying on modeled data.

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CHAPTER 4: RESEARCH QUESTION II

4.1: Accountability studies

The effect estimates from time series analyses or other types of air pollution analyses can be utilized to estimate the numbers of health outcomes prevented by air pollution interventions. One application is to use different scenarios for future pollutant levels to predict how many ED visits would be prevented or caused by certain actions. Another application is to look retrospectively and assess how many ED visits have been prevented or caused by past actions.

Previous studies have attempted to quantify the reduction in ambient pollutant levels and subsequent health benefits stemming from air pollution interventions. A sample of some of these studies is contained in Table 1.2. Many of these are pre-post studies which compare health outcomes before and after an intervention was implemented. During a nationwide strike of copper smelter workers in the US in 1967-1968, there was a 60% drop in ambient sulfate levels, which resulted in an estimated 2.5% decrease in mortality.(1) During the 2008 Beijing Summer Olympic Games, government initiatives aimed at reducing ambient air pollution (traffic restrictions, reduction of construction activities, temporary closing of pollution emitting factories) successfully reduced $PM_{2.5}$ levels by 31%.(2) The decrease in ambient $PM_{2.5}$ was associated with a significant drop in hospital visits for asthma.(3) In a long-term comparative study, researchers assessed PM_{10} changes and mortality in two Australian towns, one of which implemented coordinated strategies to reduce pollution from wood smoke. The town with the interventions displayed reductions in PM_{10} and all-cause, respiratory, and cardiovascular mortality, which was not reflected in the control town.(4)

Pre-post studies are subject to temporal confounding, as other variables which are associated with ambient air pollution or health outcomes may change over time. An alternative approach is to model the contribution of emissions to ambient pollutant levels, and contrast observed pollutant levels with counterfactual pollutant levels for the scenario where the intervention had not been implemented. While confounding can theoretically be avoided under this approach, the challenges involved in determining counterfactual pollutant levels has limited the number of studies performed. In 2003, a Congestion Charging Scheme (CCS) was introduced in London, using financial deterrents in order to reduce traffic congestion. Using data on traffic flow and fleet composition along with pollution dispersal modeling, reductions in PM_{10} attributable to the CCS were estimated, along with the resulting life-years gained.(5) The impacts of air pollution interventions in Spain were estimated using the Sparse Matrix Operator Kernel Emissions (SMOKE) system to estimate emissions reductions and the Community Multi-scale Air Quality model (CMAQ v4.6) to estimate the resulting reduction in ambient $PM_{2.5}$ levels. The interventions, through the reduction of ambient $PM_{2.5}$ levels, were estimated to prevent 8 to 15 deaths annually.(6) Another study assessed the impact of numerous changes to factors including energy consumption, fuel type, and car fleet composition in eastern Germany after German unification. These changes were estimated to have varying effects on the levels of individual pollutant species and ultimately were linked to a decrease in air pollution-associated mortality.(7)

Table 4.1. Selected air pollution intervention studies (from Henneman et al. 2017).(8)

Author	Year	Policy/event	Geographic scale	Time scale	Emissions	Air quality
Rao and Zurbenko	1994	All regulations, 1983–1991	Single monitor, New York State	Long		Ambient, meteorological detrending
Kuebler et al.	2001	All regulations, 1985–1998	National Switzerland	Long	Changes in emissions by source over time	Ambient, meteorological detrending
Greenstone	2004	1970 Clean Air Act Amendments	National U.S.	Long		Ambient, change in SO_2 concentrations in designated attainment vs. nonattainment regions
Camalier et al.	2007	All regulations, 1997–2005	Region: Eastern U.S.	Long		Ambient, meteorological detrending
Gégo et al.	2007	NO_x SIP Call	Region: Northeastern U.S.	Long	Changes in point-source emissions over time	Ambient, meteorological detrending (including wind direction analysis)
Gégo et al.	2008	NO_x SIP Call	Region: Northeastern U.S.	Long	Changes in point-source emissions over time, estimate of counterfactual	Modeled, comparing actual and counterfactual using single meteorological year
Godowitch et al.	2008	NO_x SIP Call	Region: Northeastern U.S.	Long	Changes in point-source emissions over time, estimate of counterfactual	Modeled dynamic analysis, comparing change due to emissions vs. meteorology
Bar-Weiss et al.	2008	Mobile regulations, 1997–2006	Local: tunnel	Long	Measured emission factors, before/after comparison	
Atkinson et al.	2009	Congestion charging scheme, 2003	City: London	Short		Ambient, before/after comparison
Goodman et al.	2009	Coal sale bans	National: Ireland	Long		Ambient, before/after comparison
W. Wang et al.	2009	Industrial activity reduced for 2008 Olympics in Beijing	City: Beijing	Short		Ambient, before/after comparison, back-trajectory analysis, correlations with meteorology
M. Wang et al.	2009	Reduced industrial activity for 2008 Olympics in Beijing	City: Beijing	Short		Ambient, before/after comparison
Wang and Xie	2009	Reduced industrial activity for 2008 Olympics in Beijing	City: Beijing	Short	Modeled, before/after comparison	Modeled, before/after comparison
X. Wang et al.	2009	Reduced industrial activity for 2008 Olympics in Beijing	City: Beijing	Short	Measured emission factors, before/after comparison	Ambient, before/after comparison
Y. Wang et al.	2009	Reduced industrial activity for 2008 Olympics in Beijing	City: Beijing	Short	Modeled, before/after comparison	Modeled, before/after comparison
Kean et al.	2009	Mobile regulations, 1999–2006	Local: tunnel	Long	Measured emissions factors, before/after comparison	
2010–2012 Godowitch	2010	Mobile regulations, 2002–2006	Region: Eastern U.S.	Long	Changes in emissions by source over time	Modeled dynamic analysis, comparing change due to emissions vs. meteorology
Dallman and Harley	2010	Mobile regulations, 1996–2006	National: U.S.	Long	Changes in modeled mobile emissions over time	
B. Wang et al.	2010	Reduced industrial activity for 2008 Olympics in Beijing	City: Beijing	Short	Measured emission factors, before/after comparison	Ambient, before/after comparison, source apportionment
S. Wang	2010	Reduced industrial activity for 2008 Olympics in Beijing	City: Beijing	Short	Modeled, before/after comparison	Ambient and modeled, before/after comparison
Lin et al.	2010	All regulations, 2004–2008	Region: Eastern China	Long	Changes over time estimated by satellite	Ambient, change over time (satellite measurements)
Lamsal et al.	2011	All regulations, 2003–2009	Global	Long	Changes over time estimated by satellite	
Colette	2011	All regulations, 1998–2007	Continent: Europe	Long	Changes in emissions by source over time	Modeled dynamic analysis, comparing change due to emissions vs. meteorology
Butler et al.	2011	All regulations, 1997–2008	Region: Eastern U.S.	Long	Changes in point-source emissions over time	Ambient, change over time and sensitivity to emissions
Xing et al.	2011	Reduced industrial activity for 2008 Olympics in Beijing	City: Beijing	Short	Counterfactual emissions	Modeled dynamic analysis, comparing change due to emissions vs. meteorology
Kelly et al.	2011	Congestion charging scheme introduced in 2003	City: London	Short	Modeled spatial	Ambient and modeled, before/after and control location comparison, source apportionment

Author	Year	Policy/event	Geographic scale	Time scale	Emissions	Air quality
Hao et al.	2011	Shanghai World Expo 2010	City: Shanghai	Short		Satellite-measured, before/after comparison
Harrington et al.	2012	1990 CAAA	Region: Eastern U.S.	Long	Counterfactual	Ambient, modeled counterfactual
McDonald et al.	2012	Mobile regulations, 1990–2010	Multicity: U.S.	Long	Changes over time	
Shreifels et al.	2012	SO_2 reduction goals in the 10th and 11th Five-Year Plans	National: China	Long	Changes over time	
Morgentsern et al.	2012	Title IV Phase 2 of the 1990 CAAA	Region: Eastern U.S.	Long	Change over time and counterfactual	Ambient, trends over time and counterfactual
Pegues et al.	2012	1997 8-hr ozone State Implementation Plans	National: U.S.	Long	Modeled, change over time	Ambient, change over time and location
Liu et al.	2012	Reduced industrial activity for 2008 Olympics in Beijing	City: Beijing	Short		Ambient and satellite-measured, statistically modeled changes attributable to meteorology vs. emissions
2013–2016						
He et al.	2013	All regulations, 1997–2011	Region: Eastern U.S.	Long	Changes in point-source emissions over time	Ambient, change over time
Yuan et al.	2013	All regulations, 1998–2008	City: Hong Kong	Long	Changes over time	Ambient, change over time, source apportionment, and sensitivity to emissions
McDonald et al.	2013	Mobile regulations, 1990–2010	Multicity: U.S.	Long	Changes over time	
Kuwayama et al.	2013	Adoption of clean diesel technology at a major shipping port	Local: port	Short	Measured emission factors, before/after comparison	Ambient, before/after comparison, source apportionment
Huang et al.	2013	Shanghai World Expo 2010	City: Shanghai	Short		Ambient, before/after comparison, back-trajectory analysis
Lin et al	2013	Shanghai World Expo 2010	City: Shanghai	Short		Ambient, before/after comparison, back-trajectory analysis
Lurmann et al.	2014	All regulations, 1994–2011	Region: Southern California	Long	Changes over time	Ambient, change over time
Sickles and Shadwick	2014	All regulations, 1990–2009	Region: Eastern U.S.	Long	Changes over time	Ambient, change over time
Wang et al.	2014	SO_2 and NO_x control policies, 2006–2015	Region: Eastern China	Long	Counterfactual	Modeled counterfactual
Vijayaraghavan et al.	2014	Mobile regulations, 1995–2010	City: Atlanta, GA	Long	Modeled actual	Summertime ozone (detrended)
Harley	2014	California drayage truck regulation	Local: Port of Oakland	Long	Measured emission factors, change over time	
Gan et al.	2014	All regulations, 1995–2010	National: U.S.	Long	Changes in point-source emissions over time	Ambient, multiple ground-based and satellite networks, change over time
Gan et al.	2015	All regulations, 1995–2010	National: U.S.	Long	Changes in point-source emissions over time	Modeled, multiple ground-based and satellite networks, change over time
Simon et al.	2015	All regulations, 1998–2013	National: U.S.	Long	Change over time	Ambient, trends over time
Liu et al.	2015	Reduced industrial activity for 2008 Olympics in Beijing	City: Beijing	Short		Ambient, neural network analysis and 1-D box model
Russell et al.	2016	Closure of three power plants	City: Pittsburgh, PA	Short	Fuel use used as a proxy	Ambient, before/after comparison, statistically modeled change due to emissions
van der A. et al.	2016	All regulations, 2005–2015	National: China	Long	Changes over time estimated by satellite	
Daskalakis et al.	2016	All regulations, 1980–2010	Global	Long	Counterfactual	Modeled counterfactual
Henneman et al.	in review	All regulations, 1993–2013	City: Atlanta, GA	Long	Counterfactual	Ambient, before/after comparison, source apportionment, and counterfactual

Author	Year	Policy/event	Geographic scale	Time scale	Emissions	Air quality	Dose/exposure	Health response
Pope	1989	Brief closing of steel mill, 1987–1988	City: Utah Valley	Short	Discussion of local contribution	Ambient, before/after comparison	Monthly mean and lagged mean	Respiratory illness, changes in health response rates before/after
Peters et al.	1996	1990 reduction of sulfur in fuel oil	City: Hong Kong	Short		Ambient, before/after comparison		Household survey, changes in health response rates before/after
EPA Section 812 report	1997b	1970 Clean Air Act Amendments	National: U.S.	Long	Counterfactual	Ambient, change over time and modeled counterfactual	Varied across pollutants	Multiple outcomes, change from observed to counterfactual
Wong et al.	1998	1990 reduction of sulfur in fuel oil	City: Hong Kong	Short		Ambient, before/after and more/less polluted district comparisons		Bronchial hyperreactivity, changes in health response rates before/after and in more/less polluted districts
Friedman et al.	2001	Transportation limits for 1996 Olympics	City: Atlanta	Short	Before/after comparison	Ambient, before/after comparison	Daily, 2- and 3-day lag city average	Asthma events in children, changes in health response rates before/after
Clancy et al.	2002	1990 coal sale ban	City: Dublin	Short		Ambient, before/after comparison		Mortality, changes in health response rates before/after
Hedley et al.	2002	1990 reduction of sulfur in fuel oil	City: Hong Kong	Short		Ambient, before/after and more/less polluted district comparisons		Mortality, changes in health response rates before/after
Chay and Greenstone			2003		1981–1982 recession	National: U.S.	Short	
Ambient, before/after comparison	Annual	county average	Infant mortality, changes in health response rates					
Chay et al.	2003	1970 Clean Air Act Amendments	National: U.S.	Long		Ambient annual average by county	Annual county average	Adult mortality, changes in health response rates before/after
Laden et al.	2006	Reductions in $PM_{2.5}$, 1979–1998	Multicity: U.S.	Long		Ambient, trends over time	Four annual averaging methods	Mortality, changes in health response rates with changes in concentration
Lee et al.	2007	Transportation limits for 2002 Asian Games	City: Busan, Korea	Short		Ambient, before/after comparison	Daily city average	Asthma events in children, changes in health response rates before/after
Pope et al.	2009	Reductions in $PM_{2.5}$, 1970s–2000s	National: U.S.	Long		Ambient, trends over time	Annual mean	Mortality, changes in health response rates with changes in concentration
Peters et al.	2009	Rapid industrialization of a city, 1990–2002	City: Erfuhrt, Germany	Long	Change over time	Ambient, trends over time	Daily, single monitor lagged up to 5 days	Risk of death, change over time
2010–2016 Hou et al.	2010	Reduced industrial activity for 2008 Olympics in Beijing	City: Beijing	Short	Before/after comparison	Ambient, before/after comparison	Population-weighted exposure	Mortality and morbidity, changes in health response rates before/after
Li et al.	2010	Reduced industrial activity for 2008 Olympics in Beijing	City: Beijing	Short		Ambient, before/after comparison	Daily city average	Asthma events, changes in health response rates before/after
Wu et al.	2010	Reduced industrial activity for 2008 Olympics in Beijing	City: Beijing	Short		Personal exposure, before/after comparison	Personal exposure monitoring	Association of heart rate variability with $PM_{2.5}$ exposure
Peel et al.	2010	Transportation limits for 1996 Olympics	City: Atlanta	Short	Traffic counts	Ambient, change over time and location		Relative risk for respiratory hospital visits compared with baseline period
Zigler et al.	2012	1990 CAAA—NAAQS nonattainment designation	Regional: Western U.S.	Long		Ambient, counterfactual 3-yr average	3-yr average county average	Mortality, change from observed to counterfactual
Rich et al.	2012	Reduced industrial activity for 2008 Olympics in Beijing	City: Beijing	Short		Ambient, before/after comparison	Daily, single monitor	Multiple health outcomes, changes in health response rates before/after and in various districts
Wong et al.	2012	1990 reduction of sulfur in fuel oil	City: Hong Kong	Short		Ambient, change over time and location	Daily, 1- and 2-day lag city average	Mortality, changes in health response rates before/after

Author	Year	Policy/event	Geographic scale	Time scale	Emissions	Air quality	Dose/exposure	Health response
Lin et al.	2013	NO_x Budget Trading Program	Regional: New York State	Long	Ambient, before/after and more/less polluted district comparisons	Kriged 3-day moving average	Multiple health outcomes, changes in health response rates before/after and in various districts
Dockery et al.	2013	Coal sale bans	National: Ireland	Long	Ambient, change over time and location		Mortality, changes in health response rates before/after
Chen et al.	2013	Huai River policy	National: China	Long	Ambient, change over time and location	Annual city average (central monitors)	Change in life expectancy between locations
Rich et al.	2015	Reduced industrial activity for 2008 Olympics in Beijing	City: Beijing	Short	Ambient, before/after comparison	Daily, single monitor	Change in birth weight associated with improved air quality during specific months in pregnancy
Su et al.	2015	Reduced industrial activity for 2008 Olympics in Beijing	City: Beijing	Short	Ambient, before/after comparison and 72-hr back-trajectory analysis	Daily, single monitor, 0–4 day lag	Cardiovascular disease mortality, changes in health response rates before/after
Gaudeman	2015	All regulations, 1994–2011	Multicity, California	Long	Ambient, change over time and location	All regulations, 2005–2015	Lung development associated with increase concentrations
Berhane	2016	All regulations, 1994–2011	Multicity, California	Long	Ambient, change over time and location	All regulations, 2005–2015	Bronchitic symptoms associated with increase concentrations
Zigler et al.	2016	1990 CAAA—various regulations	National: U.S.	Long	Causally modeled		Multiple health outcomes, change from observed to counterfactual

Studies which model the pollutant reductions and health benefits attributable to air pollution interventions remain scarce, highlighting a knowledge gap critical to crafting successful air pollution policy. Research connecting specific air pollution controls to reductions of harmful emissions, ambient pollutant levels, and ultimately adverse health outcomes is necessary to impart a more comprehensive knowledge of the overall impacts of assorted pollution control policies. Study Aim III assessed the health impacts of past regulatory actions aimed at reducing pollution emissions by utilizing multipollutant health models to estimate the number of cardiorespiratory ED visits that were prevented by the adoption of these policies.

4.2: Health Effects Institute, Request for Applications 11-1

The Health Effects Institute (HEI) is an independent nonprofit research organization dedicated to the study of health effects of air pollution. HEI's Request for Applications (RFA) 11-1 is a call for accountability research, aimed at quantifying the health benefits of actions aimed at curbing air pollution. To fulfill this goal, researchers at the Georgia Institute of Technology and Emory University formed a collaborative venture to assess health impacts of air pollution controls in the Atlanta metropolitan area. Georgia Institute of Technology researchers were tasked with estimating the impacts of pollution controls on ambient air pollution. Study Aim III completed the project by estimating the health benefits attributable to the reduction of ambient air pollution.

4.3: Pollution control policies affecting the Atlanta metropolitan area

There have been a number of controls on emissions implemented in the southeastern US which have resulted in measurably reduced levels of ambient pollutants in the metropolitan Atlanta area from 1999 to 2013.(9) These policies can be divided into two categories. The first category is all emissions controls affecting mobile sources: diesel and gasoline powered vehicles. The second category is emissions controls on electricity-generating units (EGUs). For Study Aim III, the impacts of 6 pollution control policies were assessed. These policies are shown in Table 3.2

Table 4.2. Pollution control policies assessed in study.

Policy	Time frame
Mobile sources	
Inspection and Maintenance	1993 – 2013
Georgia Gasoline, Tier II Gasoline standards	2000 – 2013
Heavy Duty Highway Rule	2006 – 2013
Electricity-generating units (EGUs)	
Acid Rain Program and Georgia Rules for Air Quality Control rule yy ($GRAQC_{yy}$)	1995 – 2013
Clean Air Interstate Rule/Georgia multipollutant rule	2009 – 2013
NBP and SIP Call and $GRAQC_{jjj}$	1999 – 2013

Inspection and Maintenance: The 1990 Clean Air Act Amendments establish requirements for vehicle inspection and maintenance programs in order to aid attainment of air quality standards for ground-level ozone. These requirements include the identification of passenger cars and light trucks with insufficient emissions controls and legal requirements for the remedy of these emissions controls. Enhanced inspection and maintenance has been required on automobiles

registered in 13 counties surrounding Atlanta since October 1996. The affected counties are Cherokee, Clayton, Cobb, Coweta, DeKalb, Douglas, Fayette, Forsyth, Fulton, Gwinnett, Henry, Paulding, and Rockdale. In general, the requirement covers gasoline-powered cars and light trucks, specifically 24 model years old and newer.

Georgia gasoline/ Tier II Gasoline Standards: In 1999, the EPA announced federal standards for new vehicle emissions for NO_x which would be enforced for small cars by 2004 and passenger trucks by 2009. A parallel policy was introduced which would require reduced sulfur in gasoline starting from 2004 and be fully implemented by 2006. In addition to the direct effects on reducing sulfur, the use of low-sulfur gasoline was expected to greatly reduce emissions of PM and CO. The EPA estimated that these controls would lead to a 78% decrease in PM_{10} emissions by 2015.(10) In the early 2000s, Georgia adopted standards on the volatility levels and sulfur content of gasoline sold in the 45-county Atlanta metropolitan area. Despite these regulations, the Atlanta metropolitan area failed to achieve attainment of the 1997 Clean Air Act 1-hour ozone standard and was subsequently reclassified as a severe ozone nonattainment area on January 1, 2004. As a result, Atlanta was required to participate in the federal reformulated gasoline (RFG) program which placed additional standards on gasoline. These standards would be superseded by tighter federal restrictions as of January 1, 2006.

Heavy-Duty Highway Rule: The 2007 Heavy Duty Highway Rule was promulgated in 2001 (11). Like the Tier 2 gasoline rule, this program sets standards for both

engines and fuel. The goal of this legislation was to reduce ozone levels by reducing ozone precursor emissions (NO_x and non-methane hydrocarbons or NMHCs, a component of VOCs). One major aspect of the rule was limiting sulfur content to 15 ppm or less by June 2006. According to information from the Energy Information Administration, diesel sales in Georgia went from being comprised of 91% fuel with sulfur content between 15 and 500 ppm in 2006 to 35% in 2007, with the difference being declining sales of diesel with sulfur content greater than 500 ppm and increasing sales of fuel with sulfur content less than 15 ppm. By 2008, no diesel with sulfur content greater than 500 ppm was sold, and by 2012, 100% of fuel sold in Georgia had less than 15 ppm sulfur (12).

Georgia Multipollutant Rule/ Clean Air Interstate Rule (CAIR): The EPA's CAIR instituted standards for SO_2 and NO_x emissions from EGUs and created a cap-and-trade program to incentivize the voluntary lowering of emissions. The CAIR is estimated to prevent 17,000 premature deaths, 22,000 non-fatal heart attacks, 12,300 hospital admissions, and 1.7 million lost work days by 2015.(13) Selective catalytic reduction (SCR) and flue gas desulfurization (FGD) controls were required to be installed on all large coal-fired EGUs in Georgia. SCR controls were estimated to reduce NO_x levels by 85%, while FGD controls were estimated to reduce SO_2 by at least 95%.(14)

Acid Rain Program and GRAQC$_{yy}$: The ARP was finalized and promulgated in 1993 to combat increasing SO_2 and NO_X emissions throughout the United States, especially in eastern states (15). With Title IV of the Clean Air Act Amendments in 1990, the EPA set out to reduce annual SO_2 emissions in the United States by

50% in 2010 compared to 1980 levels. In order to achieve these reductions, the EPA used a cap and trade approach for SO_2 and an emissions factor (in mass per activity) limit for NO_x that included two phases. Phase I, which began in 1995 for SO_2 and 1996 for NO_x, targeted the largest existing power plants. Starting in 2000, Phase 2 required all other plants regulated under title IV of the CAA to achieve emissions reductions. In order to ensure reductions were being made, continuous emissions monitors were required for both SO_2 and NO_x on all regulated stacks (16).

NO_x Budget Trading Program (NBP) and the associated State Implement Plan (SIP) call and $GRAQC_{jjj}$: To address the problem of ozone precursors being transported across state lines in the East, EPA issued the NO_x SIP Call in 1998. This call was meant to improve the implementation of the controls established under the Acid Rain Program. The SIP call did not place a limit on individual sources; instead, it required each state to develop a plan to reduce NO_x emissions during the ozone season that contributed to non-attainment in downwind states, particularly in the northeastern United States (17). The EPA began the NBP under the 1998 SIP call to aid states in their effort to meet their emissions budgets. The NBP was a cap-and-trade strategy that was optional; however, all 20 states and the District of Columbia used the program to help meet their NO_x SIPs by 2007. A portion of northern Georgia was included under the original draft of the NO_x SIP Call, but was later removed from the requirements of the rule due to court actions and the EPA's re-designation of Birmingham, AL and Memphis, TN nonattainment areas. Georgia began requiring seasonal NO_x controls on EGU

sources in the 20-county Atlanta non-attainment area (ANAA) beginning in 2000 under a state program ($GRAQC_{jjj}$) similar to ones adopted by other states under the SIP Call.

4.4: Counterfactual ambient pollution level estimation

Researchers at the Georgia Institute of Technology produced sets of counterfactual ambient air pollution estimates for the years 1999-2013 that represented modeled levels of air pollution under hypothetical scenarios. Counterfactual scenarios that were assessed in Study Aim III included 9 separate scenarios in which each one of the 6 pollution control policies of interest was not implemented, as well as the scenario in which none of policies regulating mobile emissions were not implemented, the scenario in which none of the policies regulating EGU emissions were implemented, and finally the scenario in which none of the 6 policies of interest were implemented. For each scenario, daily counterfactual estimates were produced for a list of 9 pollutants: carbon monoxide (CO), ozone (O_3), nitrogen dioxide (NO_2), sulfur dioxide (SO_2), fine particulate matter ($PM_{2.5}$), sulfate (SO_4^{2-}), nitrate (NO_3^-), organic carbon (OC), and elemental carbon (EC).

Data on emissions was obtained from several sources. Power plant emissions were captured with continuous emissions monitoring (CEM), and additional emissions inventories were catalogued under the Visibility Improvement State and Tribal Association of the Southeast (VISTAS). Mobile source emissions were not directly measured, but rather modeled using software programs such as MOBILE and MOVES.

MOBILE estimates emissions from hydrocarbons, CO, and NO_x from cars, trucks, buses, and motorcycles.(18) MOVES can be used to estimate emissions for a broader range of pollutants, and includes methodological advancements such as refined modeling of vehicle speed profiles.(19) Figures 4.1 and 4.2 show estimates of counterfactual pollutant emissions if specific policies regulating mobile or EGU emissions had not been implemeted.

Figure 4.1. Counterfactual pollutant emissions estimates for policies affecting electricity-generating units. Counterfactuals are for scenarios without implementation for the following policies: Acid Rain Program and $GRAQC_{yy}$, NO_x Budget Program and State Implementation Call and $GRAQC_{jjj}$, and the Clean Air Interstate Rule/Georgia multipollutant rule.

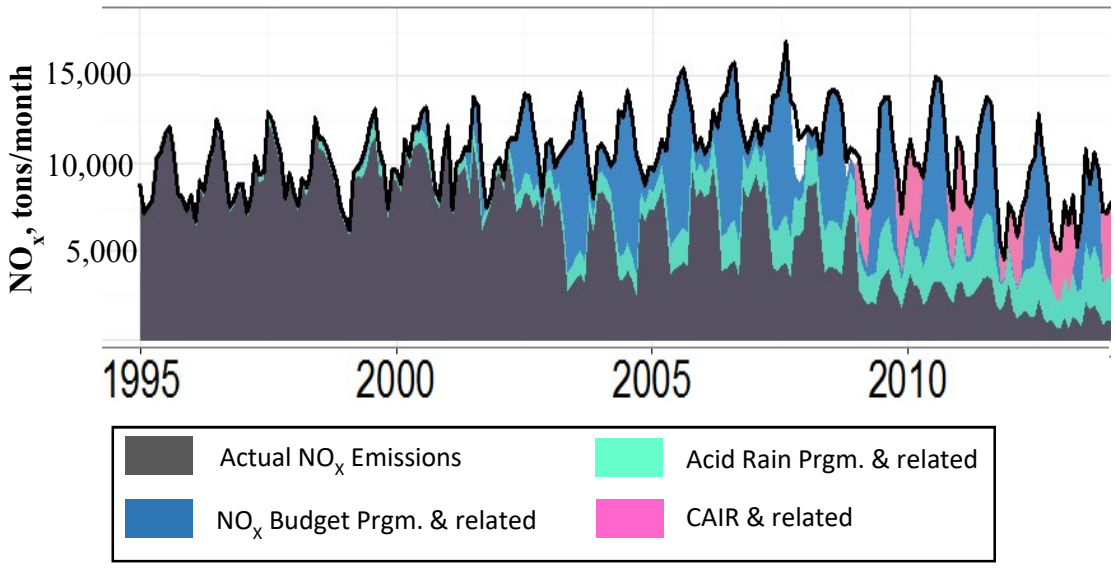
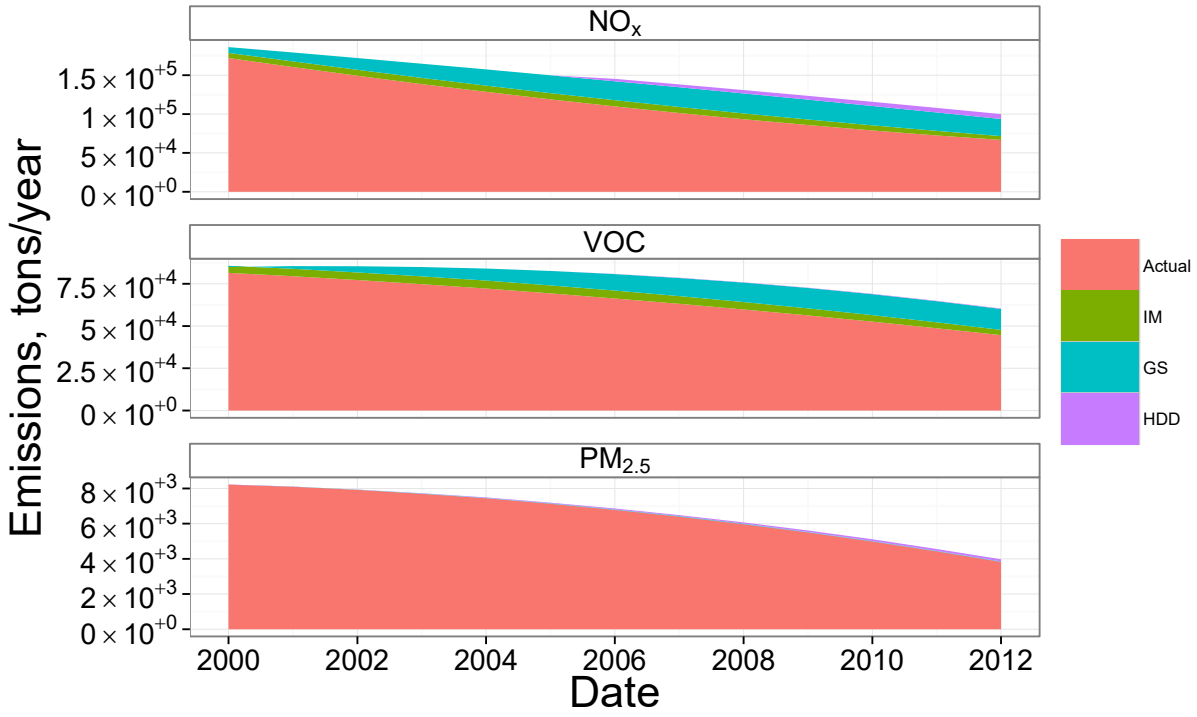


Figure 4.2. Counterfactual pollutant emissions estimates for policies affecting mobile sources. Counterfactuals are for scenarios without implementation for the following policies: Enhanced Vehicle Inspection and Maintenance (IM), the Georgia Gasoline Marketing Rule and Tier 2 Motor Vehicle Emissions Standards and Gasoline Sulfur Requirement (GS), and the Heavy-Duty Highway Rule (HDD).



Data on observed pollutant levels in the Atlanta metropolitan areas were collected from the SEARCH air quality monitors (see section 5.2). Both short-term and long-term meteorological trends can influence ambient air pollutant levels independent of emissions.(20) Detrending of pollutant time series data was performed to assess changes in pollutants controlling for meteorological changes.(21) This involved using non-linear filtering to separate the daily pollutant time series into several components: long-term (>365 days), seasonal (365 days), weekly (7 days), short-term meteorological (1-30 days), and white noise (1 day).(22) This approach was utilized to remove the effect of meteorology on ambient pollution, isolating the effect of emissions.

The Sparse Matrix Operator Kernel Emissions (SMOKE) modeling system was used to manage and process large emissions datasets.(23) These data was fed into a chemical transport model, the Community Multi-scale Air Quality model using the decoupled direct method (CMAQ-DDM/3D). CMAQ-DDM/3D was used to estimate sensitivity coefficients, which quantifies how ambient pollutant levels fluctuate with changes in emissions.(24) CMAQ -DDM/3D was used in conjunction with the Weather Research and Forecasting (WRF) model in order to best capture the dynamic pollutant/meteorology interaction processes.(25) The output from this model was simulated counterfactual pollutant estimates in the Atlanta metropolitan area.

4.5: Estimating number of ED visits prevented due to air pollution control programs

The steps which were involved in the estimation of ED visits prevented are shown in Figure 4.3. These steps were repeated for each counterfactual scenario in order to estimate the impact of each pollution control policy individually as well as the total effect of the 6 policies.

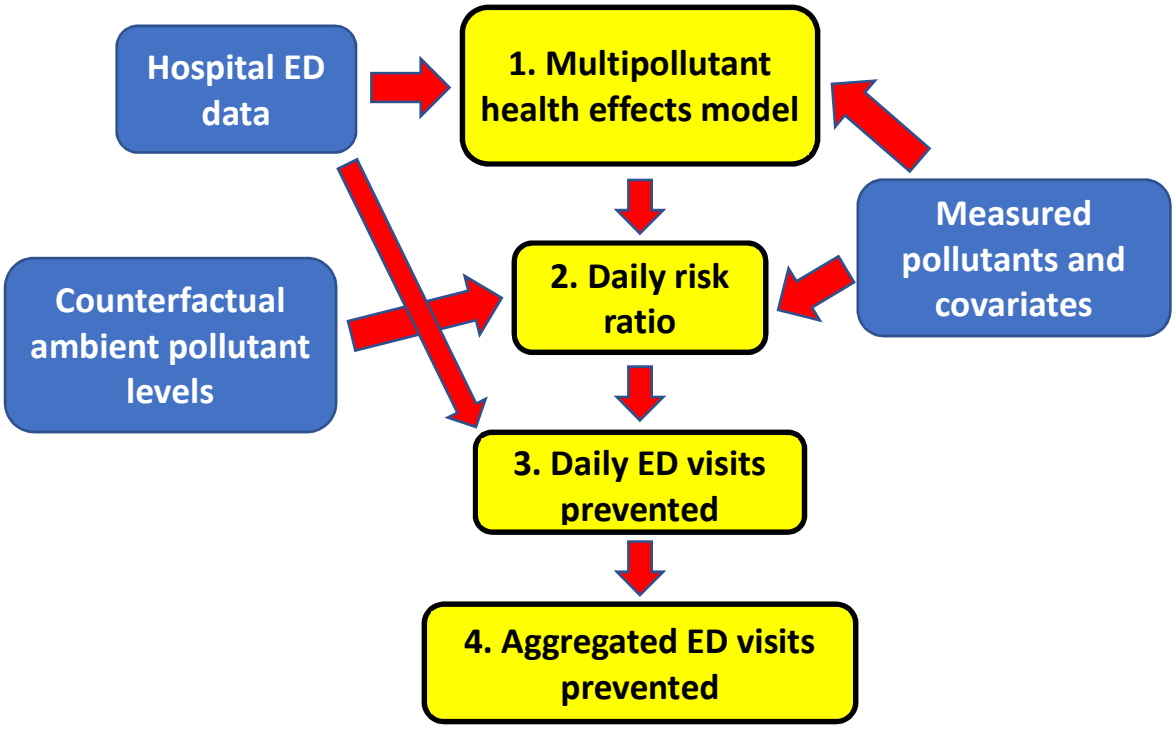
1. The multipollutant health effects model was created which estimated the associations between hospital ED data for 1999-2013 and measured pollutants and covariates.
2. The outputs of interest from the multipollutant health effects model were the coefficients for the pollutant effects. Under the counterfactual scenarios, the only predictor variables which are changed were the pollutant levels, therefore the coefficients for all covariates were disregarded from this step forward. The contrast

between measured and counterfactual pollutant levels were combined with pollutant coefficients to produce a risk ratio for each day in the study period.

3. The daily risk ratios, in conjunction with the daily time series of ED visits, were used to produce a time series of daily number of ED visits prevented by each emissions control policy.

4. The daily number of ED visits were summed over longer time periods (month, year, entire study period) to produce estimates for the number and percent of ED visits prevented during these time periods.

Figure 4.3. Steps involved in the estimation of ED visits prevented due to emissions control programs.



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CHAPTER 5: STUDY DATA AND OVERVIEW

5.1: SCAPE OP^{DTT} assay

Data collection for the measurement of particulate OP was conducted as an initiative of the Southeastern Center for Air Pollution & Epidemiology (SCAPE). SCAPE is a multidisciplinary collaboration between the Georgia Institute of Technology and Emory University researchers, and is aimed at achieving greater understanding of health-relevant air pollution mixtures. SCAPE consists of three cores (the Air Quality Core, the Biostatistics Core, and the Administrative Core) and four projects. Acquisition of air quality data for use in the proposed project was conducted by the Air Quality Core and Project 1; hospital emergency department data was collected by previous grants funding the Studies of Particles and Health in Atlanta (SOPHIA), and has fed into broader work performed by SCAPE.

To measure markers of oxidative stress, SCAPE Project 1 has developed methods for measurement of OP of ambient particulate matter.(1-4) The instrument for this study is a semi-automated dithiothreitol (DTT) system which measures the OP of water-soluble $PM_{2.5}$, referred to as OP^{DTT}. Previous studies involving DTT assays required extensive manual operation and labor, restricting the resulting number of measurements; the development of a semi-automated system allowed for the collection of a larger number of samples. These measurements were conducted in conjunction with the measurement of more standard pollutant measures.

Sampling took place at the Jefferson Street (JST) site, a mixed industrial/residential location in Atlanta, GA. JST is located at 829 Jefferson Street NW,

roughly 2 miles northwest of downtown Atlanta and about 1.4 miles from a major interstate highway (see map in Figure 5.1). The DTT assay was employed at JST from June 2012 – April 2013, producing a total of 196 days of measured OP^{DTT}. A breakdown of the sampling schedule is shown in Table 5.1. The data collection instrument utilized a high-volume sampler (HiVol, Thermo Anderson, nondenuded, nominal flow rate 1.13m^3 min^{-1}, $PM_{2.5}$ impactor). Pre-baked 8x10 inch quartz filters measured OP^{DTT} over 23 hour periods (noon-11am), then were immediately wrapped in prebaked aluminum foil and stored in a freezer. Analysis of filters for OP^{DTT} and other pollutant measures started in March 2013. Other measurements from these filters included organic carbon (OC), water-soluble organic carbon (WSOC), elemental carbon (EC), inorganic ions, water-soluble brown carbon (BrnC), and water-soluble transition metals.

Figure 5.1. 5-county Atlanta metropolitan area, showing major highways and the Jefferson street site location (JST).

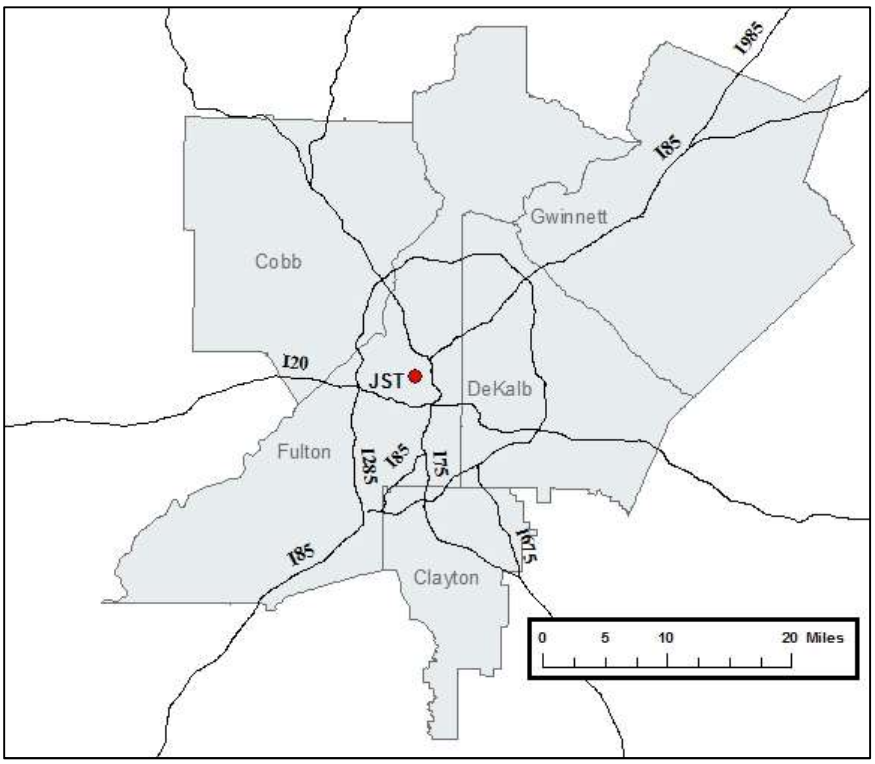


Table 5.1. Sampling schedule and number of 24-hr integrated Hi-Vol filters from Jefferson Street (JST), 2012-2013

Start date	End date	Season	Filters
June 8, 2012	July 15, 2012	Summer	31
July 24, 2012	August 31, 2012	Summer	37
September 6, 2012	October 4, 2012	Fall	26
November 16, 2012	November 30, 2012	Fall	13
December 6, 2012	January 4, 2013	Winter	22
January 27, 2013	February 27, 2013	Winter	30
March 5, 2013	March 27, 2013	Winter	23
March 30, 2013	April 12, 2013	Spring	14
Total number of filters			**196**

5.2: SEARCH Jefferson Street air quality data

Jefferson Street is also a preexisting site for the Southeastern Aerosol Research and Characterization study (SEARCH). The primary objectives for SEARCH include the characterization of temporal and spatial variability of pollutant mixtures, especially particulate matter.(5) SEARCH also emphasized the development of continuous gas and PM measurements to replace or supplement existing discrete sampling methods, which were utilized concurrently for validation purposes. Daily sampling at this site started from August 1, 1998, and overlaps with the time frame of the SCAPE data collection.

For this study, continuous or semi-continuous measurements of gases, particulate matter, and surface meteorology from SEARCH instruments were converted to daily

values. A summary of the available air quality variables is shown in Table 5.2. Time trends for selected pollutants are shown in Figure 5.3.

Table 5.2. SEARCH Atlanta area air quality raw measurements, 8/1/1998 – 1/1/2013. N=number of samples, N Miss=number of missing samples, Std Dev=standard deviation, IQR=interquartile range.

Variable	N	N Miss	Mean	Std Dev	IQR
Gas/meteorology combined I hour datasets (1998-2004)					
WSP	52,434	3,846	1.85	1.14	(0.97 - 2.56)
WDR	51,652	4,628	211.39	97.08	(123.36 - 298.36)
TEMP	53,320	2,960	17.57	8.86	(11.20 - 24.24)
RH	52,714	3,566	68.77	21.33	(52.18 - 87.27)
BP	52,532	3,748	985.63	5.36	(982.25 - 988.96)
SR	53,995	2,285	165.11	238.79	(1.17 - 285.73)
PRECIP	50,972	5,308	0.15	2.73	(0.00 - 0.00)
O3	52,596	3,684	23.69	22.49	(4.83 - 35.10)
CO	51,742	4,538	508.42	575.14	(237.12 - 508.32)
SO2	51,432	4,848	5.35	7.52	(1.22 - 6.15)
NO	53,330	2,950	26.66	58.44	(1.66 - 19.68)
NO2	50,361	5,919	20.37	14.27	(9.48 - 27.98)
HNO3	50,648	5,632	1.09	1.38	(0.10 - 1.48)
NOy	53,061	3,219	53.15	68.15	(17.14 - 56.84)
NH3 5 min (2008)					
Average_NH3_ppb_	93,116	12,292	1.62	1.10	(0.85 - 2.15)
Min_NH3_ppb_	93,116	12,292	1.39	1.06	(0.64 - 1.91)
Max_NH3_ppb_	93,116	12,292	1.87	1.25	(1.02 - 2.44)
StDev_NH3_ppb_	93,116	12,292	0.20	0.29	(0.08 - 0.25)
Median_NH3_ppb_	93,116	12,292	1.62	1.11	(0.85 - 2.15)
Count_NH3	93,116	12,292	4.98	0.16	(5.00 - 5.00)
NH3 1 hour (2008)					
Average_NH3_ppb_	8,064	720	1.61	1.03	(0.87 - 2.14)
Min_NH3_ppb_	8,064	720	1.16	0.85	(0.55 - 1.61)
Max_NH3_ppb_	8,064	720	2.14	1.42	(1.17 - 2.77)
StDev_NH3_ppb_	8,064	720	0.30	0.30	(0.13 - 0.36)
Median_NH3_ppb_	8,064	720	1.60	1.02	(0.87 - 2.13)
Count_NH3	8,064	720	11.41	1.33	(12.00 - 12.00)
NH3 24 hour (2008-2010)					
Average_NH3_ppb	313	783	1.38	0.62	(0.96 - 1.80)

Gas 5 min (2011-2013)					
Average_O3_ppb_	298,044	17,604	27.47	18.51	(13.11 - 39.08)
Min_O3_ppb_	298,044	17,604	26.22	18.36	(11.64 - 37.78)
Max_O3_ppb_	298,044	17,604	28.63	18.68	(14.45 - 40.28)
StDev_O3_ppb_	298,044	17,604	1.00	1.04	(0.35 - 1.25)
Median_O3_ppb_	298,044	17,604	27.52	18.56	(13.13 - 39.17)
Count_O3	298,044	17,604	4.99	0.14	(5.00 - 5.00)
Average_CO_ppb_	264,031	51,617	244.04	170.99	(155.14 - 260.05)
Min_CO_ppb_	264,031	51,617	234.02	163.50	(148.38 - 250.80)
Max_CO_ppb_	264,031	51,617	254.88	182.21	(161.95 - 270.32)
StDev_CO_ppb_	264,031	51,617	8.72	20.01	(3.44 - 8.81)
Median_CO_ppb_	264,031	51,617	243.84	170.87	(155.07 - 259.92)
Count_CO	264,031	51,617	4.88	0.43	(5.00 - 5.00)
Average_SO2_ppb_	260,463	55,185	1.03	2.68	(0.18 - 0.85)
Min_SO2_ppb_	260,463	55,185	0.86	2.18	(0.13 - 0.76)
Max_SO2_ppb_	260,463	55,185	1.20	3.29	(0.22 - 0.95)
StDev_SO2_ppb_	260,463	55,185	0.14	0.65	(0.03 - 0.07)
Median_SO2_ppb_	260,463	55,185	1.02	2.69	(0.18 - 0.85)
Count_SO2	260,463	55,185	4.91	0.38	(5.00 - 5.00)
Average_NO_ppb_	296,357	19,291	8.92	29.03	(0.25 - 4.16)
Min_NO_ppb_	296,357	19,291	7.24	25.37	(0.10 - 2.79)
Max_NO_ppb_	296,357	19,291	10.91	34.13	(0.43 - 5.82)
StDev_NO_ppb_	296,357	19,291	1.54	6.02	(0.08 - 1.00)
Median_NO_ppb_	296,357	19,291	8.77	29.06	(0.22 - 3.94)
Count_NO	296,357	19,291	4.99	0.13	(5.00 - 5.00)
Average_NO2_ppb_	295,966	19,682	12.47	10.53	(4.59 - 17.46)
Min_NO2_ppb_	295,966	19,682	10.56	9.35	(3.58 - 14.87)
Max_NO2_ppb_	295,966	19,682	14.58	12.37	(5.57 - 20.14)
StDev_NO2_ppb_	295,966	19,682	1.67	2.40	(0.40 - 1.97)
Median_NO2_ppb_	295,966	19,682	12.39	10.58	(4.49 - 17.37)
Count_NO2	295,966	19,682	4.98	0.18	(5.00 - 5.00)
Average_NOy_ppb_	294,837	20,811	22.72	35.31	(6.88 - 23.06)
Min_NOy_ppb_	294,837	20,811	20.34	31.88	(6.04 - 20.58)
Max_NOy_ppb_	294,837	20,811	25.38	39.66	(7.71 - 25.96)
StDev_NOy_ppb_	294,837	20,811	2.10	5.40	(0.36 - 1.99)
Median_NOy_ppb_	294,837	20,811	22.56	35.29	(6.77 - 22.94)
Count_NOy	294,837	20,811	4.99	0.10	(5.00 - 5.00)
Average_HNO3_ppb_	275,849	39,799	0.39	0.41	(0.12 - 0.51)
Min_HNO3_ppb_	275,849	39,799	0.28	0.42	(0.02 - 0.40)
Max_HNO3_ppb_	275,849	39,799	0.50	0.43	(0.21 - 0.66)
StDev_HNO3_ppb_	275,849	39,799	0.09	0.08	(0.04 - 0.11)
Median_HNO3_ppb_	275,849	39,799	0.38	0.41	(0.12 - 0.51)
Count_HNO3	275,849	39,799	4.97	0.19	(5.00 - 5.00)

Average_NH3_ppb_	189,713	125,935	1.47	0.99	(0.78 - 1.95)
Min_NH3_ppb_	189,713	125,935	1.24	0.93	(0.57 - 1.71)
Max_NH3_ppb_	189,713	125,935	1.72	1.12	(0.95 - 2.23)
StDev_NH3_ppb_	189,713	125,935	0.20	0.23	(0.08 - 0.23)
Median_NH3_ppb_	189,713	125,935	1.47	0.99	(0.77 - 1.95)
Count_NH3	189,713	125,935	4.99	0.12	(5.00 - 5.00)
Gas 1 hour (2005-2013)					
Average_O3_ppb_	76,850	2,038	25.84	19.23	(10.52 - 37.25)
Min_O3_ppb_	76,850	2,038	21.25	18.48	(5.11 - 32.18)
Max_O3_ppb_	76,850	2,038	29.76	19.92	(15.07 - 41.41)
StDev_O3_ppb_	76,850	2,038	2.75	2.25	(1.24 - 3.63)
Median_O3_ppb_	76,850	2,038	26.03	19.46	(10.39 - 37.67)
Count_O3	76,850	2,038	11.63	1.11	(12.00 - 12.00)
Average_CO_ppb_	75,208	3,680	302.85	257.51	(180.07 - 314.55)
Min_CO_ppb_	75,208	3,680	263.02	211.01	(162.70 - 275.85)
Max_CO_ppb_	75,208	3,680	356.08	347.75	(199.13 - 364.19)
StDev_CO_ppb_	75,208	3,680	30.72	62.55	(8.83 - 28.06)
Median_CO_ppb_	75,208	3,680	303.34	256.43	(180.68 - 315.07)
Count_CO	75,208	3,680	10.51	0.85	(10.00 - 11.00)
Average_SO2_ppb_	75,343	3,545	2.61	5.29	(0.37 - 2.47)
Min_SO2_ppb_	75,343	3,545	1.48	2.92	(0.22 - 1.56)
Max_SO2_ppb_	75,343	3,545	4.45	9.88	(0.55 - 3.58)
StDev_SO2_ppb_	75,343	3,545	1.00	2.76	(0.07 - 0.57)
Median_SO2_ppb_	75,343	3,545	2.55	5.34	(0.35 - 2.37)
Count_SO2	75,343	3,545	10.46	0.88	(10.00 - 11.00)
Average_NO_ppb_	75,573	3,315	13.42	35.83	(0.61 - 7.53)
Min_NO_ppb_	75,573	3,315	7.31	25.33	(0.08 - 2.64)
Max_NO_ppb_	75,573	3,315	23.94	55.18	(1.70 - 17.24)
StDev_NO_ppb_	75,573	3,315	5.44	13.21	(0.41 - 4.20)
Median_NO_ppb_	75,573	3,315	12.41	35.40	(0.35 - 6.31)
Count_NO	75,573	3,315	11.61	1.13	(12.00 - 12.00)
Average_NO2_ppb_	71,575	7,313	15.65	12.06	(6.29 - 22.20)
Min_NO2_ppb_	71,575	7,313	11.15	9.77	(3.79 - 15.76)
Max_NO2_ppb_	71,575	7,313	22.13	15.52	(10.12 - 30.70)
StDev_NO2_ppb_	71,575	7,313	3.45	2.88	(1.47 - 4.52)
Median_NO2_ppb_	71,575	7,313	15.30	12.24	(5.82 - 21.85)
Count_NO2	71,575	7,313	11.51	1.21	(12.00 - 12.00)
Average_NOy_ppb_	76,370	2,518	30.66	42.90	(9.26 - 31.80)
Min_NOy_ppb_	76,370	2,518	21.47	32.30	(6.31 - 21.96)
Max_NOy_ppb_	76,370	2,518	44.77	60.94	(13.93 - 46.75)
StDev_NOy_ppb_	76,370	2,518	7.63	12.99	(1.90 - 7.60)
Median_NOy_ppb_	76,370	2,518	29.56	42.60	(8.64 - 30.66)

Count_NOy	76,370	2,518	11.49	1.25	(12.00 - 12.00)
Average_HNO3_ppb_	32,568	46,320	0.41	0.44	(0.13 - 0.53)
Min_HNO3_ppb_	32,568	46,320	0.28	0.43	(0.01 - 0.39)
Max_HNO3_ppb_	32,568	46,320	0.56	0.47	(0.25 - 0.71)
StDev_HNO3_ppb_	32,568	46,320	0.08	0.06	(0.05 - 0.10)
Median_HNO3_ppb_	32,568	46,320	0.41	0.44	(0.14 - 0.53)
Count_HNO3	32,568	46,320	11.13	1.46	(11.00 - 12.00)
Average_NH3_ppb_	24,279	54,609	1.67	1.14	(0.87 - 2.18)
Min_NH3_ppb_	24,279	54,609	1.24	0.93	(0.58 - 1.70)
Max_NH3_ppb_	24,279	54,609	2.20	1.54	(1.16 - 2.83)
StDev_NH3_ppb_	24,279	54,609	0.30	0.30	(0.13 - 0.36)
Median_NH3_ppb_	24,279	54,609	1.65	1.14	(0.86 - 2.16)
Count_NH3	24,279	54,609	11.46	1.32	(12.00 - 12.00)
Met 5 min (2011-2013)					
Average_WSP_m_s_	309,280	6,368	1.67	1.11	(0.80 - 2.32)
Min_WSP_m_s_	309,280	6,368	1.19	0.91	(0.50 - 1.69)
Max_WSP_m_s_	309,280	6,368	2.18	1.38	(1.08 - 3.01)
StDev_WSP_m_s_	309,280	6,368	0.40	0.28	(0.19 - 0.54)
Median_WSP_m_s_	309,280	6,368	1.65	1.12	(0.78 - 2.30)
Count_WSP	309,280	6,368	4.99	0.08	(5.00 - 5.00)
Average_WDR_Deg_	309,530	6,118	206.50	90.34	(127.75 - 285.74)
Min_WDR_Deg_	309,530	6,118	179.01	92.38	(96.60 - 256.95)
Max_WDR_Deg_	309,530	6,118	229.72	88.63	(151.29 - 310.33)
StDev_WDR_Deg_	309,530	6,118	24.07	43.55	(7.03 - 19.26)
Median_WDR_Deg_	309,530	6,118	206.27	88.51	(127.61 - 284.14)
Count_WDR	309,530	6,118	4.99	0.08	(5.00 - 5.00)
Average_TEMP_Deg_C_	310,964	4,684	17.37	8.46	(10.88 - 23.93)
Min_TEMP_Deg_C_	310,964	4,684	17.30	8.45	(10.82 - 23.87)
Max_TEMP_Deg_C_	310,964	4,684	17.44	8.48	(10.94 - 24.00)
StDev_TEMP_Deg_C_	310,964	4,684	0.06	0.06	(0.02 - 0.07)
Median_TEMP_Deg_C_	310,964	4,684	17.37	8.46	(10.88 - 23.93)
Count_TEMP	310,964	4,684	4.99	0.08	(5.00 - 5.00)
Average_RH___	310,715	4,933	67.73	21.15	(51.14 - 86.10)
Min_RH___	310,715	4,933	67.25	21.28	(50.54 - 85.70)
Max_RH___	310,715	4,933	68.22	21.01	(51.76 - 86.50)
StDev_RH___	310,715	4,933	0.40	0.39	(0.14 - 0.53)
Median_RH___	310,715	4,933	67.72	21.16	(51.14 - 86.09)
Count_RH	310,715	4,933	4.99	0.08	(5.00 - 5.00)
Average_BP_mbar_	311,316	4,332	983.43	5.25	(980.04 - 986.87)
Min_BP_mbar_	311,316	4,332	983.41	5.25	(980.01 - 986.84)
Max_BP_mbar_	311,316	4,332	983.46	5.25	(980.07 - 986.89)
StDev_BP_mbar_	311,316	4,332	0.02	0.02	(0.01 - 0.03)

Median_BP_mbar_	311,316	4,332	983.43	5.25	(980.04 - 986.87)
Count_BP	311,316	4,332	4.99	0.08	(5.00 - 5.00)
Average_SR_W_m2_	311,104	4,544	187.50	281.98	(0.00 - 308.42)
Min_SR_W_m2_	311,104	4,544	168.56	261.42	(0.00 - 258.71)
Max_SR_W_m2_	311,104	4,544	205.69	307.10	(0.00 - 343.12)
StDev_SR_W_m2_	311,104	4,544	15.76	46.88	(0.05 - 6.21)
Median_SR_W_m2_	311,104	4,544	187.90	285.16	(0.00 - 300.30)
Count_SR	311,104	4,544	5.00	0.07	(5.00 - 5.00)
Average_RAINFALL_Inches_	311,998	3,650	5.30	5.06	(1.11 - 8.29)
Min_RAINFALL_Inches_	311,998	3,650	5.30	5.06	(1.11 - 8.29)
Max_RAINFALL_Inches_	311,998	3,650	5.30	5.06	(1.11 - 8.29)
StDev_RAINFALL_Inches_	311,998	3,650	0.00	0.00	(0.00 - 0.00)
Median_RAINFALL_Inches_	311,998	3,650	5.30	5.06	(1.11 - 8.29)
Count_RAINFALL	311,998	3,650	4.99	0.08	(5.00 - 5.00)
Average_2M_TEMP_Deg_C_	292,380	23,268	17.68	8.57	(11.10 - 24.16)
Min_2M_TEMP_Deg_C_	292,380	23,268	17.61	8.55	(11.02 - 24.10)
Max_2M_TEMP_Deg_C_	292,380	23,268	17.77	8.60	(11.16 - 24.24)
StDev_2M_TEMP_Deg_C_	292,380	23,268	0.07	0.07	(0.02 - 0.08)
Median_2M_TEMP_Deg_C_	292,380	23,268	17.69	8.57	(11.10 - 24.17)
Count_2M_TEMP	292,380	23,268	4.99	0.08	(5.00 - 5.00)
Average_2M_RH___	292,394	23,254	68.73	20.47	(52.65 - 86.70)
Min_2M_RH___	292,394	23,254	68.18	20.71	(51.84 - 86.34)
Max_2M_RH___	292,394	23,254	69.30	20.21	(53.50 - 87.10)
StDev_2M_RH___	292,394	23,254	0.46	0.53	(0.13 - 0.62)
Median_2M_RH___	292,394	23,254	68.72	20.48	(52.61 - 86.70)
Count_2M_RH	292,394	23,254	4.99	0.08	(5.00 - 5.00)
Average_2M_SWS___	303,998	11,650	2.60	58.90	(0.22 - 0.52)
Min_2M_SWS___	303,998	11,650	2.47	57.73	(0.21 - 0.50)
Max_2M_SWS___	303,998	11,650	2.75	61.71	(0.22 - 0.52)
StDev_2M_SWS___	303,998	11,650	0.35	10.09	(0.00 - 0.01)
Median_2M_SWS___	303,998	11,650	2.60	59.55	(0.22 - 0.52)
Count_2M_SWS	303,998	11,650	4.99	0.08	(5.00 - 5.00)
Met 5 min (2005-2013)					
Average_WSP_m_s_	76,604	2,284	1.80	1.04	(1.01 - 2.45)
Min_WSP_m_s_	76,604	2,284	1.22	0.87	(0.57 - 1.73)
Max_WSP_m_s_	76,604	2,284	2.45	1.28	(1.47 - 3.26)
StDev_WSP_m_s_	76,604	2,284	0.38	0.20	(0.23 - 0.48)
Median_WSP_m_s_	76,604	2,284	1.79	1.05	(0.99 - 2.44)
Count_WSP	76,604	2,284	11.97	0.28	(12.00 - 12.00)
Average_WDR_Deg_	76,622	2,266	195.04	104.07	(94.88 - 292.40)
Min_WDR_Deg_	76,622	2,266	142.02	103.77	(51.29 - 237.74)
Max_WDR_Deg_	76,622	2,266	239.89	101.40	(143.87 - 331.90)

StDev_WDR_Deg_	76,622	2,266	37.82	54.76	(7.67 - 35.26)
Median_WDR_Deg_	76,622	2,266	194.57	99.45	(97.46 - 288.14)
Count_WDR	76,622	2,266	11.97	0.28	(12.00 - 12.00)
Average_TEMP_Deg_C_	77,953	935	17.23	9.13	(10.35 - 24.22)
Min_TEMP_Deg_C_	77,953	935	16.77	9.08	(9.90 - 23.74)
Max_TEMP_Deg_C_	77,953	935	17.70	9.17	(10.81 - 24.68)
StDev_TEMP_Deg_C_	77,953	935	0.31	0.28	(0.13 - 0.40)
Median_TEMP_Deg_C_	77,953	935	17.23	9.13	(10.35 - 24.22)
Count_TEMP	77,953	935	11.97	0.28	(12.00 - 12.00)
Average_RH___	77,911	977	67.06	21.66	(49.65 - 86.08)
Min_RH___	77,911	977	64.89	21.89	(47.10 - 83.80)
Max_RH___	77,911	977	69.22	21.45	(52.11 - 88.28)
StDev_RH___	77,911	977	1.44	1.39	(0.59 - 1.84)
Median_RH___	77,911	977	67.08	21.72	(49.59 - 86.19)
Count_RH	77,911	977	11.95	0.32	(12.00 - 12.00)
Average_BP_mbar_	78,007	881	983.14	5.30	(979.87 - 986.45)
Min_BP_mbar_	78,007	881	982.92	5.31	(979.66 - 986.25)
Max_BP_mbar_	78,007	881	983.36	5.28	(980.09 - 986.64)
StDev_BP_mbar_	78,007	881	0.14	0.11	(0.07 - 0.19)
Median_BP_mbar_	78,007	881	983.14	5.30	(979.86 - 986.45)
Count_BP	78,007	881	11.97	0.24	(12.00 - 12.00)
Average_PRECIP_Inches_	12,055	66,833	0.15	1.14	(0.00 - 0.00)
Min_PRECIP_Inches_	12,055	66,833	0.00	0.02	(0.00 - 0.00)
Max_PRECIP_Inches_	12,055	66,833	0.05	0.39	(0.00 - 0.00)
StDev_PRECIP_Inches_	12,055	66,833	0.15	1.10	(0.00 - 0.00)
Median_PRECIP_Inches_	12,055	66,833	0.01	0.06	(0.00 - 0.00)
Count_PRECIP	12,055	66,833	11.98	0.26	(12.00 - 12.00)
Average_SR_W_m2_	77,080	1,808	189.88	276.44	(0.22 - 333.39)
Min_SR_W_m2_	77,080	1,808	131.77	220.15	(0.00 - 189.09)
Max_SR_W_m2_	77,080	1,808	247.49	335.58	(0.36 - 476.20)
StDev_SR_W_m2_	77,080	1,808	38.10	60.61	(0.06 - 56.23)
Median_SR_W_m2_	77,080	1,808	190.13	282.25	(0.18 - 324.93)
Count_SR	77,080	1,808	11.96	0.29	(12.00 - 12.00)
Average_RAINFALL_Inches_	56,763	22,125	5.09	5.75	(0.95 - 6.84)
Min_RAINFALL_Inches_	56,763	22,125	5.08	5.75	(0.95 - 6.84)
Max_RAINFALL_Inches_	56,763	22,125	5.09	5.75	(0.96 - 6.84)
StDev_RAINFALL_Inches_	56,763	22,125	0.00	0.08	(0.00 - 0.00)
Median_RAINFALL_Inches_	56,763	22,125	5.09	5.75	(0.95 - 6.84)
Count_RAINFALL	56,763	22,125	11.97	0.26	(12.00 - 12.00)
Average_2M_TEMP_Deg_C_	24,358	54,530	17.69	8.56	(11.10 - 24.15)
Min_2M_TEMP_Deg_C_	24,358	54,530	17.18	8.49	(10.62 - 23.65)
Max_2M_TEMP_Deg_C_	24,358	54,530	18.20	8.64	(11.57 - 24.70)
StDev_2M_TEMP_Deg_C_	24,358	54,530	0.34	0.29	(0.14 - 0.45)

Median_2M_TEMP_Deg_C_	24,358	54,530	17.68	8.56	(11.10 - 24.14)
Count_2M_TEMP	24,358	54,530	11.98	0.20	(12.00 - 12.00)
Average_2M_RH___	24,392	54,496	68.72	20.37	(52.70 - 86.58)
Min_2M_RH___	24,392	54,496	66.53	20.68	(50.17 - 84.36)
Max_2M_RH___	24,392	54,496	70.87	20.09	(55.31 - 88.76)
StDev_2M_RH___	24,392	54,496	1.43	1.36	(0.62 - 1.84)
Median_2M_RH___	24,392	54,496	68.73	20.43	(52.60 - 86.64)
Count_2M_RH	24,392	54,496	11.98	0.20	(12.00 - 12.00)
Average_2M_SWS___	25,350	53,538	2.60	55.17	(0.22 - 0.57)
Min_2M_SWS___	25,350	53,538	1.87	48.30	(0.21 - 0.46)
Max_2M_SWS___	25,350	53,538	3.73	71.78	(0.23 - 0.89)
StDev_2M_SWS___	25,350	53,538	0.72	21.45	(0.00 - 0.09)
Median_2M_SWS___	25,350	53,538	2.60	58.53	(0.22 - 0.52)
Count_2M_SWS	25,350	53,538	11.98	0.22	(12.00 - 12.00)
PM coarse (1998-2013)					
Coarse_Mass_ug_m3	4,693	1,019	8.07	4.60	(4.93 - 10.19)
Coarse_SO4_ug_m3	3,727	1,985	0.29	0.58	(0.10 - 0.31)
Coarse_NO3_ug_m3	3,727	1,985	0.46	0.63	(0.18 - 0.54)
Coarse_NH4_ug_m3	3,727	1,985	0.09	0.46	(0.00 - 0.04)
CoarseMMO_ug_m3	3,320	2,392	3.18	2.30	(1.53 - 4.17)
WSM_SUM_ug_m3	3,183	2,529	0.08	0.46	(0.01 - 0.03)
WS_Cr_ug_m3	3,598	2,114	0.12	0.94	(0.00 - 0.00)
WS_Cu_ug_m3	3,589	2,123	0.03	0.24	(0.00 - 0.00)
WS_Fe_ug_m3	3,593	2,119	0.08	0.62	(0.00 - 0.02)
WS_Mn_ug_m3	3,594	2,118	0.06	0.60	(0.00 - 0.00)
WS_Ni_ug_m3	3,600	2,112	0.12	0.94	(0.00 - 0.00)
WS_V_ug_m3	3,592	2,120	0.13	1.02	(0.00 - 0.00)
Al2O3_ug_m3	2,913	2,799	0.62	0.56	(0.26 - 0.81)
SiO2_ug_m3	2,905	2,807	1.48	1.11	(0.67 - 1.96)
K2O_ug_m3	2,905	2,807	0.24	0.83	(0.08 - 0.19)
CaO_ug_m3	2,913	2,799	0.44	0.38	(0.21 - 0.57)
TiO2_ug_m3	2,905	2,807	0.15	0.67	(0.02 - 0.07)
Fe2O3_ug_m3	2,905	2,807	0.59	0.43	(0.30 - 0.76)
Coarse_S	2,828	2,884	0.12	0.09	(0.06 - 0.14)
XRF_Al_ug_m3	493	5,219	0.40	1.16	(0.10 - 0.30)
XRF_Ca_ug_m3	493	5,219	0.31	0.86	(0.11 - 0.29)
XRF_Cu_ug_m3	489	5,223	0.64	1.78	(0.00 - 0.01)
XRF_Fe_ug_m3	492	5,220	0.37	0.57	(0.17 - 0.42)
XRF_K_ug_m3	493	5,219	0.80	2.08	(0.06 - 0.14)
XRF_Mn_ug_m3	493	5,219	0.58	1.51	(0.00 - 0.01)
XRF_Pb_ug_m3	489	5,223	1.23	2.94	(0.00 - 0.00)
XRF_S_ug_m3	491	5,221	0.70	1.83	(0.05 - 0.14)

XRF_Si_ug_m3	493	5,219	0.53	0.56	(0.24 - 0.65)
XRF_Ti_ug_m3	493	5,219	0.48	1.33	(0.01 - 0.04)
XRF_Zn_ug_m3	489	5,223	0.77	2.04	(0.00 - 0.01)
Coarse_Cl_ug_m3	432	5,280	0.08	0.26	(0.01 - 0.03)
PMcoarse_Calcium_ug_m3	434	5,278	0.22	0.14	(0.12 - 0.29)
PMcoarse_Magnesium_ug_m3	434	5,278	0.03	0.03	(0.02 - 0.04)
PMcoarse_Potassium_ug_m3	435	5,277	0.02	0.02	(0.01 - 0.03)
PMcoarse_Sodium_ug_m3	420	5,292	0.14	0.26	(0.01 - 0.16)
PMcoarse_XRF_Na__ug_m3_	198	5,514	0.07	0.11	(0.02 - 0.08)
PMcoarse_Zn_68__ng_m3_	367	5,345	5.01	8.45	(2.55 - 5.65)
PMcoarse_As_75__ng_m3_	393	5,319	0.05	0.07	(0.01 - 0.06)
PMcoarse_Se_82__ng_m3_	422	5,290	0.09	0.10	(0.03 - 0.12)
PMcoarse_Cd_114__ng_m3_	424	5,288	0.01	0.01	(0.01 - 0.01)
PMcoarse_Ba_137__ng_m3_	425	5,287	7.04	4.99	(3.84 - 8.81)
PMcoarse_La_139__ng_m3_	425	5,287	0.02	0.03	(0.01 - 0.02)
PMcoarse_Pb_208__ng_m3_	198	5,514	0.15	0.47	(0.00 - 0.16)
PM fine (1998-2007)					
FRM_Mass	3,008	463	16.99	8.27	(10.85 - 21.58)
FRM_SO4	757	2,714	5.51	3.49	(2.89 - 7.30)
FRM_NO3	762	2,709	0.27	0.63	(0.03 - 0.16)
FRM_NH4	766	2,705	2.05	1.26	(1.10 - 2.68)
PCM1_Mass	672	2,799	18.06	8.77	(11.12 - 23.55)
PCM1_SO4	3,220	251	4.74	3.33	(2.33 - 6.11)
PCM1_NO3	3,218	253	0.93	0.81	(0.39 - 1.22)
PCM1_Vol_NO3	3,217	254	0.74	0.51	(0.37 - 0.99)
PCM1_Teflon_NO3	3,218	253	0.19	0.51	(0.01 - 0.09)
PCM1_NH4	2,483	988	2.39	1.41	(1.33 - 3.13)
PCM1_Vol_NH4	2,499	972	0.67	0.56	(0.30 - 0.89)
PCM1_Teflon_NH4	3,204	267	1.67	1.14	(0.84 - 2.15)
PM25_MajorMetalOxides	2,946	525	0.53	0.48	(0.28 - 0.63)
PM25_WSM_SUM	3,254	217	0.03	0.03	(0.02 - 0.04)
PCM2_SO4	723	2,748	5.46	3.64	(2.79 - 6.95)
PCM2_NO3	723	2,748	1.11	0.87	(0.51 - 1.46)
PCM2_NH4	722	2,749	1.99	1.32	(1.04 - 2.53)
PCM2_CL	723	2,748	0.11	0.08	(0.06 - 0.13)
PCM3_EC	3,327	144	1.55	1.10	(0.83 - 1.92)
PCM3_OC	3,328	143	4.19	2.32	(2.65 - 5.10)
XRF_As	2,946	525	0.00	0.00	(0.00 - 0.00)
XRF_Ba	2,946	525	0.02	0.01	(0.01 - 0.01)
XRF_Br	2,946	525	0.00	0.01	(0.00 - 0.00)
XRF_Cu	2,946	525	0.01	0.02	(0.00 - 0.00)
XRF_Mn	2,946	525	0.00	0.00	(0.00 - 0.00)

XRF_Pb	2,946	525	0.01	0.02	(0.00 - 0.01)
XRF_Sb	2,946	525	0.00	0.01	(0.00 - 0.00)
XRF_Se	2,946	525	0.00	0.00	(0.00 - 0.00)
XRF_Sn	2,946	525	0.00	0.00	(0.00 - 0.00)
XRF_Ti	2,946	525	0.00	0.00	(0.00 - 0.00)
XRF_Zn	2,946	525	0.01	0.01	(0.01 - 0.01)
WS_Chromium	3,243	228	0.00	0.00	(0.00 - 0.00)
WS_Copper	3,237	234	0.00	0.02	(0.00 - 0.00)
WS_Iron	3,235	236	0.03	0.02	(0.01 - 0.04)
WS_Manganese	3,231	240	0.00	0.00	(0.00 - 0.00)
WS_Nickel	3,246	225	0.00	0.00	(0.00 - 0.00)
WS_Vanadium	3,231	240	0.00	0.00	(0.00 - 0.00)
Al2O3	2,946	525	0.06	0.10	(0.01 - 0.07)
SiO2	2,946	525	0.22	0.25	(0.10 - 0.26)
K2O	2,946	525	0.08	0.09	(0.04 - 0.09)
CaO	2,946	525	0.06	0.05	(0.03 - 0.08)
TiO2	2,946	525	0.01	0.01	(0.00 - 0.00)
Fe2O3	2,946	525	0.11	0.09	(0.06 - 0.14)
XRF_S	2,946	525	1.58	1.02	(0.84 - 2.01)
TEOM_Mass	2,266	1,205	15.57	8.06	(9.54 - 20.00)
BackupPCM3_EC	353	3,118	0.03	0.10	(0.00 - 0.02)
BackupPCM3_OC	353	3,118	0.68	0.45	(0.39 - 0.85)
VAR49	504	2,967	1.40	0.70	(0.92 - 1.78)
BE_MASS_PM25	3,122	349	18.15	8.72	(11.68 - 22.93)
BE_NO3_PM25	3,293	178	0.94	0.81	(0.40 - 1.23)
BE_SO4_PM25	3,376	95	4.75	3.33	(2.34 - 6.13)
BE_SO4_PM25_1	3,376	95	4.75	3.33	(2.34 - 6.13)
BE_NH4_PM25	3,201	270	1.89	1.17	(1.06 - 2.39)
BE_EC_PM25	3,327	144	1.55	1.10	(0.83 - 1.92)
BE_OM_PM25	3,328	143	6.46	3.54	(4.10 - 7.93)
BE_MMO_PM25	2,946	525	0.53	0.48	(0.28 - 0.63)
BE_OTHER_PM25	2,742	729	2.24	2.66	(0.63 - 3.55)
FRM_EQ_MASS_PM25	3,436	35	17.02	8.34	(10.75 - 21.61)
FRM_EQ_NO3_PM25	3,368	103	0.20	0.51	(0.01 - 0.10)
FRM_EQ_SO4_PM25	3,376	95	4.75	3.33	(2.34 - 6.13)
FRM_EQ_SO4_PM25_1	3,376	95	4.75	3.33	(2.34 - 6.13)
FRM_EQ_NH4_PM25	3,376	95	1.67	1.12	(0.86 - 2.13)
FRM_EQ_EC_PM25	3,327	144	1.55	1.10	(0.83 - 1.92)
FRM_EQ_OM_PM25	3,328	143	5.87	3.25	(3.71 - 7.14)
FRM_EQ_MMO_PM25	2,946	525	0.53	0.48	(0.28 - 0.63)
FRM_EQ_OTHER_PM25	2,806	665	2.60	2.63	(0.97 - 3.91)
PM fine (2008-2013)					

FRM_Mass	108	2,851	11.43	4.51	(7.93 - 13.70)
PCM1_SO4	106	2,853	2.66	1.33	(1.62 - 3.49)
PCM1_NO3	106	2,853	1.15	0.74	(0.60 - 1.55)
PM25_WSM_SUM	106	2,853	3.10	1.81	(1.88 - 3.71)
PM25_MajorMetalOxides	77	2,882	0.56	1.46	(0.21 - 0.40)
PCM3_EC	107	2,852	1.02	0.87	(0.52 - 1.23)
PCM3_OC	107	2,852	3.03	1.63	(1.78 - 4.08)
XRF_As	77	2,882	4.52	1.33	(5.05 - 5.05)
XRF_Ba	77	2,882	1.45	0.02	(1.45 - 1.45)
XRF_Br	77	2,882	3.31	1.67	(2.01 - 4.17)
XRF_Cu	77	2,882	4.59	2.35	(2.20 - 6.16)
XRF_Mn	77	2,882	3.78	1.73	(4.00 - 4.00)
XRF_Pb	77	2,882	2.44	2.25	(1.17 - 2.60)
XRF_Sb	77	2,882	2.73	1.50	(2.12 - 2.14)
XRF_Se	77	2,882	3.42	2.07	(2.03 - 3.51)
XRF_Sn	77	2,882	3.54	0.04	(3.53 - 3.53)
XRF_Ti	77	2,882	2.27	0.52	(2.14 - 2.14)
XRF_Zn	77	2,882	4.09	2.81	(1.35 - 6.70)
WS_Chromium	94	2,865	4.96	0.91	(5.20 - 5.20)
WS_Copper	94	2,865	4.17	1.46	(3.95 - 3.95)
WS_Iron	94	2,865	2.85	2.44	(1.42 - 2.71)
WS_Manganese	94	2,865	4.42	2.61	(1.80 - 6.51)
WS_Nickel	94	2,865	5.21	0.08	(5.20 - 5.20)
WS_Vanadium	94	2,865	2.92	0.04	(2.91 - 2.91)
PCM1_Vol_NO3	106	2,853	0.65	0.35	(0.39 - 0.87)
PCM1_Teflon_NO3	106	2,853	2.30	2.90	(0.21 - 3.04)
PCM1_Teflon_NH4	94	2,865	1.03	0.48	(0.66 - 1.43)
Al2O3	71	2,888	3.96	1.87	(2.22 - 6.05)
SiO2	75	2,884	3.83	3.66	(0.14 - 7.57)
K2O	77	2,882	4.98	2.93	(3.41 - 7.34)
CaO	77	2,882	3.74	1.74	(2.41 - 4.50)
TiO2	77	2,882	3.78	0.87	(3.57 - 3.57)
Fe2O3	77	2,882	3.95	2.91	(0.26 - 6.24)
XRF_S	77	2,882	0.78	0.32	(0.54 - 1.01)
PCM3E1TC	90	2,869	1.46	0.89	(0.74 - 2.05)
PCM3E2TC	90	2,869	0.45	1.46	(0.14 - 0.22)
PCM3E3TC	90	2,869	0.13	0.56	(0.00 - 0.00)
PCM3ECTC	90	2,869	1.01	0.66	(0.53 - 1.34)
PCM3EHTC	90	2,869	0.46	1.46	(0.14 - 0.22)
PCM3O1TC	90	2,869	0.65	1.08	(0.27 - 0.69)
PCM3O2TC	90	2,869	0.74	0.43	(0.44 - 0.91)
PCM3O3TC	90	2,869	0.81	0.51	(0.44 - 1.14)
PCM3O4TC	90	2,869	0.72	1.33	(0.28 - 0.71)

PCM3OCTC	90	2,869	3.14	1.68	(1.85 - 4.20)
PCM3OPTC	90	2,869	0.63	0.36	(0.37 - 0.81)
PCM3OHTC	90	2,869	2.65	1.48	(1.56 - 3.53)
PCM3TCTC	90	2,869	4.15	2.27	(2.35 - 5.39)
PM25_Mass__ug_m3_	1,932	1,027	11.50	5.13	(7.58 - 14.55)
PM25_Tef_Chloride__ug_m3_	1,063	1,896	0.01	0.03	(0.00 - 0.01)
PM25_Tef_Nitrate__ug_m3_	1,063	1,896	0.24	0.50	(0.04 - 0.17)
PM25_Tef_Sulfate__ug_m3_	1,063	1,896	2.85	1.82	(1.61 - 3.64)
PM25_Tef_Ammonium__ug_m3_	1,063	1,896	1.02	0.57	(0.60 - 1.27)
PM25_Tef_Calcium__ug_m3_	1,063	1,896	0.03	0.02	(0.02 - 0.04)
PM25_Tef_Magnesium__ug_m3_	1,062	1,897	0.01	0.01	(0.00 - 0.01)
PM25_Tef_Potassium__ug_m3_	1,063	1,896	0.04	0.06	(0.01 - 0.04)
PM25_Tef_Sodium__ug_m3_	1,040	1,919	0.05	0.08	(0.01 - 0.06)
PM25_Nyl_Chloride__ug_m3_	1,035	1,924	0.04	0.03	(0.02 - 0.04)
PM25_Nyl_Nitrate__ug_m3_	1,072	1,887	0.35	0.30	(0.16 - 0.43)
PM25_total_Cl__ug_m3_	780	2,179	0.05	0.05	(0.02 - 0.05)
PM25_total_NO3__ug_m3_	817	2,142	0.61	0.71	(0.23 - 0.66)
OCTC__ug_m3_	824	2,135	2.86	1.40	(1.89 - 3.50)
ECTC__ug_m3_	816	2,143	0.82	0.51	(0.47 - 1.02)
O1TC__ug_m3_	824	2,135	0.33	0.33	(0.12 - 0.42)
O2TC__ug_m3_	824	2,135	0.75	0.40	(0.48 - 0.94)
O3TC__ug_m3_	824	2,135	0.81	0.42	(0.52 - 0.98)
O4TC__ug_m3_	824	2,135	0.43	0.22	(0.28 - 0.53)
OPTC__ug_m3_	824	2,135	0.54	0.31	(0.33 - 0.67)
E1TC__ug_m3_	824	2,135	0.57	0.54	(0.21 - 0.77)
E2TC__ug_m3_	824	2,135	0.79	0.75	(0.26 - 1.12)
E3TC__ug_m3_	824	2,135	0.00	0.01	(0.00 - 0.00)
PM25_WS_V_51__ng_m3_	803	2,156	0.21	0.19	(0.08 - 0.29)
PM25_WS_Cr_52__ng_m3_	803	2,156	0.13	0.14	(0.06 - 0.15)
PM25_WS_Mn_55__ng_m3_	803	2,156	1.18	0.92	(0.60 - 1.53)
PM25_WS_Fe_56__ng_m3_	803	2,156	15.94	11.53	(7.32 - 21.86)
PM25_WS_Ni_60__ng_m3_	803	2,156	0.32	0.70	(0.10 - 0.27)
PM25_WS_Cu_63__ng_m3_	803	2,156	3.63	7.00	(1.25 - 3.47)
PM25_WS_Zn_68__ng_m3_	703	2,256	9.49	6.40	(5.06 - 12.53)
PM25_WS_As_75__ng_m3_	803	2,156	0.65	0.48	(0.37 - 0.78)
PM25_WS_Se_82__ng_m3_	803	2,156	0.88	0.61	(0.46 - 1.16)
PM25_WS_Cd_114__ng_m3_	803	2,156	0.08	0.09	(0.04 - 0.10)
PM25_WS_Ba_137__ng_m3_	803	2,156	3.22	2.76	(1.40 - 4.17)
PM25_WS_La_139__ng_m3_	803	2,156	0.01	0.01	(0.00 - 0.01)
PM25_WS_Pb_208__ng_m3_	803	2,156	1.57	3.83	(0.59 - 1.55)
XRF_Na__ug_m3_	2,254	705	0.04	0.04	(0.01 - 0.05)
XRF_Al__ug_m3_	2,255	704	0.05	0.06	(0.02 - 0.06)
XRF_Si__ug_m3_	2,255	704	0.09	0.12	(0.03 - 0.11)

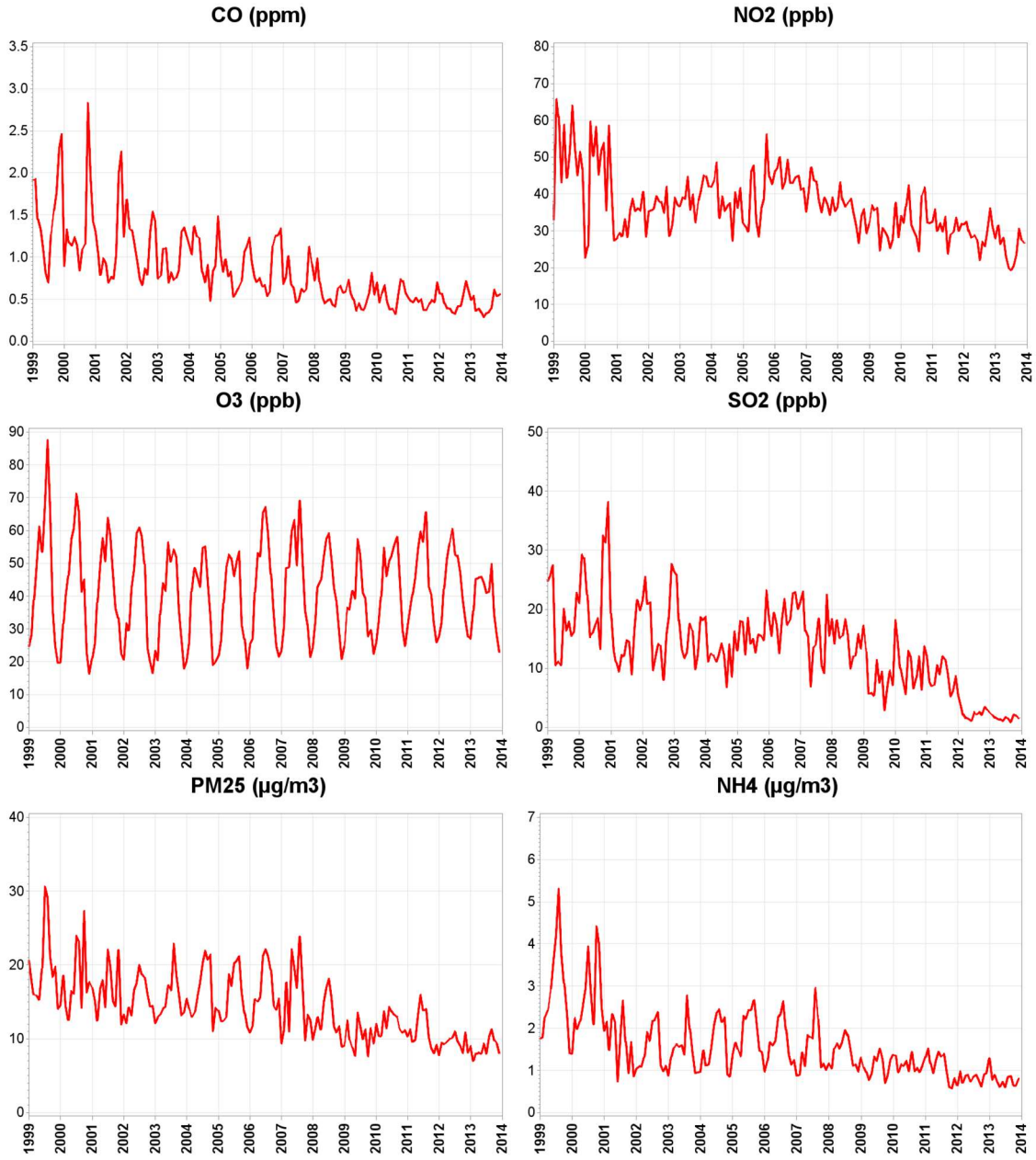
XRF_S__ug_m3_	2,253	706	0.82	0.46	(0.50 - 1.04)
XRF_K__ug_m3_	2,255	704	0.06	0.12	(0.03 - 0.07)
XRF_Ca__ug_m3_	2,255	704	0.03	0.02	(0.02 - 0.04)
XRF_Ti__ug_m3_	2,255	704	0.00	0.00	(0.00 - 0.01)
XRF_Mn__ug_m3_	2,255	704	0.00	0.00	(0.00 - 0.00)
XRF_Fe__ug_m3_	2,255	704	0.08	0.06	(0.04 - 0.10)
XRF_Cu__ug_m3_	2,255	704	0.01	0.01	(0.00 - 0.01)
XRF_Zn__ug_m3_	2,255	704	0.01	0.01	(0.01 - 0.01)
XRF_Pb__ug_m3_	2,255	704	0.00	0.01	(0.00 - 0.00)
PM25_MMO__ug_m3_	1,552	1,407	0.53	0.51	(0.25 - 0.63)
PM25_WS_V_51__ng_m3_1	115	2,844	0.19	0.20	(0.06 - 0.26)
PM25_WS_Cr_52__ng_m3_1	115	2,844	0.10	0.08	(0.06 - 0.12)
PM25_WS_Mn_55__ng_m3_1	115	2,844	1.72	1.49	(0.88 - 2.04)
PM25_WS_Fe_56__ng_m3_1	115	2,844	12.22	6.48	(6.82 - 16.53)
PM25_WS_Ni_60__ng_m3_1	115	2,844	0.80	1.33	(0.19 - 0.83)
PM25_WS_Cu_63__ng_m3_1	115	2,844	3.20	2.49	(1.56 - 4.18)
PM25_WS_Zn_68__ng_m3_1	107	2,852	7.62	4.23	(4.93 - 9.34)
PM25_WS_As_75__ng_m3_1	115	2,844	0.48	0.51	(0.27 - 0.58)
PM25_WS_Se_82__ng_m3_1	115	2,844	0.42	0.21	(0.26 - 0.51)
PM25_WS_Cd_114__ng_m3_1	115	2,844	0.05	0.04	(0.03 - 0.07)
PM25_WS_Ba_137__ng_m3_1	115	2,844	4.86	3.65	(2.45 - 6.06)
PM25_WS_La_139__ng_m3_1	115	2,844	0.01	0.01	(0.01 - 0.02)
PM25_WS_Pb_208__ng_m3_1	115	2,844	1.00	0.99	(0.40 - 1.17)
FRM_PM25_Mass__ug_m3_	709	2,250	9.16	3.73	(6.45 - 11.46)
PM25_Total_Chloride__ug_m3_	238	2,721	0.04	0.06	(0.02 - 0.04)
PM25_Total_Nitrate__ug_m3_	238	2,721	0.51	0.50	(0.20 - 0.66)
PM2_5_MMO__ug_m3_	703	2,256	0.51	0.53	(0.27 - 0.58)
Continuous carbon 1 hour (2005-2006)					
Average_AETH_ug_m3_	16,516	1,004	1.48	1.49	(0.63 - 1.68)
Average_5400_TC_ug_m3_	4,209	13,311	7.39	4.10	(4.54 - 9.10)
Average_OptEC_ug_m3_	10,555	6,965	1.49	1.77	(0.53 - 1.63)
Average_TC_ug_m3_	10,386	7,134	6.53	5.27	(3.24 - 8.04)
Continuous PM 1 hour (2000-2004)					
DAS_TEOM_ug_m3	39,042	4,806	15.64	10.84	(8.10 - 20.63)
TEOM_ug_m3	29,102	14,746	15.23	10.13	(7.96 - 20.31)
NO3_ug_m3	28,972	14,876	0.86	1.04	(0.13 - 1.10)
NH4_ug_m3	29,264	14,584	1.53	1.25	(0.65 - 2.08)
SO4_ug_m3	28,787	15,061	4.57	4.18	(1.87 - 5.81)
PSAP_Bap__1_m_	1,752	42,096	-0.27	11.11	(0.00 - 0.00)
AETH_BC_ug_m3	39,544	4,304	1.32	1.54	(0.48 - 1.53)
_400_TC_ug_m3	37,773	6,075	5.90	5.23	(2.97 - 7.07)
NEPH_Bsp__1_m_	27,150	16,698	0.69	1.87	(0.00 - 0.00)

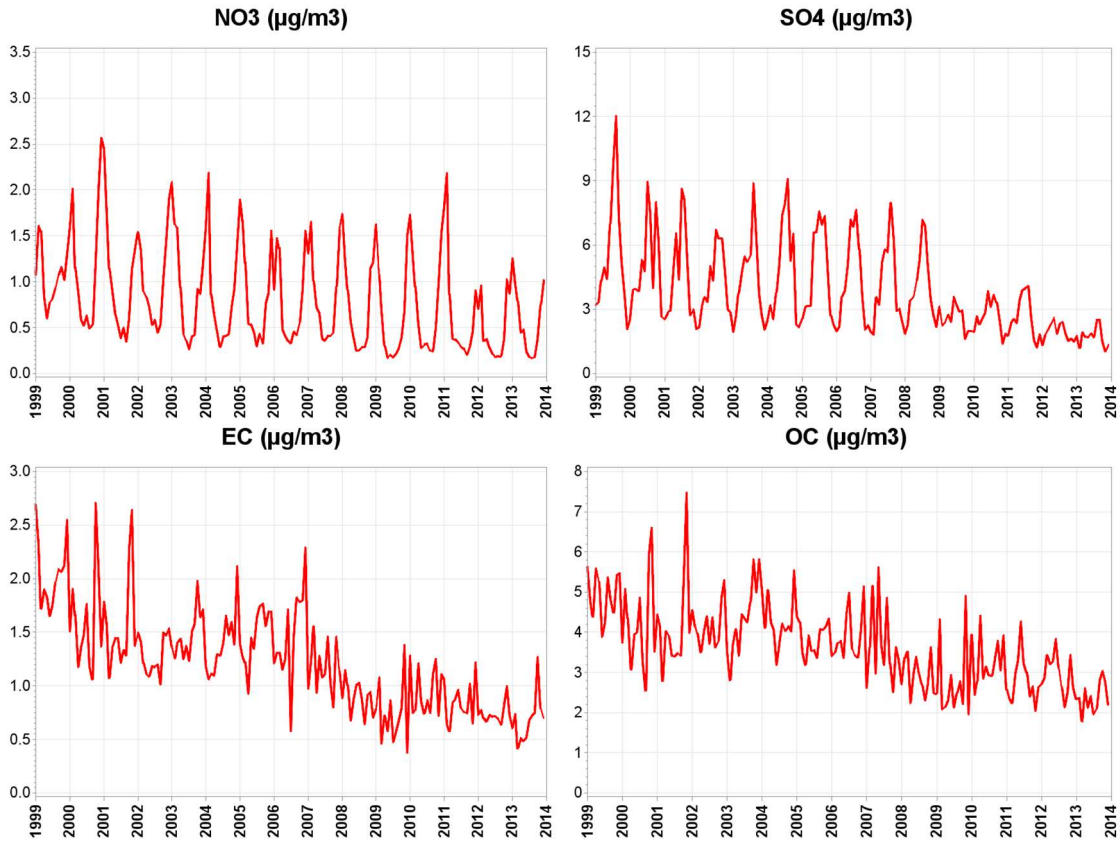
Continuous PM 1 hour (2005-2013)					
Average_SO4_ug_m3_	72,866	6,022	3.24	2.88	(1.43 - 4.06)
Min_SO4_ug_m3_	72,866	6,022	2.85	2.65	(1.18 - 3.61)
Max_SO4_ug_m3_	72,866	6,022	3.67	3.20	(1.69 - 4.54)
StDev_SO4_ug_m3_	72,866	6,022	0.27	0.35	(0.12 - 0.28)
Median_SO4_ug_m3_	72,866	6,022	3.26	2.89	(1.45 - 4.08)
Count_SO4	72,866	6,022	10.22	1.21	(10.00 - 11.00)
Average_NO3_ug_m3_	71,715	7,173	0.69	0.87	(0.17 - 0.86)
Min_NO3_ug_m3_	71,715	7,173	0.48	0.79	(0.04 - 0.61)
Max_NO3_ug_m3_	71,715	7,173	0.93	1.02	(0.31 - 1.16)
StDev_NO3_ug_m3_	71,715	7,173	0.14	0.15	(0.06 - 0.16)
Median_NO3_ug_m3_	71,715	7,173	0.69	0.87	(0.17 - 0.86)
Count_NO3	71,716	7,172	11.13	1.44	(11.00 - 12.00)
Average_NH4_ug_m3_	72,540	6,348	1.28	0.91	(0.67 - 1.64)
Min_NH4_ug_m3_	72,540	6,348	1.15	0.86	(0.57 - 1.49)
Max_NH4_ug_m3_	72,540	6,348	1.43	0.99	(0.76 - 1.81)
StDev_NH4_ug_m3_	72,540	6,348	0.09	0.10	(0.04 - 0.10)
Median_NH4_ug_m3_	72,540	6,348	1.28	0.91	(0.66 - 1.64)
Count_NH4	72,540	6,348	11.41	1.23	(12.00 - 12.00)
Average_AETH_BC_ug_m3_	8,621	70,267	1.17	1.10	(0.53 - 1.35)
Min_AETH_BC_ug_m3_	8,621	70,267	0.81	0.84	(0.32 - 0.99)
Max_AETH_BC_ug_m3_	8,621	70,267	1.70	1.67	(0.78 - 1.90)
StDev_AETH_BC_ug_m3_	8,621	70,267	0.28	0.37	(0.12 - 0.29)
Median_AETH_BC_ug_m3_	8,621	70,267	1.13	1.08	(0.52 - 1.31)
Count_AETH	58,549	20,339	11.70	0.78	(12.00 - 12.00)
Average_TEOM_ug_m3_	57,836	21,052	11.47	7.13	(6.73 - 14.62)
Min_TEOM_ug_m3_	57,836	21,052	9.26	6.67	(4.80 - 12.35)
Max_TEOM_ug_m3_	57,836	21,052	13.79	8.00	(8.59 - 17.13)
StDev_TEOM_ug_m3_	57,836	21,052	1.45	1.11	(0.86 - 1.72)
Median_TEOM_ug_m3_	57,836	21,052	11.47	7.12	(6.73 - 14.62)
Count_TEOM	57,836	21,052	11.73	0.88	(12.00 - 12.00)
Average_OptEC_ug_m3_	54,272	24,616	0.86	0.82	(0.40 - 0.99)
Count_OptEC	54,272	24,616	1.00	0.00	(1.00 - 1.00)
Average_TC_ug_m3_	53,543	25,345	4.22	2.77	(2.37 - 5.29)
Count_TC	53,543	25,345	1.00	0.00	(1.00 - 1.00)
Average_AETH_ug_m3_	49,928	28,960	0.80	0.73	(0.39 - 0.92)
Min_AETH_ug_m3_	49,928	28,960	0.49	0.57	(0.18 - 0.57)
Max_AETH_ug_m3_	49,928	28,960	1.21	1.13	(0.62 - 1.37)
StDev_AETH_ug_m3_	49,928	28,960	0.22	0.25	(0.10 - 0.26)
Median_AETH_ug_m3_	49,928	28,960	0.78	0.72	(0.39 - 0.90)
Min_OptEC_ug_m3_	46,721	32,167	0.81	0.75	(0.39 - 0.93)
Max_OptEC_ug_m3_	46,721	32,167	0.81	0.75	(0.39 - 0.93)
StDev_OptEC_ug_m3_	46,721	32,167	0.00	0.00	(0.00 - 0.00)

Median_OptEC_ug_m3_	46,721	32,167	0.81	0.75	(0.39 - 0.93)
Min_TC_ug_m3_	46,483	32,405	4.09	2.66	(2.31 - 5.15)
Max_TC_ug_m3_	46,483	32,405	4.09	2.66	(2.31 - 5.15)
StDev_TC_ug_m3_	46,483	32,405	0.00	0.00	(0.00 - 0.00)
Median_TC_ug_m3_	46,483	32,405	4.09	2.66	(2.31 - 5.15)
Nephelometer 5 min (2013)					
Average_NEPH_Mm_1_	101,523	3,597	29.23	18.32	(15.50 - 38.80)
Min_NEPH_Mm_1_	101,523	3,597	28.11	17.83	(14.64 - 37.60)
Max_NEPH_Mm_1_	101,523	3,597	30.41	19.39	(16.37 - 40.07)
StDev_NEPH_Mm_1_	101,523	3,597	0.94	2.60	(0.54 - 1.07)
Median_NEPH_Mm_1_	101,523	3,597	29.21	18.26	(15.49 - 38.79)
Count_NEPH	101,523	3,597	4.99	0.13	(5.00 - 5.00)
Average_Babs_Mm_1_	99,110	6,010	12.64	12.18	(5.48 - 15.24)
Min_Babs_Mm_1_	99,110	6,010	10.62	11.52	(3.83 - 13.28)
Max_Babs_Mm_1_	99,110	6,010	14.92	14.25	(6.97 - 17.72)
StDev_Babs_Mm_1_	99,110	6,010	1.78	3.12	(0.50 - 2.17)
Median_Babs_Mm_1_	99,110	6,010	12.51	12.10	(5.42 - 15.11)
Count_Babs	99,110	6,010	5.00	0.07	(5.00 - 5.00)
Average_RH___	103,109	2,011	70.44	22.10	(53.41 - 90.39)
Min_RH___	103,109	2,011	69.96	22.26	(52.75 - 90.04)
Max_RH___	103,109	2,011	70.92	21.93	(54.16 - 90.72)
StDev_RH___	103,109	2,011	0.39	0.42	(0.12 - 0.53)
Median_RH___	103,109	2,011	70.43	22.11	(53.40 - 90.40)
Count_RH	103,109	2,011	5.00	0.07	(5.00 - 5.00)
Average_NEPH_RH___	103,459	1,661	12.41	3.86	(10.00 - 14.25)
Min_NEPH_RH___	103,459	1,661	12.30	3.83	(10.00 - 14.00)
Max_NEPH_RH___	103,459	1,661	12.51	3.90	(10.00 - 15.00)
StDev_NEPH_RH___	103,459	1,661	0.10	0.21	(0.00 - 0.07)
Median_NEPH_RH___	103,459	1,661	12.41	3.87	(10.00 - 14.00)
Count_NEPH_RH	103,459	1,661	4.99	0.08	(5.00 - 5.00)
Nephelometer 1 hour (2007-2013)					
Average_NEPH_Mm_1_	60,226	1,142	36.98	29.14	(18.62 - 47.86)
Min_NEPH_Mm_1_	60,226	1,142	33.81	26.97	(16.62 - 44.00)
Max_NEPH_Mm_1_	60,226	1,142	40.91	32.90	(20.79 - 52.66)
StDev_NEPH_Mm_1_	60,226	1,142	2.32	4.26	(0.80 - 2.51)
Median_NEPH_Mm_1_	60,226	1,142	36.81	29.09	(18.48 - 47.71)
Count_NEPH	60,226	1,142	11.77	0.79	(12.00 - 12.00)
Average_RH___	60,543	825	66.64	21.74	(49.20 - 85.63)
Min_RH___	60,543	825	64.48	21.98	(46.67 - 83.36)
Max_RH___	60,543	825	68.77	21.54	(51.60 - 87.82)
StDev_RH___	60,543	825	1.43	1.39	(0.59 - 1.82)
Median_RH___	60,543	825	66.66	21.80	(49.15 - 85.74)

Count_RH	60,543	825	11.96	0.28	(12.00 - 12.00)
Average_NEPH_RH___	60,710	658	9.87	3.43	(8.00 - 11.94)
Min_NEPH_RH___	60,710	658	9.40	3.44	(7.46 - 11.29)
Max_NEPH_RH___	60,710	658	10.27	3.62	(8.00 - 12.00)
StDev_NEPH_RH___	60,710	658	0.31	0.52	(0.01 - 0.43)
Median_NEPH_RH___	60,710	658	9.88	3.45	(8.00 - 12.00)
Count_NEPH_RH	60,710	658	11.99	0.11	(12.00 - 12.00)
Average_Babs_Mm_1_	49,898	11,470	12.99	12.19	(5.91 - 15.29)
Min_Babs_Mm_1_	49,898	11,470	7.76	9.61	(2.42 - 9.53)
Max_Babs_Mm_1_	49,898	11,470	19.77	18.85	(9.62 - 22.88)
StDev_Babs_Mm_1_	49,898	11,470	3.68	4.21	(1.81 - 4.16)
Median_Babs_Mm_1_	49,898	11,470	12.69	11.93	(5.80 - 14.98)
Count_Babs	49,898	11,470	11.66	0.81	(12.00 - 12.00)
TEOM 1 hour (2005-2012)					
Average_TEOM_ug_m3_	58,023	3,345	12.54	7.60	(7.28 - 15.95)
Min_TEOM_ug_m3_	58,023	3,345	10.19	7.06	(5.31 - 13.51)
Max_TEOM_ug_m3_	58,023	3,345	15.03	8.66	(9.16 - 18.64)
StDev_TEOM_ug_m3_	58,023	3,345	1.55	1.25	(0.87 - 1.83)
Median_TEOM_ug_m3_	58,023	3,345	12.53	7.59	(7.28 - 15.95)
Count_TEOM	58,023	3,345	11.76	0.83	(12.00 - 12.00)
Estimated source impacts (1998-2010)					
GV	4134	394	0.84	0.74	(0.39 - 1.05)
DV	4134	394	1.20	1.04	(0.51 - 1.59)
DUST	4134	394	0.38	0.49	(0.17 - 0.42)
BURN	4134	394	2.92	2.52	(1.25 - 3.70)
COAL	4134	394	0.15	0.13	(0.06 - 0.20)
AMSULF	4134	394	3.46	3.27	(1.27 - 4.68)
AMBSULF	4134	394	1.98	1.84	(0.84 - 2.56)
AMNITR	4134	394	1.08	1.00	(0.42 - 1.41)
SOC	4134	394	1.71	1.59	(0.57 - 2.46)

Figure 5.2. Mean monthly values for selected pollutants measured at Jefferson Street, 1999-2013.





5.3: Atlanta emergency department data set

Data were collected on emergency department (ED) visits for the people living in the Atlanta metropolitan area between January 1, 1999 and December 31, 2013.(6) Computerized billing records for individual-level data were pulled from 42 acute care hospitals. A single dataset was created by combining data from individual hospitals from 1999-2004 with a comprehensive dataset from the Georgia Hospital Association from 2005-2013.

Patient variables included date of admission, the primary International Classification of Diseases 9th Revision (ICD-9) diagnostic code, patient date of birth, sex, race, and 5-digit residential ZIP code. ED visits were included if the patient ZIP

code was located wholly or partially within the 5 primary urban counties of metropolitan Atlanta (Fulton, DeKalb, Gwinnett, Cobb, Clayton). A similar dataset was defined for patients from the larger 20-county Atlanta metropolitan area, with these additional Georgia counties included: Barrow, Bartow, Carroll, Cherokee, Coweta, Douglas, Fayette, Forsyth, Henry, Newton, Paulding, Pickens, Rockdale, Spalding, and Walton.

ED data have been thoroughly cleaned prior to analysis. Data cleaning included resolving ambiguities, standardizing variables, identifying potential inconsistencies, and determining periods of invalid data for each hospital. Hospital indicators were generated to distinguish periods of available and useable data for each hospital. Table 5.3 gives a summary of the 42 hospitals used in this analysis.

Table 5.3. Hospitals contributing data to the Atlanta emergency department dataset, 1999-2013. ED visits are for all patients within 20-county Atlanta metropolitan area. Days represent the number of days for which the hospital contributes data (out of a possible 5,463).

Hospital ID	Days	ED visits
1	5,424	580,340
2	3,881	204,092
3	5,463	583,540
4	5,463	1,149,954
5	5,461	567,080
6	5,463	620,205
7	3,072	396,770
8	5,414	877,985
9	2,787	82,007
10	5,463	282,659
11	5,463	655,774
12	2,458	128,539
13	5,463	674,140
14	5,369	295,939
15	5,341	602,623
16	4,732	499,854
17	4,511	1,691,979
18	5,463	1,635,250
19	5,412	787,394
20	5,463	1,527,051
21	5,092	154,726
22	5,159	393,299
23	5,463	469,093
24	2,901	122,651
25	5,368	396,073
26	5,463	692,772
27	4,124	371,918
28	5,463	425,780
29	5,463	633,807

30	609	27,748
31	5,463	540,059
32	3,189	320,652
33	4,678	304,432
34	5,417	1,053,896
35	5,463	478,237
36	5,462	1,083,219
37	1,827	66,307
38	5,157	481,315
39	5,155	360,745
40	3,637	240,266
41	304	4,991
42	1,727	3,002

Review of clinical outcomes potentially linked to ambient air pollution has been covered in Chapter 2.1. Based on this literature review, a number of outcomes of interest were identified. These outcomes were described by defined sets of ICD-9 codes listed as the primary cause for ED visits. Outcomes of interest include general categories for cardiovascular disease and respiratory disease, as well as more specific cardiorespiratory subcategories. Outcomes of interest selected for these studies are listed in Table 5.4.

Table 5.4. Outcomes of interest and respective ICD-9 codes 1999 –2013.

Category	ICD-9 codes	No. of cases (1999-2013)
All emergency department visits (not used in studies)	[001-999, E/V]	16,191,785
Respiratory disease	[460-465, 466.0, 466.1, 466.11, 466.19, 477, 480-486, 491-493, 496, 786.07]	1,637,338
Asthma or wheezing	[493, 786.07]	374,126
Chronic obstructive pulmonary disease (COPD)	[491, 492, 496]	74,853
Pneumonia	[480-486]	200,551

Upper respiratory infection (URI)	[460-465, 466.0, 477]	926,547
Cardiovascular disease	[410-414, 427, 428, 433-437, 440, 443-445, 451-453]	416,392
Ischemic heart disease (IHD)	[410-414]	99,666
Congestive heart failure (CHF)	[428]	105,561

ED visits for all selected categories in the 5-county Atlanta metropolitan area increased from 1999-2013, ranging from increases of 43.5% for pneumonia to 225.0% for congestive heart failure (Figure 5.3). Population also increased during that time period (Figure 5.4), increasing from 2,850,396 in 1999 to 3,541,663 in 2013 in the 5-county area (a 24.3% increase), from 4,009,836 in 1999 to 5,351,272 in 2013 in the 20-county area (a 33.5% increase), and from 8,227,303 in 1999 to 9,994,759 in 2013 in all of Georgia (a 24.2% increase) (7). While increased population and changing disease incidence likely contributed to the increase of reported ED visits, the substantially higher increases in ED visits also are likely a function of improved hospital coverage. The switch to consolidated Georgia Hospital Association data in 2005 coincided with a large observed increase in ED visits; after 2005, changes in ED visits mostly leveled off, with subsequent change of rates of ED visits from 2005-2013 ranging from -15.8% for pneumonia to 29.4% for COPD.

Figure 5.3. Number of ED visits by outcome category, 1999-2013, relative to 1999 numbers.

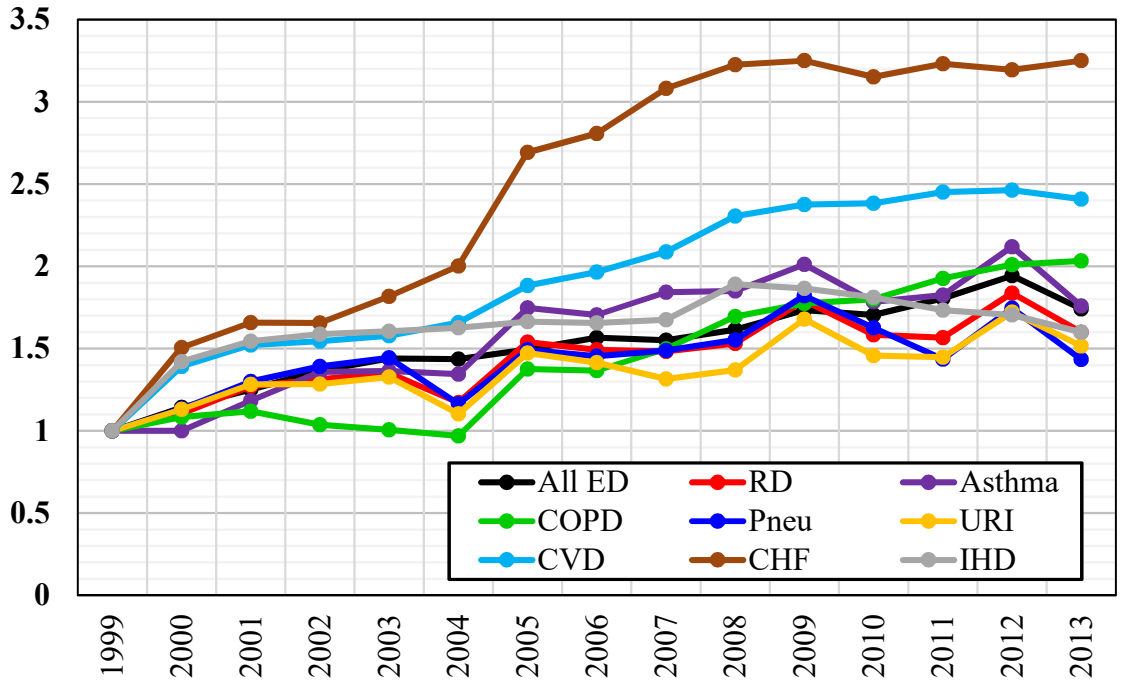
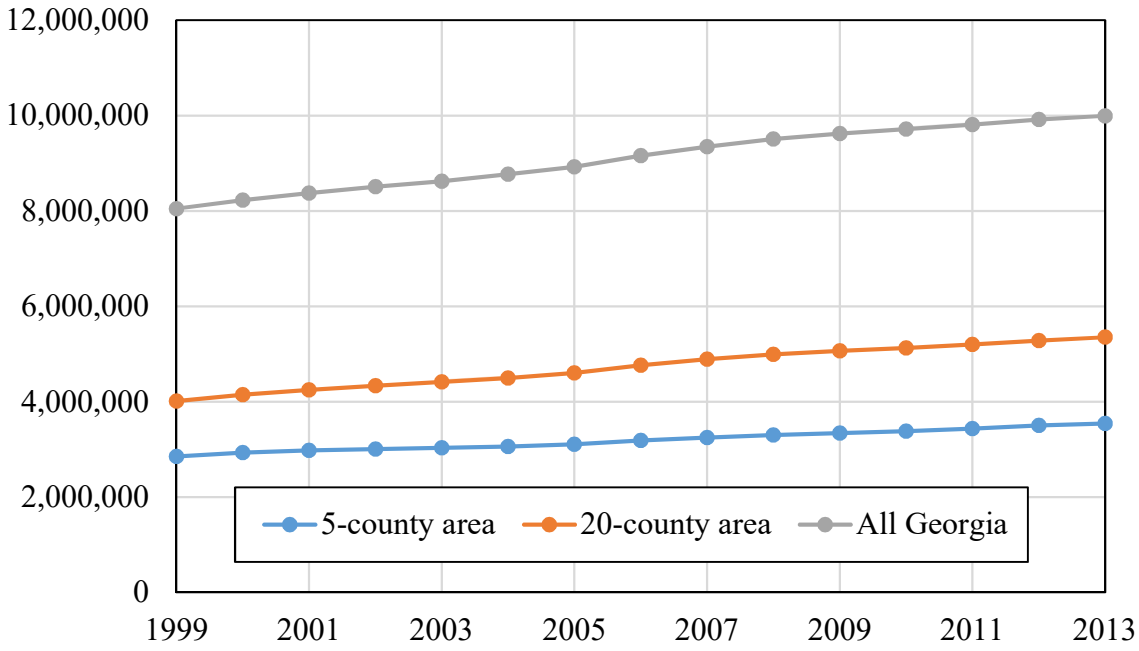


Figure 5.4. Annual population in the Atlanta area, 1999-2013.



5.4: Summary of study aims

The goal of Aim I was to assess associations between measured OP^{DTT} and cardiorespiratory ED visits. We incorporated established time series models in order to control for potential temporal confounding, adjusting the covariates to account for a smaller number of observations. Bipollutant models were assessed in order to verify health associations for OP^{DTT} independent from other air quality indicators.

The goal of Aim II was to model OP^{DTT} over a long time period, then estimate associations between modeled OP^{DTT} and cardiorespiratory ED visits. Regressions were run to generate estimated coefficients for the relationships between measured OP^{DTT} and concurrent air quality measurements. These coefficients were applied to a larger retrospective dataset in order to generate estimates of daily OP^{DTT} for that time period during which DTT was not directly measured. We used established air pollution health effect models to estimate associations between retrospective daily estimates of OP^{DTT} and ED visits for a number of cardiovascular and respiratory outcomes. This analysis tested if these OP^{DTT} estimates were useful predictors of ED visits, and provided further evidence that OP is an important pathways for the initiation of clinical outcomes from air pollution.

The goal of Aim III was to estimate the number of ED visits from 1999-2013 that had been prevented in the Atlanta metropolitan area as a result of reduced air pollution due to emissions controls. For each selected cardiorespiratory ED category, multipollutant regression models were run to determine the association between the outcome and pollutants. Resulting regression coefficients were applied to the difference between observed and counterfactual ED visits to estimate the number and percent of ED

visits prevented. By running these analyses for different counterfactual scenarios, we were able to assess the health impacts of identified air pollution control policies.

5.5: References

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6: AIM I: ASSOCIATIONS BETWEEN AMBIENT FINE PARTICULATE OXIDATIVE POTENTIAL AND CARDIORESPIRATORY EMERGENCY DEPARTMENT VISITS

6.1: Abstract

Background: Oxidative potential (OP) has been proposed as a measure of toxicity of ambient particulate matter (PM).

Objectives: Address an important research gap by using long-term daily OP measurements to conduct population-level analysis of the health effects of measured ambient OP.

Methods: A semi-automated dithiothreitol (DTT) analytical system was used to measure daily average OP (OP^{DTT}) in water-soluble fine PM at a central monitor site in Atlanta, GA for 196 days during June 2012 – April 2013. Daily counts of emergency department (ED) visits for cardiorespiratory outcomes were obtained for the 5-county Atlanta metropolitan area for this period. Poisson log-linear regression models were used to conduct time-series analyses of the relationship between ED visits for the selected cardiorespiratory outcomes and the 3-day moving average of OP^{DTT}. Bipollutant regression models were run to estimate the health associations of OP^{DTT} while controlling for other pollutants.

Results: OP^{DTT} was significantly associated with ED visits for respiratory disease (RR=1.03, 95% CI=1.00-1.05 per interquartile range increase in OP^{DTT}), asthma (RR=1.12, 95% CI=1.03-1.22), and ischemic heart disease (RR=1.19, 95% CI=1.03-

1.38). Associations of borderline significance were observed for upper respiratory infections and a combined cardiovascular diseases group, and no association was observed for chronic obstructive pulmonary disease, pneumonia, or congestive heart failure. OP^{DTT} remained a significant predictor of asthma and ischemic heart disease in most bipollutant models controlling for other pollutant measures.

Conclusions: OP^{DTT} was associated with ED visits for multiple cardiorespiratory outcomes, providing support for the utility of OP^{DTT} as a measure of fine particle toxicity.

6.2: Introduction

Fine particulate matter (PM with aerodynamic diameter <2.5 microns, or $PM_{2.5}$) has been associated with hospital admissions and emergency department (ED) visits for several respiratory outcomes (e.g., asthma, chronic obstructive pulmonary disease, and bronchitis) and cardiovascular outcomes (e.g. myocardial infarction, coronary heart disease, and stroke).(1-4) Given that fine PM is a heterogeneous mixture and distinct particulate components could have different health effects, measurement of mass concentration may not be an ideal way to quantify risk to human health. One proposed mechanism for the toxicity of PM is through oxidative stress-driven pathways.

Fine particulate matter can contain a variety of species that contribute to its oxidative potential (OP), including transition metals (e.g., copper, iron), quinones, polycyclic aromatic hydrocarbons (PAHs), and elemental carbon.(5-7) Several assays have been developed to attempt to measure the OP of ambient fine PM. The electron spin resistance (ESR) assay measures the capacity of PM to convert hydrogen peroxide to

hydroxyl radicals.(8) Assays for ascorbic acid (AA) and glutathione (GSH), two antioxidants, measure the level of depletion of these compounds when added to PM sample extract.(9) The dithiothreitol (DTT) assay mimics the *in vivo* generation of superoxide radicals by particles transferring electrons from nicotinamide adenine dinucleotide (NADH) and nicotinamide adenine dinucleotide phosphate (NADPH) to oxygen.(10, 11) Cellular assays, such as those using rat alveolar macrophage (NR8383) cells, can directly measure the oxidation of intracellular probes.(12) For this study, a semi-automated system was used to measure DTT activity as a measure of OP (OP^{DTT}) of water-soluble fine PM in order to generate a time-series of daily OP^{DTT} measurements for a central site in Atlanta.

Exposure to high levels of diesel exhaust and other sources of particulate matter have been repeatedly shown to be associated with measureable amounts of oxidative stress.(13, 14) Additionally, exposure to diesel exhaust can result in acute oxidative stress and inflammatory responses in peripheral blood as well as airway tissues.(15) Inhalation of particulate matter is associated with the release of cytokines, activated immune cells, and other mediators of inflammation in the upper and lower airways.(16, 17) This respiratory inflammation can lead to exacerbation of asthma symptoms, chronic bronchitis, and decreased gas exchange. The release of proinflammatory mediators into the bloodstream results in elevated levels of white blood cells, platelets, and the enzyme myeloperoxidase; these changes are linked to vasoconstriction, atherosclerosis, and endothelial dysfunction, all major risk factors for future cardiac outcomes.(18, 19) These inflammatory pathways are hypothesized to be driven or mediated by oxidative stress caused by the *in vivo* generation of reactive oxygen species.(14, 20)

Exposure to pollutant mixtures with high OP have been linked to the exacerbation of a variety of respiratory (including chronic obstructive pulmonary disease, asthma, chronic bronchitis, and emphysema) and cardiovascular conditions (including myocardial infarction, stroke, ischemic heart disease, and coronary heart disease).(21-27) These studies strengthen the evidence that OP may be a major determinant of the toxicity of PM. However, since these health effects may involve other biological mechanisms of toxicity, it is unclear whether the observed harms are truly attributable to OP. In each of two studies that exposed volunteers to PM mixtures of similar concentration but different composition, exposure to a mixture high in metals with considerable OP such as zinc, copper, and iron produced significantly higher inflammatory responses.(28, 29) Panel studies show that $PM_{2.5}$ OP is linked to decreased lung function in children with asthma and markers of inflammation in elderly subjects.(30, 31) OP levels at home addresses for children have been associated with increased asthma incidence and decreased lung function.(32)

In a large-scale case-crossover study in Ontario, Canada using city-level estimates of long-term $PM_{2.5}$ OP, glutathione-related OP was found to modify the association between fine particulate matter and respiratory disease, but ascorbate-related OP did not modify this association.(33) Different OP measurement assays may be sensitive to dissimilar sets of particulate compounds that may be linked to different cardiorespiratory health effects.(34) Measurements of daily $PM_{2.5}$ OP would help to better characterize the results from this study.

Since many methods for measuring OP are labor-intensive, studies of the health effects of OP have typically been over relatively short time periods and have compared

relatively minor clinical outcomes within small study groups. While limited previous studies have assessed population-level health impacts of modeled ambient OP,(35, 36) associations with directly measured OP have yet to be assessed. Given that modeled ambient OP may be prone to substantial measurement errors, population-level studies assessing effects of measured OP are needed to: 1) provide stronger evidence of OP as a major mechanism of harm for PM, 2) determine health outcomes for people exposed to ambient levels of OP, not just experimental doses; and 3) quantify health effects at the population level. The study we report on here is, to our knowledge, the first to assess population-level associations of measured OP in ambient PM and therefore helped to meet these critical research gaps.

6.3: Methods

Air sampling took place from June 2012 – April 2013 at a mixed industrial/residential location in Atlanta, GA (Jefferson Street), roughly 2 miles northwest of downtown Atlanta and about 1.4 miles from a major interstate highway. To measure oxidative potential, we used a semi-automated system that measures the capacity of water-soluble $PM_{2.5}$ to generate reactive oxygen species using the DTT assay. Our OP^{DTT} method and this Atlanta sampling campaign have been described extensively in previous publications.(37-40) Particles were collected with a high-volume sampler (HiVol, Thermo Anderson, nondenuded, nominal flow rate 1.13m^3 min^{-1}, $PM_{2.5}$ cut size by impactor) onto pre-baked 8x10 inch quartz filters to collect $PM_{2.5}$ over 23 hour periods (noon-11am daily). After sampling, filters were immediately wrapped in prebaked aluminum foil and stored in a freezer. Analysis of filters for OP^{DTT} and other pollutant

measures started in March 2013. A fraction of the high volume filter was extracted in water, the extract was filtered and then DTT activity was determined with the automated analytical system, which allowed for consistent DTT analysis on a large number of filter samples with less effort compared to manual analysis. As detailed in previous work, this system has a high analytical precision (Coefficient of Variation of 12% for standards, 4% for ambient samples).(37) Daily measurements on additional particulate and gaseous pollutants were also taken at this location; methods for their collection have been previously described.(41-43) Meteorological data collected at Hartsfield-Jackson airport, about 8 miles south of downtown Atlanta, were also acquired.

Computerized billing records on ED visits made at 38 acute care hospitals in the Atlanta metropolitan area were acquired from the Georgia Hospital Association for the study period.(44) Patient variables included date of admission, all recorded International Classification of Diseases 9th Revision (ICD-9) diagnostic codes, date of birth, sex, race, and 5-digit residential ZIP code. ED visits were included in the study if the patient residential ZIP code was located wholly or partially within the 5 primary urban counties of metropolitan Atlanta (Fulton, DeKalb, Gwinnett, Cobb, Clayton). Daily counts of ED visits were calculated for the following outcome categories based on primary ICD-9 codes: asthma (ICD-9 codes 493, 786.07), chronic obstructive pulmonary disease (COPD) (491, 492, 496), pneumonia (480-486), upper respiratory infection (URI) (460-465, 466.0, 477), congestive heart failure (CHF) (428), and ischemic heart disease (IHD) (410-414). In addition, daily counts were determined for combined categories of all respiratory diseases (460-465, 466.0, 466.1, 466.11, 466.19, 477, 480-486, 491-493, 496,

786.07) and all cardiovascular diseases (410-414, 427, 428, 433-437, 440, 443-445, 451-453).

We estimated associations between OP^{DTT} and daily counts of ED visits for the selected cardiorespiratory outcomes using Poisson log-linear models accounting for overdispersion. The exposure of interest was the 3-day moving average of OP^{DTT} (the average of OP^{DTT} on the same day as the ED visit, 1 day previous, and 2 days previous), as our prior studies have shown consistent associations of multi-day elevated pollutant levels.(45-47) Observations without 3 consecutive daily OP^{DTT} measurements were excluded from the analysis. To control for seasonal trends, the models included cubic splines with monthly knots. The models also controlled for weekdays and federal holidays, as well as temperature (cubic polynomial of the lag 0-2 moving average of daily maximum temperature), dew point (cubic polynomial of the lag 0-2 moving average of daily mean dew point), and indicator variables for periods of hospital data contribution. To determine the utility of OP^{DTT} as a measure of ambient air toxicity independent of other pollutant measures, we ran bipollutant models that included OP^{DTT} and one of several common pollutant measures. These pollutant measures were: $PM_{2.5}$ total mass, carbon monoxide (CO), nitrogen dioxide (NO_2), ozone (O_3), and sulfur dioxide (SO_2), as well as the following $PM_{2.5}$ components: sulfate (SO_4), elemental carbon (EC), organic carbon (OC), ammonium (NH_4), nitrate (NO_3), water-soluble manganese (Mn), water-soluble iron (Fe), and water-soluble copper (Cu). Health associations were measured as risk ratio (RR) per interquartile range (IQR) of daily OP^{DTT} or other pollutants.

All analyses were performed using SAS version 9.3 (SAS Institute, Inc., Cary, NC).

6.4: Results

There were 196 days of daily OP^{DTT} levels recorded from June 2012 – April 2013. Mean daily OP^{DTT} was 0.32 nmol/min/m^3 (range: 0.05-0.83, interquartile range: 0.21). OP^{DTT} tended to be highest from November through January (Figure 6.1). OP^{DTT} was most strongly correlated with EC (r=0.56), $PM_{2.5}$ (r =0.55), and OC (r =0.51) (Table 6.1). For the days with OP^{DTT} measurements, there were 730,000 total ED visits; on average there were 390.8 daily ED visits per day for all respiratory diseases, of which 85.1 visits were for asthma, 19.7 visits for COPD, 227.4 visits for URI, and 45.2 visits for pneumonia. There was a mean of 98.8 ED visits per day for all cardiovascular diseases, of which 25.4 visits were for CHF and 19.6 visits were for IHD.

After excluding data for which the full 3-day moving average of OP^{DTT} was unavailable, there were 156 days of observations used for the time-series analyses. OP^{DTT} was significantly positively associated with the combined respiratory disease group (RR=1.03, 95% CI=1.00-1.05) and positively associated, but not significantly, with the combined cardiovascular disease group (RR=1.05, 95% CI=0.98-1.12) (Figure 6.2). Within more specific outcome categories, OP^{DTT} was significantly positively associated with asthma (RR=1.12, 95% CI=1.03-1.22) and IHD (RR=1.19, 95% CI=1.03-1.38). OP^{DTT} was not significantly associated with CHF, COPD, pneumonia, or URI (although the association with URI was suggestive).

Since OP^{DTT} was strongly associated with asthma ED visits, we examined 13 separate bipollutant models including both OP^{DTT} and another pollutant to see if OP^{DTT}

remained a significant predictor of asthma while controlling for other pollutants. In every model, the risk ratio point estimate for OP^{DTT} was above 1 (Figure 6.3). In 11 of the 13 models, the risk ratio point estimate for OP^{DTT} was greater than the risk ratio for the other pollutant included; the only exceptions were models that included $PM_{2.5}$ or OC. OP^{DTT} was significantly associated with asthma ED visits in bipollutant models that included CO, NO_2, NO_3, O_3, SO_2, SO_4, Mn, Fe, and Cu.

In bipollutant models with IHD as the outcome, the estimated health associations for OP^{DTT} were even stronger. In every bipollutant model, the risk ratio point estimate for OP^{DTT} was above 1 and OP^{DTT} had a higher risk ratio point estimate than the other pollutant included. (Figure 6.4). In all but two models, OP^{DTT} was significantly and positively associated with IHD; the exceptions were models that included $PM_{2.5}$ and CO, although the risk ratio point estimate for OP^{DTT} was of borderline significance and still strong in magnitude.

6.5: Discussion

To our knowledge, this study represents the first report of population-level health associations for directly measured OP, with a focus on OP measured using the DTT assay. The study draws upon a comprehensive hospital database consisting of data from all acute care hospitals with emergency departments (except the Veterans' Affairs medical center) serving an area with over 3.3 million residents.(48) Daily measurements of collocated air quality data for OP^{DTT} and a large number of other pollutants, as well as meteorological variables, allowed for assessment of correlations and control of potential

confounders. The Poisson log-linear regression models build upon our previous analyses in the Atlanta metropolitan area and utilize the strengths of established quantitative methodologies.

OP^{DTT} was a significant predictor of ED visits for respiratory disease, asthma, and IHD. We ran multiple two-pollutant models to help assess whether OP^{DTT} was merely a proxy for another pollutant. OP^{DTT} was more strongly associated with asthma ED visits than the other pollutant measure in most bipollutant models. $PM_{2.5}$ had a slightly higher risk ratio for asthma than OP^{DTT} in a bipollutant model (1.07 compared to 1.05), though these risk ratios were both lower than the corresponding RRs from single-pollutant models; the same was also true for OC and OP^{DTT}. This finding is consistent with water-soluble OP explaining part of the respiratory toxicity of $PM_{2.5}$ and OC; these mixtures may also cause adverse effects either through oxidative stress mediated by water-insoluble particles or through pathways unrelated to OP. For IHD visits, OP^{DTT} was more strongly predictive than the other pollutant measure in every two-pollutant model. These results provide evidence that OP may offer additional information about health risks of air pollution beyond the risks captured by other pollutant measures.

OP^{DTT} observations were available for 196 days from June 2012 – April 2013. While this represents a larger sample size than available for prior studies of OP, this is still relatively few observations compared to other time-series analyses of acute effects of air pollution.(49, 50) Only 156 observations with full data were used in the time-series analyses, which also included numerous covariates (39 additional model parameters) to control for potential temporal confounders. Consequently, the risk ratio estimates had relatively large confidence intervals. The fact that this study showed statistically

significant effects of OP^{DTT} on cardiorespiratory ED visits for this sample size indicates that OP^{DTT} may be a relatively strong predictor of health outcomes. Furthermore, where results were suggestive for certain outcomes (such as URI and the combined CVD ED visits), there may be a true positive association with OP^{DTT}, but the sample size was not sufficient to detect a significant effect. The results of this study should provide a strong impetus to produce longer time series of measurements of OP^{DTT} and other characterizations of OP in order to produce more stable risk estimates for multiple outcome groups and further elucidate particulate matter toxicity.

Temporal relationships between air pollutants and health outcomes may differ by specific pollutants or outcomes, and we used the three-day moving average – a previously utilized *a priori* lag structure – to account for possible multi-day effects of elevated pollutant levels.(46, 47, 51) When testing the associations between OP^{DTT} and same-day ED visits, there were no statistically significant associations, suggesting that many adverse health outcomes of oxidative stress may not be immediately fully realized. In addition, the use of pollutant measurements at a single location to predict health outcomes over a large metropolitan area is not ideal. However, previous work by our group showed that different urban locations in Atlanta had similar daily OP^{DTT} measurements.(10, 37) In addition, a previous analysis of exposure measurement error in Atlanta demonstrated that the use of measurements from urban monitors (within 20 miles of the city center) located different distances from geographic subpopulations produced similar associations between pollutants and health outcomes, particularly for secondary pollutants, suggesting the viability of using a single central monitor as a surrogate for ambient pollutant levels experienced by a population spread out over a sizable

metropolitan area.(44) Zeger et al. suggest that if pollutant measurements in a time series analysis are close to the average pollutant exposure levels for the population of interest (i.e., Berkson-type error), then the associations between pollutants and health outcomes should have minimal bias. On the other hand, if the measurements differ meaningfully from population average exposures, bias can be created with the direction most likely toward the null.(52) Goldman et al. investigated the effects of measurement error on associations between pollutants and health outcomes using Poisson log-linear models similar to those used in this study; associations were all biased toward the null, though less for Berkson-type errors.(53) Furthermore, the other pollutants considered in this study were also measured at the same central location; therefore the significant health associations for OP^{DTT} in bipollutant models are not readily explained by measurements being from a single location.

Various prior analyses of these data indicate that the main sources of aerosol OP include biomass burning and vehicle emissions through tail pipe and tire and brake wear and that atmospheric processing following emissions plays a key role in the observed DTT activities.(10, 40, 54) However, OP^{DTT} may be more closely linked to different sources by season.(37) Further analysis of OP^{DTT} measured over different seasons and geographic area would be useful to determine variability in associations with adverse health outcomes.

6.6: Conclusions

The health effects of $PM_{2.5}$ OP have been previously explored in panel studies assessing markers of toxicity, small cohort studies assessing health outcomes in subjects with differing levels of exposure, and case-crossover studies analyzing relationships between OP and health outcomes over time. In this ground-breaking study, we present support for the measurement of OP^{DTT} as a predictor of acute cardiorespiratory outcomes in a population-level study of a large metropolitan area. These results provide key evidence for OP as an important and useful integrated indicator of particulate matter toxicity for future air pollution studies.

Fig 6.1: Monthly distribution of the oxidative potential of water-soluble PM2.5 as measured by the DTT assay (OPDTT), June 2012 – April 2013, Atlanta, GA. Boxes encompass 25th through 75th percentiles, middle horizontal line represents the median, whiskers extend to the most extreme point within 1.5 interquartile ranges of the box, dots indicate outliers.

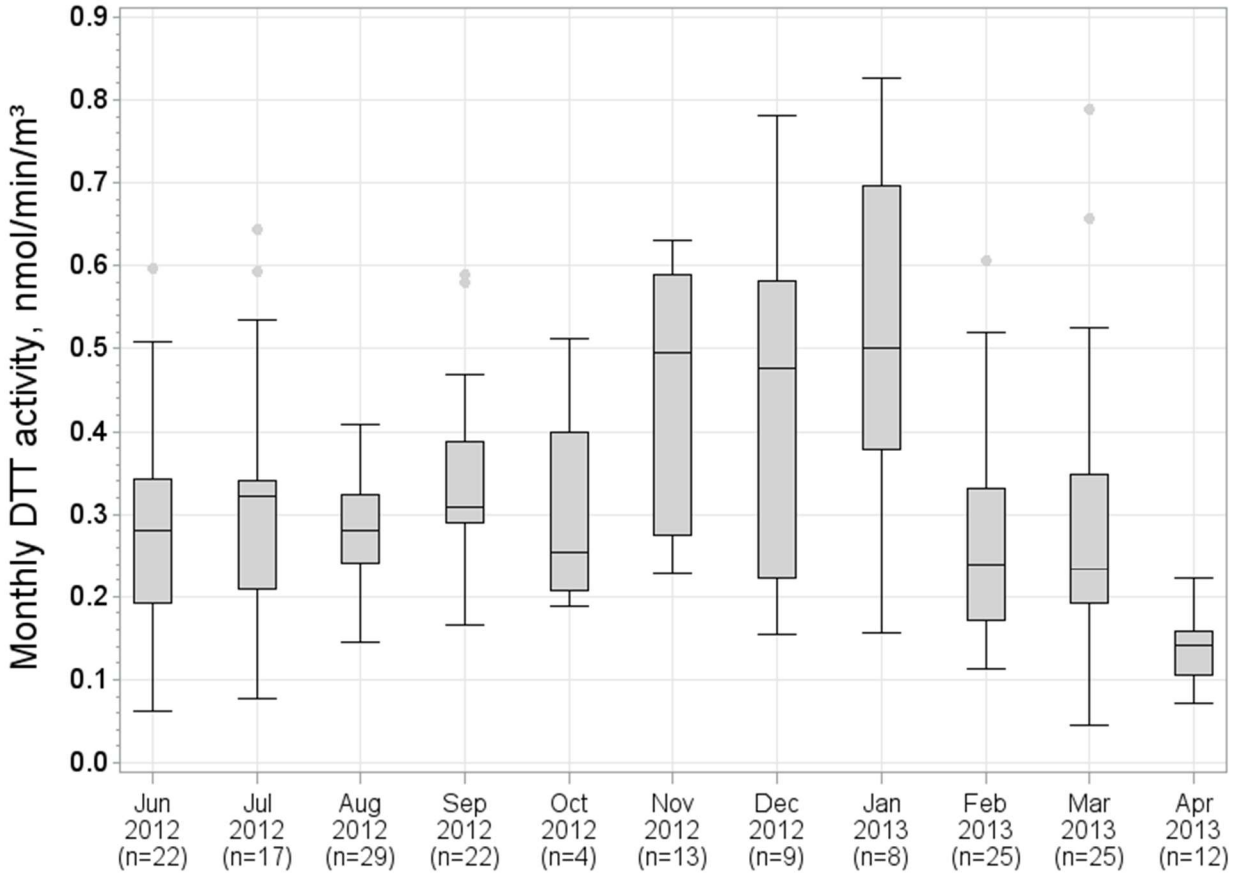


Table 6.1: Pearson correlation coefficients between the oxidative potential of water-soluble $PM_{2.5}$ as measured by the DTT assay (OP^{DTT}) and other air quality variables, June 2012 – April 2013, Atlanta, GA. Abbreviations: CO=carbon monoxide, NO2=nitrogen dioxide, O3=ozone, SO2=sulfur dioxide, PM25=fine particulate matter, and the following components of $PM_{2.5}$: EC=elemental carbon, NH4=ammonium, NO3=nitrate, OC=organic carbon, SO4=sulfate, Mn=manganese, Fe=iron, Cu=copper.

	OP^{DTT}	**$PM_{2.5}$**	**CO**	**EC**	**NH_4**	**NO_2**	**NO_3**	**O_3**	**OC**	**SO_2**	**SO_4**	**Mn**	**Fe**	**Cu**
OP^{DTT}	-	0.55	0.46	0.56	0.26	0.27	0.24	0.01	0.51	0.28	0.14	0.42	0.43	0.41
$PM_{2.5}$	0.55	-	0.44	0.65	0.63	0.36	0.14	0.41	0.86	0.24	0.66	0.38	0.62	0.48
CO	0.46	0.44	-	0.78	0.11	0.72	0.25	0.02	0.46	0.46	0.08	0.29	0.40	0.45
EC	0.56	0.65	0.78	-	0.23	0.59	0.22	0.07	0.70	0.45	0.21	0.40	0.51	0.50
NH_4	0.26	0.63	0.11	0.23	-	0.10	0.42	0.08	0.33	-0.03	0.83	0.07	0.31	0.22
NO_2	0.27	0.36	0.72	0.59	0.10	-	0.26	0.15	0.42	0.27	0.09	0.24	0.33	0.39
NO_3	0.24	0.14	0.25	0.22	0.42	0.26	-	-0.48	0.07	0.06	0.08	-0.01	-0.02	-0.05
O_3	0.01	0.41	0.02	0.07	0.08	0.15	-0.48	-	0.43	-0.01	0.31	0.19	0.37	0.28
OC	0.51	0.86	0.46	0.70	0.33	0.42	0.07	0.43	-	0.19	0.35	0.39	0.60	0.43
SO_2	0.28	0.24	0.46	0.45	-0.03	0.27	0.06	-0.01	0.19	-	0.01	0.22	0.17	0.19
SO_4	0.14	0.66	0.08	0.21	0.83	0.09	0.08	0.31	0.35	0.01	-	0.13	0.41	0.27
Mn	0.42	0.38	0.29	0.40	0.07	0.24	-0.01	0.19	0.39	0.22	0.13	-	0.63	0.38
Fe	0.43	0.62	0.40	0.51	0.31	0.33	-0.02	0.37	0.60	0.17	0.41	0.63	-	0.70
Cu	0.41	0.48	0.45	0.50	0.22	0.39	-0.05	0.28	0.43	0.19	0.27	0.38	0.70	-

Fig 6.2: Risk ratio for emergency department (ED) visit outcomes per interquartile range (IQR) of the oxidative potential of water-soluble $PM_{2.5}$ as measured by the DTT assay (OP^{DTT}), with 95% confidence intervals, June 2012 – April 2013, Atlanta, GA. Abbreviations: RD=all respiratory diseases (combined), COPD=chronic obstructive pulmonary disease, Pneu=pneumonia, URI=upper respiratory infection, CVD=all cardiovascular diseases (combined), CHF=coronary heart failure, IHD=ischemic heart disease.

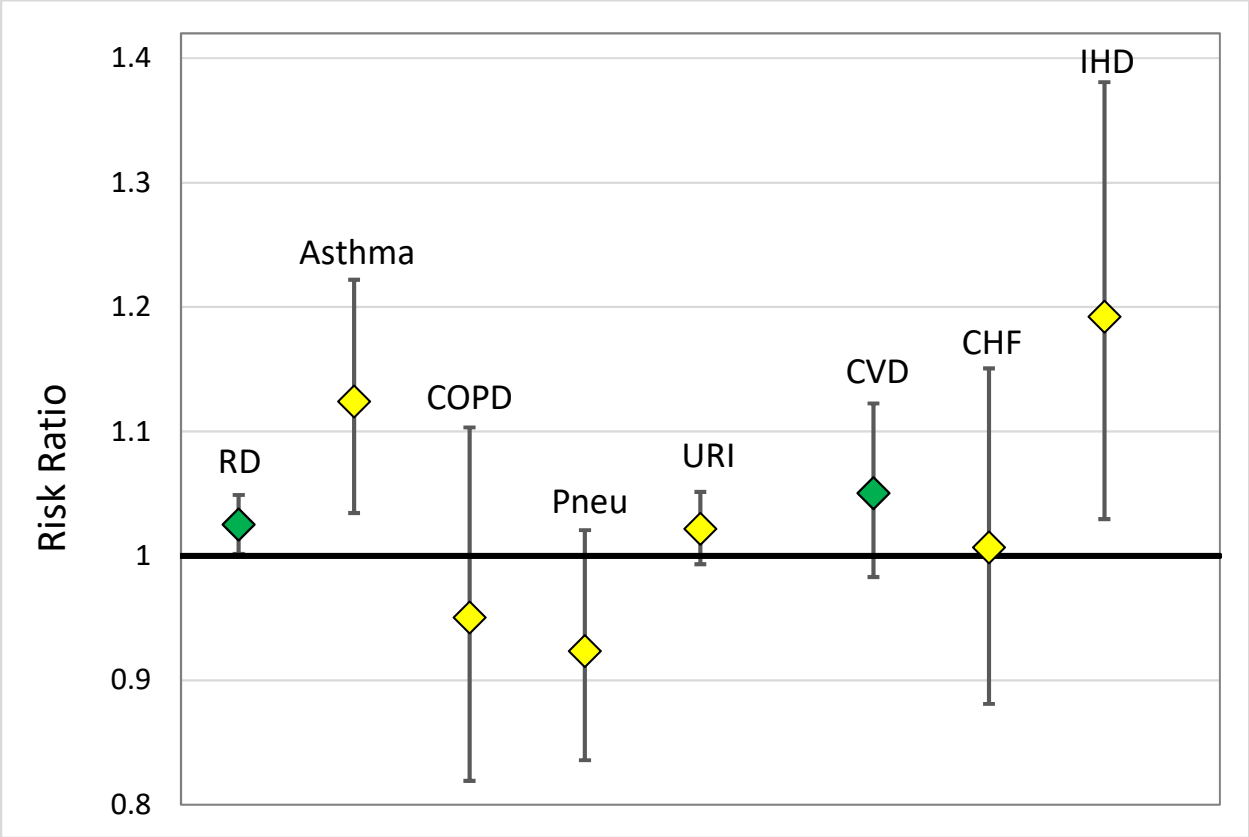


Fig 6.3: Asthma risk ratios for the oxidative potential of water-soluble $PM_{2.5}$ as measured by the DTT assay (OP^{DTT}) and other pollutant measures in two-pollutant models, with 95% confidence intervals, June 2012 – April 2013, Atlanta, GA. Risk ratio for OP^{DTT} (red markers) are per interquartile range (IQR) of OP^{DTT}; risk ratio for all other pollutant measures (blue markers) are per IQR of that particular pollutant. Abbreviations: CO=carbon monoxide, NO2=nitrogen dioxide, O3=ozone, SO2=sulfur dioxide, PM25=fine particulate matter, and the following components of $PM_{2.5}$: EC=elemental carbon, NH4=ammonium, NO3=nitrate, OC=organic carbon, SO4=sulfate, Mn=manganese, Fe=iron, Cu=copper.

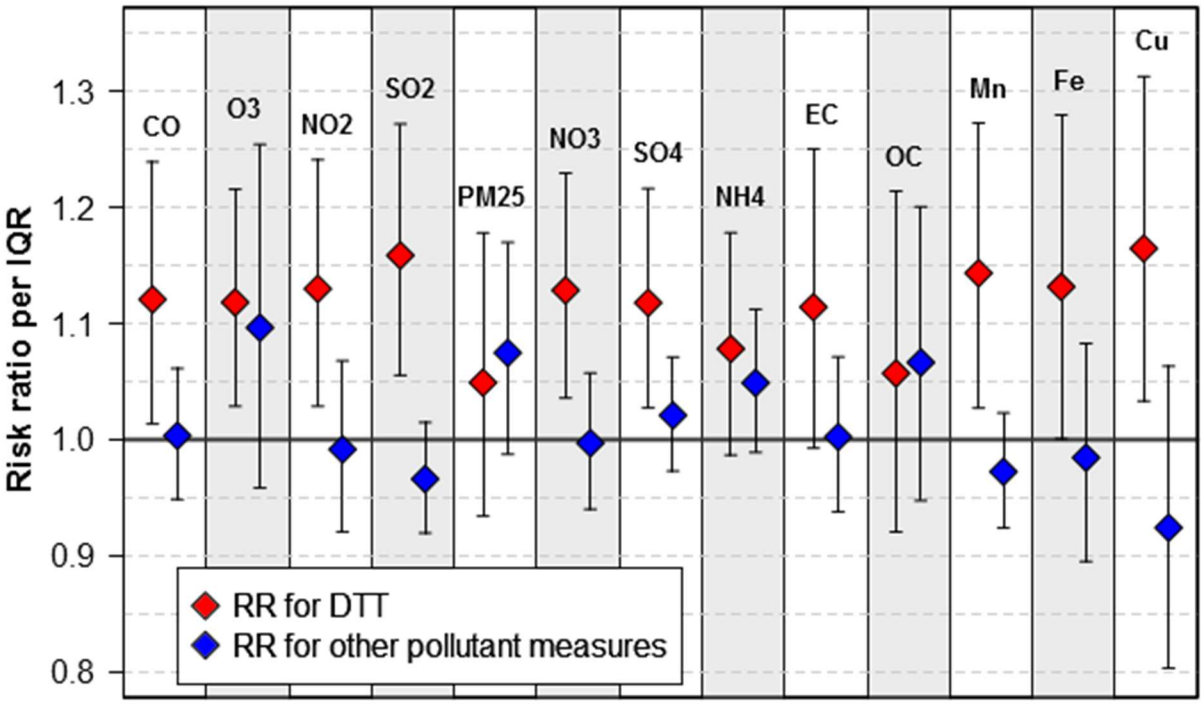
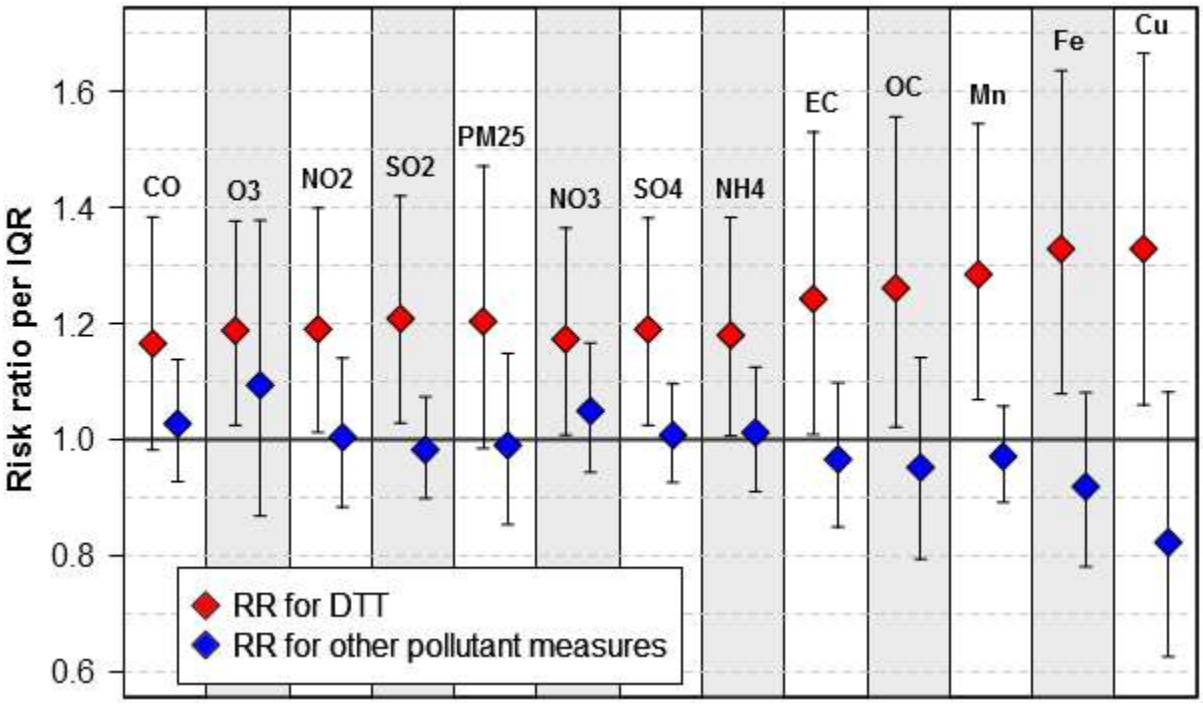


Fig 6.4: Ischemic heart disease (IHD) risk ratios for the oxidative potential of water-soluble $PM_{2.5}$ as measured by the DTT assay (OP^{DTT}) and other pollutant measures in two-pollutant models, with 95% confidence intervals. Risk ratio for OP^{DTT} (red markers) are per interquartile range (IQR) of OP^{DTT}; risk ratio for all other pollutant measures (blue markers) are per IQR of that particular pollutant. Abbreviations: CO=carbon monoxide, NO2=nitrogen dioxide, O3=ozone, SO2=sulfur dioxide, PM25=fine particulate matter, and the following components of $PM_{2.5}$: EC=elemental carbon, NH4=ammonium, NO3=nitrate, OC=organic carbon, SO4=sulfate, Mn=manganese, Fe=iron, Cu=copper.



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7: AIM II: ASSOCIATIONS BETWEEN MODELED FINE PARTICLE OXIDATIVE POTENTIAL AND CARDIORESPIRATORY EMERGENCY DEPARTMENT VISITS IN A LONG-TERM TIME SERIES STUDY

7.1: Abstract

Background: Oxidative potential (OP) has been proposed as a major mechanism of particulate matter toxicity, but time and labor constraints have generally thus far prevented large-scale ambient OP measurements for long-term, population-based studies.

Methods: We used measurements of fine particulate matter ($PM_{2.5}$) OP captured by a dithiothreitol assay (OP^{DTT}) for 196 days in Atlanta, GA, along with concurrent air pollutant concentrations and meteorology measurements to develop a predictive model for OP^{DTT}. This model was applied to historical air quality measurements from 1/1/1999 – 12/31/2013 in order to generate modeled daily time series of OP^{DTT} for a period when direct measurements of OP^{DTT} were not available. Poisson log-linear models were then applied to estimate associations between modeled OP^{DTT} and emergency department (ED) visits for selected cardiorespiratory categories in the 5-county Atlanta metropolitan area.

Results: Modeled OP^{DTT} was associated with ED visits for respiratory disease (risk ratio = 1.006, 95% confidence interval = 1.001-1.011) and asthma (RR = 1.010, 95% CI = 1.004-1.017). These associations were stronger for the period from 1999-2005. In bipollutant models with $PM_{2.5}$ mass and OP^{DTT}, the positive associations of OP^{DTT} with ED visits for respiratory disease, asthma, chronic obstructive pulmonary disorder,

pneumonia, and congestive heart failure were not attenuated while the associations for $PM_{2.5}$ became null.

Conclusions: Significant associations between modeled OP^{DTT} and cardiorespiratory ED visits, as well as the relative importance of OP^{DTT} compared to total $PM_{2.5}$ mass in bipollutant models, provide additional evidence that OP may be an important aspect of $PM_{2.5}$ toxicity.

7.2: Introduction

Oxidative potential (OP) has been hypothesized to be an important marker for the toxicity of fine particulate matter (PM with aerodynamic diameter <2.5 microns, or $PM_{2.5}$). Through the *in vivo* generation of reactive oxygen species, $PM_{2.5}$ OP may initiate inflammatory cascades that lead to adverse cardiorespiratory outcomes.(1, 2) Exposure to diesel exhaust and other sources of $PM_{2.5}$ have been associated with measureable amounts of oxidative stress, leading to inflammatory responses in peripheral blood and airway tissues. Inhalation of particulate matter has been shown to be associated with the release of cytokines, activated immune cells, and other mediators of inflammation in the upper and lower airways, which can lead to asthma, bronchitis, and other respiratory outcomes.(3, 4) Similarly, $PM_{2.5}$-driven release of proinflammatory mediators into the bloodstream can lead to vasoconstriction, atherosclerosis, and endothelial dysfunction, all major risk factors for future cardiac outcomes.(5, 6) Studies have shown that inhalation of aerosol OP is linked to increased inflammatory responses and decreased lung function.(7-10)

Current methods for measuring OP are labor-intensive and time consuming, thus most existing studies of the health effects of OP have involved few measurements. The largest known study to date involves ~700 daily measurements using glutathione and ascorbate OP assays: this study showed generally positive but nonsignificant associations between OP and hospital admissions for respiratory and cardiovascular diseases in young adults.(11) An alternative to extensive OP measurement is modeling aerosol OP over space or time from a smaller number of OP measurements to enable use and evaluation of OP in longer retrospective studies. Using land-use regression to estimate OP at

individual addresses, residential ambient OP levels were found to be associated with increased asthma incidence and decreased lung function.(12) Another study that combined glutathione OP assays with spatial emissions-dispersion models did not find evidence that OP increased progression of atherosclerosis.(13) Long-term city-level $PM_{2.5}$ OP extrapolated from a small number of measurements was shown to modify the association between $PM_{2.5}$ and emergency room visits for respiratory illness and myocardial infarctions.(14, 15)

Recently, we conducted a study in the Atlanta, GA metropolitan area, which showed acute health associations for ambient water-soluble $PM_{2.5}$ OP (*submitted*). This study measured OP using a dithiothreitol (DTT) assay daily for 196 days, and estimates from time series models were positive and statistically significant for the associations of OP^{DTT} with daily counts of ED visits for several cardiorespiratory outcomes. In additional studies using source apportionment models constructed from these OP^{DTT} measurements, modeled backcast OP^{DTT} was associated with ED visits for asthma and congestive heart failure.(16, 17) While these results suggest OP^{DTT} may be a useful health indicator, more studies are needed to build the evidence base regarding the health effects of $PM_{2.5}$ OP. In this study, we make further use of this dataset of measured OP^{DTT} along with extensive databases of air quality measurements and hospital ED visits in the Atlanta area. Our goal was to model daily $PM_{2.5}$ OP back in time to 1999 and perform a 15-year study of OP health associations.

7.3: Methods

OP measurement

Ambient air sampling for $PM_{2.5}$ OP took place over 196 days from June 2012 – April 2013 at a mixed industrial/residential location in Atlanta, GA (Jefferson Street), roughly 2 miles northwest of downtown Atlanta and about 1.4 miles from a major interstate highway. To measure OP, we used a semi-automated system that measures the capacity of water-soluble $PM_{2.5}$ to generate reactive oxygen species using the DTT assay (OP^{DTT}). Our OP^{DTT} method and this Atlanta sampling campaign have been described extensively in previous publications.(18-21) Particles were collected with a high-volume sampler (HiVol, Thermo Anderson, nondenuded, nominal flow rate 1.13m3 min-1, $PM_{2.5}$ cut size by impactor) onto pre-baked 8x10 inch quartz filters to collect $PM_{2.5}$ over 23 hour periods (noon-11am daily). After sampling, filters were immediately wrapped in prebaked aluminum foil and stored in a freezer. Analysis of filters for OP^{DTT} and other pollutant measures started in March 2013. A fraction of the high volume filter was extracted in water, the extract was filtered and then OP^{DTT} was determined with the automated analytical system, which allowed for consistent OP^{DTT} analysis on a large number of filter samples with less effort than manual analysis. As detailed in previous work, this system has a high analytical precision (Coefficient of Variation of 12% for standards, 4% for ambient samples).(18)

Modeling OP as a function of other air quality variables

We used daily OP^{DTT} measurements for 196 days during the period June 2012 – April 2013 to build linear regression models for OP^{DTT} using daily air pollutant concentration and meteorology variables.

Daily measurements of gaseous pollutants, $PM_{2.5}$ components, meteorology, and temporal variables were made from 1/1/1999 – 12/31/2013. All gases and particulate compounds were also measured at the same Jefferson Street location as part of the Southern Aerosol Research and Characterization Study (SEARCH) project; details on their measurement have been previously reported.(22-24) Meteorology measurements were made at Hartsfield-Jackson Atlanta airport, approximately 10 miles south of Jefferson Street. The full list of variables available for this study is in Table 7.1.

The goal of this phase of the study was to accurately estimate daily backcast OP^{DTT} for the 1999-2013 study period. We constructed a predictive model for OP^{DTT} using daily measurements of OP^{DTT} and concurrently measured predictor variables from June 2012 – April 2013. The models then were used to estimate (backcast) OP^{DTT} using daily measurements of the same predictors from 1/1/1999 – 12/31/2013. Developing models based solely on statistical criteria could be inadequate, so additional criteria were also considered. Measurements that included mixtures of components (such as total $PM_{2.5}$ mass or organic carbon) may have changed in composition over the 15-year study period and therefore the associations with OP^{DTT} may be meaningfully different over time, so we did not use these variables in our models. Variables believed to be closely linked to OP would likely maintain a more consistent association with OP^{DTT} compared to variables that may be more indirect proxies for OP. Finally, there was some consideration of the relative strengths of a larger model that would maximize model fit versus a smaller model that would include only strong predictors of OP^{DTT}. Models with more predictor variables may be susceptible to overfitting and poorer precision for coefficient estimates, yielding inaccurate backcast OP^{DTT} estimates. As backcast

estimates could not be validated with actual measurements of OP^{DTT}, we decided that in addition to our primary model for predicting OP^{DTT}, we would also construct secondary models using different methodological approaches in order to convey uncertainty in the process of backcasting OP^{DTT}.

Our primary model for predicting OP^{DTT} was constructed with the idea of choosing variables we believed would be strongly predictive of oxidative potential based on knowledge of atmospheric oxidative chemistry and other factors. This included $PM_{2.5}$ components that may directly contribute to measured OP^{DTT}, gases that are indicators for pollution from different sources, and important meteorological variables. Twelve *a priori* predictive variables were selected: EC, Fe, Cu, Mn, K, NH_4, CO, NO_y, O_3, temperature, dew point, and precipitation. A model predicting OP^{DTT} from these variables was fit, and any nonsignificant predictor variables were eliminated through backward selection, with variables sequentially removed by highest p-value testing for association with OP^{DTT} until all remaining predictors were significantly associated with OP^{DTT} ($p<0.05$).

OP^{DTT} was measured over 23-hour periods from noon-11am, while most reported air quality measurements were reported using midnight to midnight values. For all predictor variables, we used 2-day moving average values of the two days overlapped by the OP^{DTT} measurement. We tested for further lagged associations by looking at correlations between OP^{DTT} and air quality measurements from days prior, but found little support for using additional lags compared to concurrent measurements. Nonlinear relationships were also considered: associations were tested between OP^{DTT} and cubic polynomials of predictor variables, and between OP^{DTT} and logged predictor variables, as

well as between logged OP^{DTT} and unaltered predictor variables. Preliminary findings showed that associations generally were not substantially improved compared to linear associations, therefore cubic polynomial and log terms were not used in the final models. For NH_4 and SO_4, we divided measured values by the 365-day moving average to adjust for long-term trends.

This model was created in order to estimate joint associations between predictor variables and OP^{DTT}. The estimate regression coefficients of these models for the June 2012 – April 2013 period were then applied to measured daily predictor values from 1/1/1999 – 12/31/2013 in order to produce three sets of daily backcast estimates of OP^{DTT}.

Secondary models

Two additional models for predicting OP^{DTT} (which will be referred to as Model B and Model C) were constructed using stepwise selection. At each sequential step, we added a predictor variable that most increased the adjusted r^2 value, and then tested to see if replacing any existing model variable with any other potential predictor would increase the adjusted r^2 value. Replacements maximizing adjusted r^2 would continue to be performed until no possible additional replacement existed which would further increase the adjusted r^2. Interaction terms were considered, but models were required to be hierarchically well-formulated: interaction terms could only be included if their component variables were already in the model, and those component variables could not be eliminated while they were present in interaction terms.

For Model B, the motivation was to construct a small model containing the strongest predictors: to avoid potential model overfitting or inclusion of predictors only marginally predictive of OP^{DTT}, this model was restricted to six predictor variables. Model C was constructed with the central goal of maximizing fit for measured OP^{DTT}, so we allowed for the addition of more predictor variables as long as each new addition was significantly associated with OP^{DTT}, up to a maximum of 20 model parameters. Model C also allowed for temporal indicators (season and weekday). For gas and meteorology variables, which had hourly data available, we used created noon-11am mean values: though this method was not consistent with that used for particulate measurements, it did result in greater model fit.

The criteria for the construction of the primary and secondary models for predicting OP^{DTT} were decided prior to assessing health associations in order to deter any preferential selection of positive results.

Hospital emergency department (ED) visit data

Data were collected on emergency department (ED) visits for the people living in the Atlanta, GA metropolitan area between January 1, 1999 and December 31, 2013. Computerized billing records for patient-level data were pulled from 42 acute care hospitals. A single patient-level dataset was created by combining data obtained directly from individual participating hospitals for the period 1999-2004 with a pre-combined dataset from the Georgia Hospital Association (GHA) for the period 2005-2013. Patient variables included date of admission, the primary International Classification of Diseases 9th Revision (ICD-9) diagnostic code, patient date of birth, sex, race, and 5-digit residential ZIP code. ED visits were included if the patient ZIP code was located wholly

or partially within the five primary urban counties of metropolitan Atlanta (Fulton, DeKalb, Gwinnett, Cobb, Clayton). Hospital indicators were generated to distinguish periods of available and useable data for each hospital.

Daily counts of ED visits were calculated for several cardiorespiratory outcome categories based on primary ICD-9 codes. We used daily counts of ED visits for all respiratory diseases (RD) (ICD-9 codes 460-465, 466.0, 466.1, 466.11, 466.19, 477, 480-486, 491-493, 496, 786.07) as well as the RD subcategories of asthma ED visits (ICD-9 codes 493, 786.07), chronic obstructive pulmonary disease (COPD) (ICD-9 codes 491, 492, 496), and pneumonia (ICD-9 codes 480-486). We also used daily counts of ED visits for all cardiovascular diseases (CVD) (ICD-9 codes 410-414, 427, 428, 433-437, 440, 443-445, 451-453) as well as the CVD subcategories of congestive heart failure (CHF) (ICD-9 code 428) and ischemic heart disease (IHD) (ICD-9 codes 410-414).

Health associations of backcast DTT

We estimated associations between modeled daily OP^{DTT} and daily counts of ED visits for the selected cardiorespiratory outcomes using Poisson log-linear models accounting for overdispersion; the methodology for these models had been developed through substantial previous work by our study team.(25-31) To maintain consistent methodology with our prior studies which demonstrated multi-day associations between pollutants and respiratory outcomes,(28, 29, 32, 33) 3-day moving averages (average of OP^{DTT} levels same-day, 1 day prior, and 2 days prior, or lag 0-2) were chosen *a priori* as the relevant exposure values for respiratory outcomes (ED visits for RD, asthma, COPD, and pneumonia). For cardiovascular outcomes (ED visits for CVD, CHF, and IHD), same-day OP^{DTT} values (lag 0) were used as had been done in previous studies.(27, 34)

To control for long-term trends, the models included cubic splines with monthly knots. The models controlled for season as a categorical variable (winter=Dec-Feb, spring=Mar-May, summer=Jun-Aug, autumn=Sep-Nov), weekdays and federal holidays, as well as the day after Christmas, the day after Thanksgiving, and the actual date of certain holidays (Christmas, New Year's Day, Veteran's Day, Independence Day) when not on the day of the federal holiday. Meteorology covariates included temperature (cubic polynomial of the daily maximum temperature and the cubic polynomial of the lag 1-2 daily minimum temperature), dew point (cubic polynomial of the lag 0-2 moving average of daily mean dew point), and indicator variables for periods of hospital data contribution. To determine the utility of OP^{DTT} as a measure of ambient air toxicity independent of overall $PM_{2.5}$, we ran similar models with $PM_{2.5}$ total mass as the primary exposure, as well as bipollutant models with both OP^{DTT} and $PM_{2.5}$. Health associations were measured as risk ratio (RR) per interquartile range (IQR) of daily observed OP^{DTT} or $PM_{2.5}$ mass (during the period of OP^{DTT} measurement).

Due to the implementation of pollution control policies, ambient levels of multiple pollutants in the Atlanta metropolitan area have dropped substantially over the study period.(35) As associations between pollutants and health may be more readily quantifiable at higher concentrations, we also ran the health associations models over the first half of the study period (1/1/1999-12/31/2005).

Accounting for uncertainty in backcast OP^{DTT} estimates

Typically, for studies that utilize modeled exposure data, confidence intervals reflect uncertainty in the association between the exposure and outcome; the modeled data is essentially treated as fixed. This approach ignores potential biases or uncertainty

inherent in using modeled, not measured, exposure data. We used Monte Carlo methods to capture both the uncertainty in estimating associations between modeled OP^{DTT} and cardiorespiratory ED visits as well as the uncertainty in daily backcast OP^{DTT} estimates. We used the observed parameter estimates of the backcast OP^{DTT} model and the estimated variance-covariance structure to generate 100 sets of estimated coefficient values using a multivariate normal distribution, which were used to produce 100 sets of predicted daily backcast OP^{DTT} estimates. Randomized daily residuals were added to the daily predicted OP^{DTT} estimates based on a normal distribution with the observed residual variance from the predictive model for the 196-day period; this produced 100 sets of finalized daily backcast OP^{DTT} estimates. For each of these 100 sets of OP^{DTT} values, we took 100 sample risk ratios based on the estimated association with cardiorespiratory ED visits, thus generating 10,000 risk ratios for each outcome. The mean and the 2.5^{th} and 97.5^{th} percentiles of these 10,000 risk ratios were used for the point estimate and 95% confidence interval.

All analyses were performed using SAS version 9.4 (SAS Institute, Inc., Cary, NC) and R version 3.01 (The R Foundation for Statistical Computing, 2013).

7.4: Results

OP^{DTT} measurements

OP^{DTT} levels were recorded for 196 days from June 2012 – April 2013. Mean daily OP^{DTT} was 0.32 nmol/min/m^3 (range: 0.05-0.83, interquartile range: 0.21), and OP^{DTT} tended to be higher from November through January.

OP^{DTT} backcast modeling results

Three variables (Fe, Cu, and precipitation) were not associated with OP^{DTT}, leaving a 9-variable predictive model (EC, Mn, K, NH_4, CO, NO_y, O_3, temperature, and dew point); model coefficients are shown in Table 7.2. The r^2 value was 0.595 (adjusted r^2=0.573). Estimated backcast OP^{DTT} values were generally higher in the early years (Figure 7.1), with an estimated mean OP^{DTT} activity of 0.72 nmol/min/m^3 in 1999.

Hospital ED visit data

From 1999-2013 in the 5-county Atlanta metropolitan area, there were 1,637,338 recorded ED visits for respiratory disease (a mean of 299.7 per day), of which 374,126 were for asthma (68.5 per day), 74,853 were for chronic obstructive pulmonary disease (13.7 per day), and 200,551 were for pneumonia (36.7 per day). There were 416,392 recorded ED visits for cardiovascular disease (76.2 per day) of which 105,561 were for congestive heart failure (19.3 per day) and 99,666 were for ischemic heart disease (18.2 per day).

Health associations

Daily values of backcast OP^{DTT} for 1999-2013 were associated with ED visits for RD (risk ratio=1.006, 95% confidence interval=1.001-1.011) and asthma (RR=1.010, 95% CI=1.004-1.017) (Figure 7.2). Point estimates for risk ratios were positive for all seven cardiorespiratory outcomes. Backcast OP^{DTT} estimates over the first half of the study period (1999-2005) generally had stronger associations with cardiorespiratory ED visits. OP^{DTT} was associated with ED visits for RD (RR=1.011, 95% CI=1.006-1.018) and asthma (RR=1.018, 95% CI=1.009-1.029) (Figure 7.3).

Daily values of $PM_{2.5}$ mass from 1999-2013 were also associated with ED visits for RD (RR=1.005, 95% CI=1.001-1.009), asthma (RR=1.008, 95% CI=1.002-1.014), and CVD (RR=1.004, 95% CI=1.000-1.008), and risk ratio point estimates were above 1 for all cardiorespiratory outcomes. In bipollutant models with OP^{DTT} and $PM_{2.5}$, the health associations for OP^{DTT} were not substantially attenuated for RD, asthma, and COPD, pneumonia, and CHF, while health associations for $PM_{2.5}$ went to the null (Figure 7.4). $PM_{2.5}$ had higher risk ratio estimates than OP^{DTT} for CVD and IHD ED visits in bipollutant models.

Secondary models

The 6-variable Model B had r^2=0.587 and the 12-variable Model C had r^2=0.740; summary information for these models are shown in Table 7.3, with full regression coefficient estimates presented in Tables 7.4-7.5. The correlation between daily backcast OP^{DTT} estimates for the Primary Model and Model B was r=0.913, between the Primary Model and Model C was r=0.707, and between Model B and Model C was r=0.687. Backcast estimates were generally highest for Model C (Figure 7.5), which had estimated mean OP^{DTT} values of 1.13 nmol/min/m^3 for 1999; however, Model C also estimated negative OP^{DTT} values for 13 days.

Associations with cardiorespiratory ED visits are shown in Figure 7.6. In general, Model B had weaker health associations than the Primary Model, and Model C had the weakest health associations.

7.5: Discussion

This study provided further evidence that OP is an important indicator of $PM_{2.5}$ toxicity. We used established time-series regressions that controlled for a variety of potential temporal confounders, and we found that modeled OP^{DTT} was significantly associated with ED visits for respiratory disease and asthma. In several bipollutant models with $PM_{2.5}$, associations between OP^{DTT} and cardiorespiratory ED visits were not attenuated while the effect of $PM_{2.5}$ was null, supporting the interpretation that OP is a driver of $PM_{2.5}$ effects.

Observed associations between OP^{DTT} and ED visits were stronger for the 1999-2005 time period compared to associations for the entire 1999-2013 period. Similar patterns in strength of association had previously been found for other air pollution analyses conducted in the Atlanta area (unpublished data). Measured ambient levels of most pollutants were significantly lower in the latter half of the 1999-2013 study period compared to the earlier half, and this decline was also observed for all backcast OP^{DTT} estimates. One possible explanation for the stronger health associations from 1999-2005 was that the higher pollutant concentrations, along with larger daily variability, made health associations more readily quantifiable. Other hypotheses may include nonlinear associations between pollutants and ED visits, changes in the relationship between ambient and personal exposure (e.g., tighter buildings over time), or simply random error.

The Primary Model had the strongest associations with cardiorespiratory ED visits, while Model C generally had the weakest associations. The Primary Model was constructed by making informed decisions for the *a priori* selection of variables believed to be strongly predictive of OP^{DTT}. The large number of terms in the Model C led to a

loss of precision in parameter estimates; combined with the inclusion of multiple interaction terms, this caused inflated daily variability of OP^{DTT} estimates, resulting in a few implausible values like negative or improbably large OP^{DTT} values. Model fit for the 2012-2013 time period may not necessarily be the most important quality of a predictive model for backcasting to earlier time periods; rather, the careful selection of variables that would be expected to be closely linked to OP^{DTT} may be critical. However, without any way to validate the backcast OP^{DTT} estimates, we are unable to make any conclusive determinations regarding the relative success of the three models. Despite the methodological difference in these models, they produced well-correlated daily backcast OP^{DTT} estimates as well as similar trends toward positive associations with cardiorespiratory ED visits. Importantly, we chose the form of the final models prior to conducting health association analyses in order to avoid bias toward the selection of positive results. Furthermore, we utilized Monte Carlo simulation to capture the uncertainty in the modeling of backcast OP^{DTT}. The simulated 95% confidence intervals presented in this study incorporated the uncertainty in the parameter estimates of the predictive model, the uncertainty in the backcasting of daily OP^{DTT} values based on this model, and the uncertainty in the estimation of the associations between modeled backcast OP^{DTT} and cardiorespiratory ED visits.

EC and NH_4 were strongly predictive of OP^{DTT}, and were included in all three predictive models. EC is a marker for traffic pollution, especially from diesel emissions; prior studies have shown associations between EC and oxidative stress-linked inflammation.(36-38) NH_4, on the other hand, is a secondary aerosol generally formed by reactions between NH_3 (largely from agricultural operations), but largely follows

concentrations of SO_4^{2-} plus NO_3^-, which are secondary products of power plant or traffic emissions.(39) Higher NH_4^+ concentrations may be indicative of a certain combinations of pollutant emissions and atmospheric processing of those emissions, with NH_4^+ acting as a tracer for secondary species that can significantly increase OP^{DTT}.(40, 41) Previous studies did not find positive associations between OP^{DTT} and NH_4^+,(42, 43) suggesting that these relationships may be conditional on factors such as geographic location, seasonality, aerosol oxidation processes or atmospheric conditions.

Previous studies using the same 196 daily measurements of OP^{DTT} had used associations with modeled $PM_{2.5}$ source impacts in order to backcast daily estimates of OP^{DTT}; these backcast OP^{DTT} estimates were associated with ED visits for asthma and CHF.(16, 17) This current study expands upon those analyses by utilizing a larger number of potential predictor variables that were measured, not modeled. Using measured predictors removes one possible source of error, and the availability of individual pollutant species and meteorological variables allow for the investigation of additional relationships that may not have been detected using source apportionment. Furthermore, this current study expands upon previous analyses in multiple ways: the study period was expanded to 1999-2013; nonlinear associations and interaction terms were assessed; additional temporal lags were considered; different modeling considerations were taken into account; and associations with additional cardiorespiratory outcomes were reported.

This study only assessed health associations with modeled water-soluble $PM_{2.5}$ OP^{DTT}, which does not consider OP^{DTT} associated with solid particle surfaces of $PM_{2.5}$ such as soot or EC.(43) In addition, different assays for OP such as DTT, glutathione,

and ascorbate are often poorly correlated and may capture different aerosol components that generate OP.(44) OP^{DTT} may be largely driven by transition metal ions as well as organic aerosols linked to incomplete combustion, such as biomass burning (18), while ascorbate (40) and glutathione depletion may be more associated with brake and tire wear.(16, 45-47) Epidemiologic assessments using any single OP assay likely only capture a fraction of the total health effects of aerosol OP, but OP^{DTT} may be more comprehensive than others.(17)

7.6: Conclusion

This study applied unique methodologies to create a modeled time series of daily OP^{DTT} estimates, which was supported by secondary models. We utilized a substantial hospital ED dataset and well-established epidemiologic models to perform the largest population-based analysis of the cardiorespiratory effects of OP^{DTT} conducted to date. Estimated health associations incorporated uncertainty in in the modeling of backcast OP^{DTT} values. The results provide additional evidence that OP is an important measure of $PM_{2.5}$ toxicity and should continue to be a key aspect of future air pollution studies.

Figure 7.1. Distribution of daily backcast OP^{DTT} values for each year, Atlanta, GA, 1999-2013. Boxes represent the 25th through the 75th percentiles of daily OP^{DTT} values; median values are horizontal white lines within each box, and mean values are yellow dots. Whiskers extend to the most extreme points within 1.5 interquartile ranges of the box, while and outliers outside the whiskers are represented by blue dots.

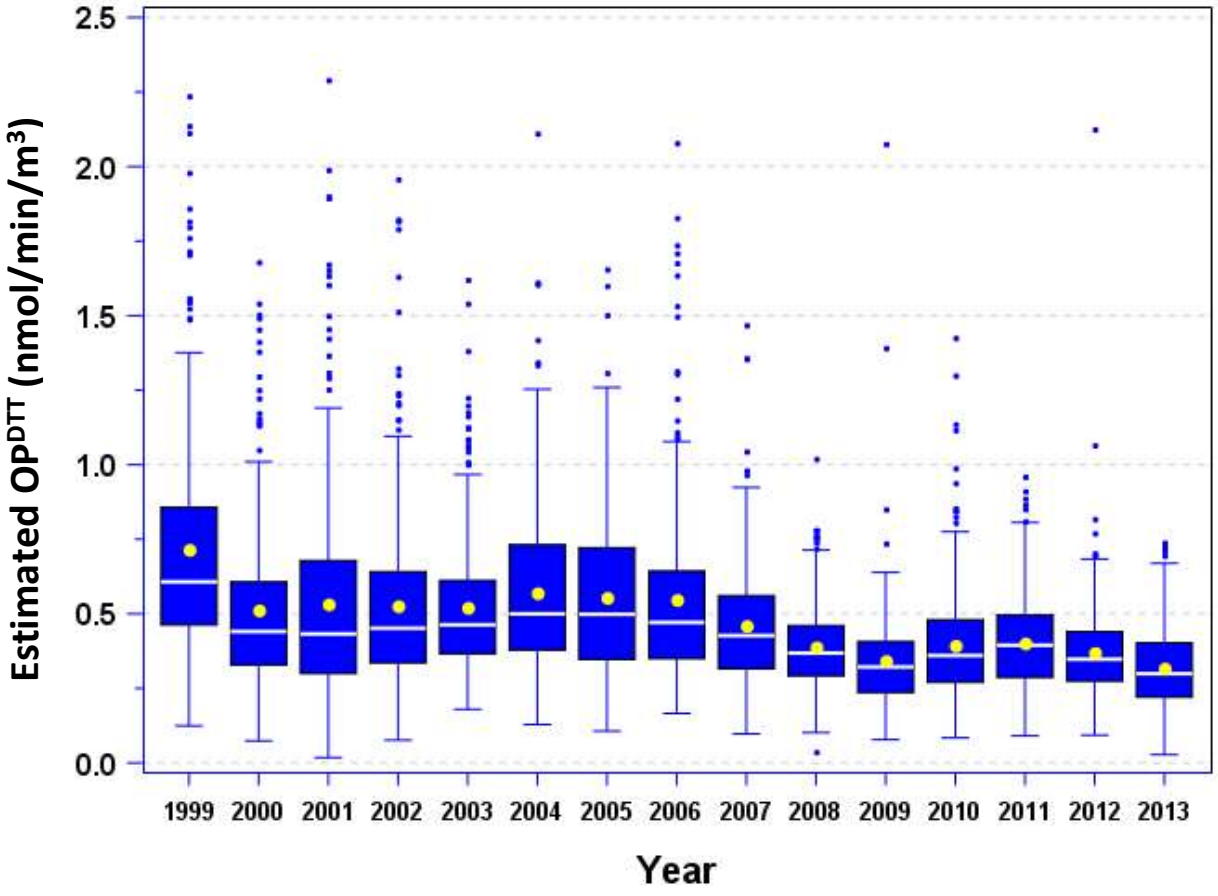


Figure 7.2: Associations between oxidative potential OP^{DTT} and seven categories of cardiorespiratory ED visits, 5-county Atlanta metropolitan area, 1999-2013. RD = all respiratory disease, COPD = chronic obstructive pulmonary disease, Pneu = pneumonia, CVD = all cardiovascular disease, CHF = congestive heart failure, IHD = ischemic heart disease, IQR = interquartile range.

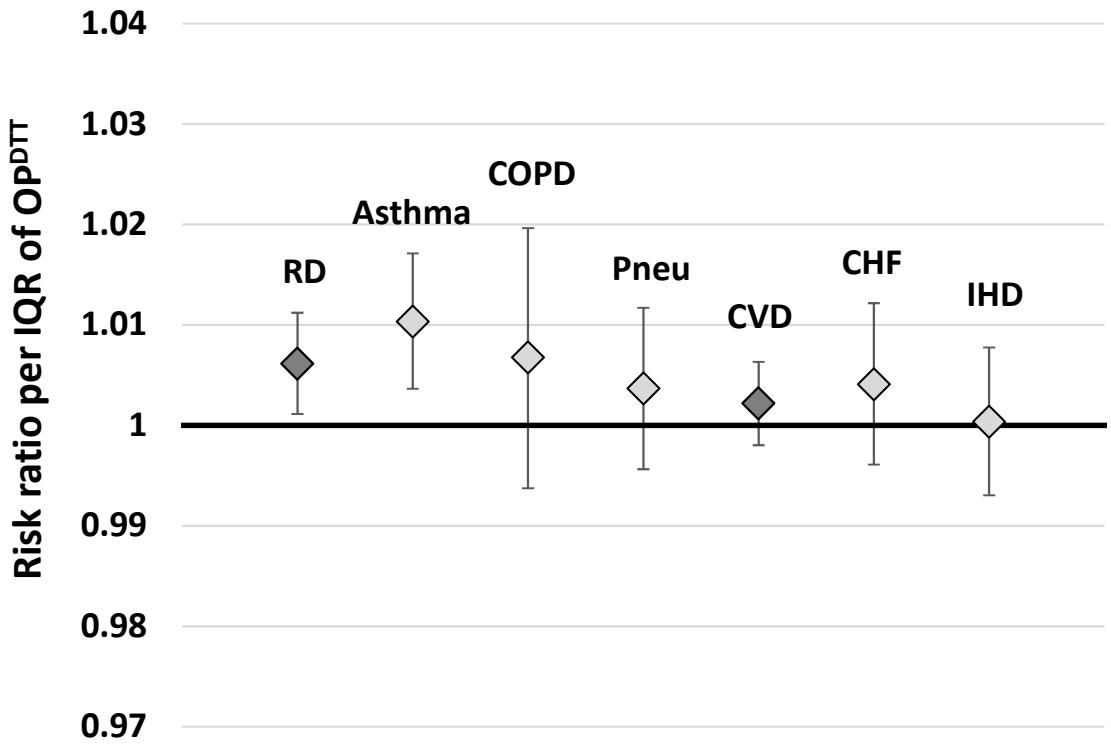


Figure 7.3: Associations between OP^{DTT} and seven categories of cardiorespiratory ED visits, 5-county Atlanta metropolitan area, earlier time period, 1999-2005. RD = all respiratory disease, COPD = chronic obstructive pulmonary disease, Pneu = pneumonia, CVD = all cardiovascular disease, CHF = congestive heart failure, IHD = ischemic heart disease, IQR = interquartile range.

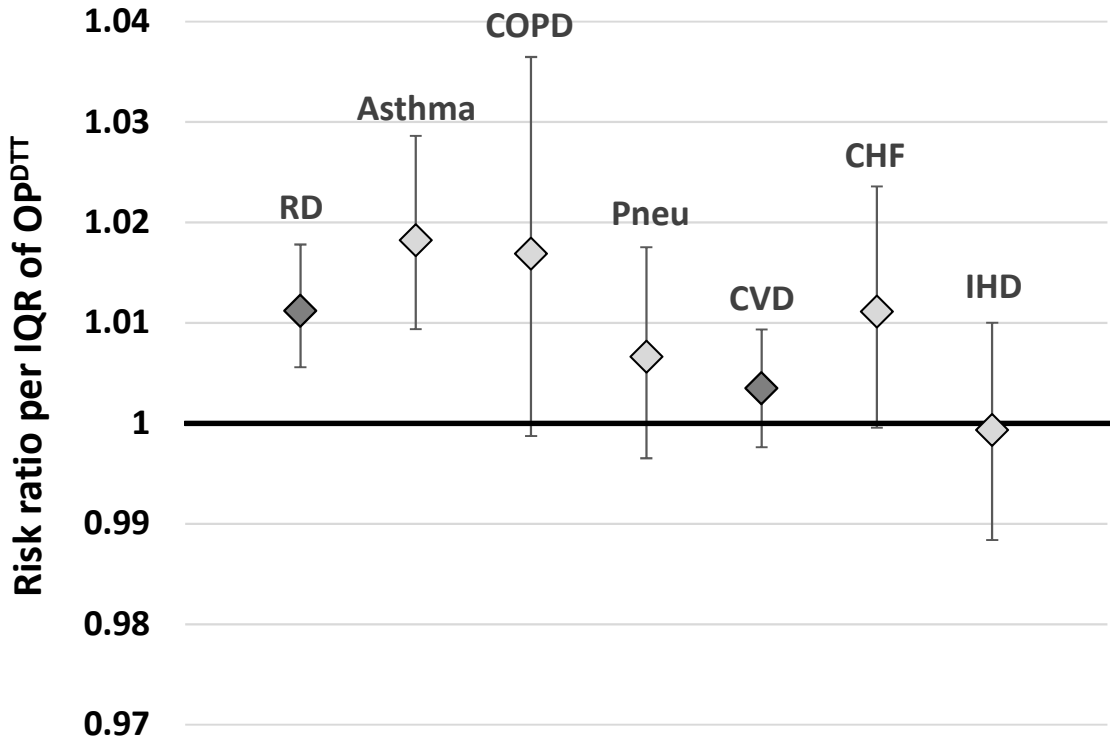


Figure 7.4: Associations with seven categories of cardiorespiratory ED visits for OP^{DTT} (blue) and $PM_{2.5}$ (green) in bipollutant models, 5-county Atlanta metropolitan area, earlier time period, 1999-2005. RD = all respiratory disease, COPD = chronic obstructive pulmonary disease, Pneu = pneumonia, CVD = all cardiovascular disease, CHF = congestive heart failure, IHD = ischemic heart disease, IQR = interquartile range.

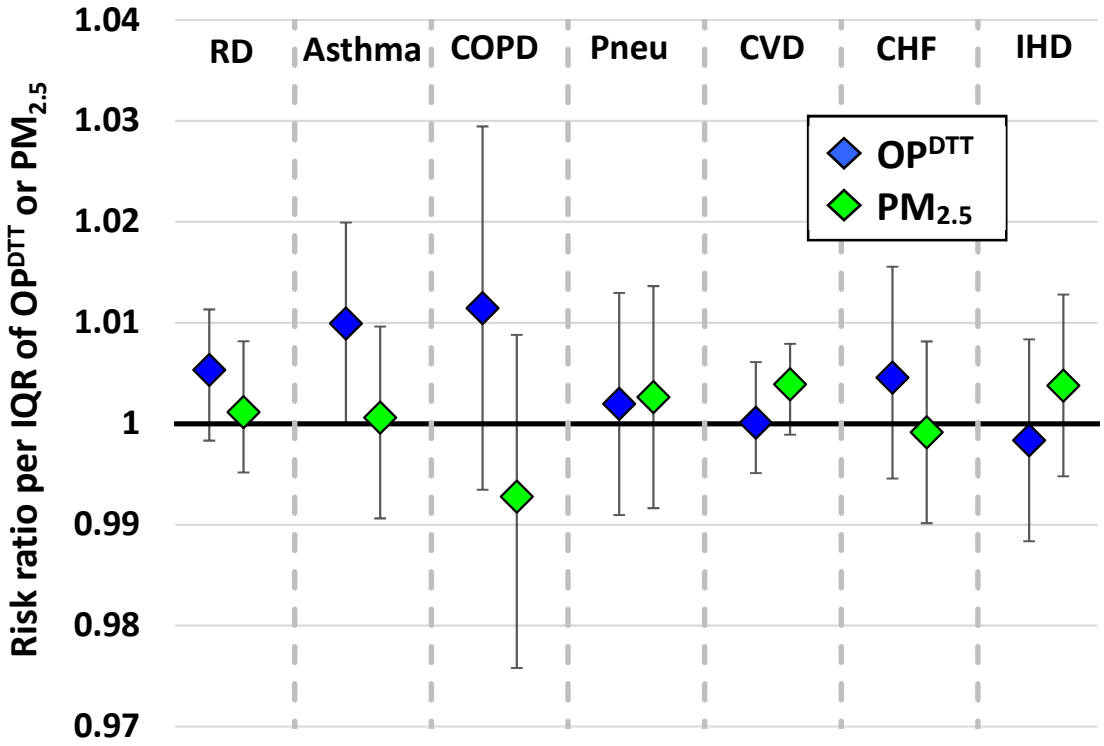


Table 7.1. Potential predictor variables available for OP^{DTT} modeling purposes.

Category	Variables
Gases	ozone (O_3), carbon monoxide (CO), nitrogen oxide (NO), nitrogen dioxide (NO_2), nitrogen oxides (NO_y)
$PM_{2.5}$ components	nitrate (NO_3), sulfate (SO_4), ammonium (NH_4), elemental carbon (EC), copper (Cu), manganese (Mn), lead (Pb), titanium (Ti), zinc (Zn), aluminum (Al), silicon (Si), potassium (K), calcium (Ca), iron (Fe)
Meteorology	mean daily temperature (Temp), maximum daily temperature, minimum daily temperature, mean dew point (DewPt), barometric pressure, total precipitation (Precip), wind speed, cloud ceiling, visibility
Temporal indicators	season (winter=Dec-Feb, spring=Mar-May, summer=Jun-Aug, autumn=Sep-Nov), day of week (w/federal holidays as separate value)

Table 7.2: Parameter estimates for all variables in the Primary Model for predicting OP^{DTT}. EC = elemental carbon, Temp = temperature, DewPt = dew point, all other abbreviations are chemical compounds/elements.

Parameter	Coefficient estimate (95% confidence interval)
Intercept	0.034 (-0.083, 0.150)
EC	0.214 (0.037, 0.391)
Mn	16.506 (5.152, 27.861)
K	1.208 (0.367, 2.049)
NH_4	0.101 (0.057, 0.146)
CO	0.779 (0.235, 1.323)
NO_y	-0.005 (-0.010, -0.001)
O_3	-0.004 (-0.007, -0.001)
Temp	0.125 (0.050, 0.201)
DewPt	-0.151 (-0.223, -0.080)

Table 7.3. Description of models used to predict daily OP^{DTT} measurements, Atlanta, GA, 2012-2013.

Model	No. of variables	No. of parameters*	Variables	r^2	Adj. r^2
Primary	**9**	**9**	**EC, Mn, K, NH_4, CO, NO_y, O_3, Temp, DewPt**	**0.595**	**0.573**
Model B	**6**	**9**	**NH_4, Ca, EC, Si, Zn, K**	**0.587**	**0.573**
Model C	**12**	**20**	**CO, NH_4, Season, Ca, EC, Precip, CO*Season, EC*Season, Fe, NH_4*Season, NH_4*Ca, CO*NH_4**	**0.740**	**0.707**

* Season is a categorical variable equivalent to three binary indicators, thus counts as three parameters (including each time season is used in a product term)

EC=elemental carbon, Temp=temperature, DewPt=dew point, all other abbreviations are chemical compounds/elements

Table 7.4: Parameter estimates for all variables in Model B. EC = elemental carbon, all other abbreviations are chemical compounds/elements.

Parameter	Coefficient estimate (95% confidence interval)
Intercept	-0.030 (-0.083, 0.023)
NH_4	0.097 (0.056, 0.138)
Ca	4.145 (2.639, 5.650)
EC	0.195 (0.120, 0.270)
Si	-0.663 (-0.944, -0.381)
Zn	6.095 (1.383, 10.808)
K	1.090 (0.104, 2.077)

Table 7.5: Parameter estimates for all variables in Model C. Season1 is winter, season2 is spring, season3 is summer, and the reference season is fall. EC = elemental carbon, Precip = precipitation, all other abbreviations are chemical compounds/elements.

Parameter	Coefficient estimate (95% confidence interval)
Intercept	0.018 (-0.124, 0.159)
CO	1.738 (1.049, 2.427)
NH_4	0.073 (-0.066, 0.212)
season1	-0.097 (-0.236, 0.041)
season2	-0.235 (-0.459, -0.011)
season3	-0.019 (-0.159, 0.121)
Ca	1.053 (-0.723, 2.830)
EC	-0.086 (-0.264, 0.092)
Precip	-0.260 (-0.368, -0.152)
Fe	-1.346 (-2.143, -0.550)
CO*season1	-0.697 (-1.279, -0.115)
CO*season2	1.600 (0.480, 2.719)
CO*season3	-0.880 (-1.540, -0.220)
season1*EC	0.349 (0.129, 0.570)
season2*EC	0.010 (-0.243, 0.263)
season3*EC	0.134 (-0.120, 0.387)
NH_4*season1	0.073 (-0.029, 0.176)
NH_4*season2	-0.140 (-0.315, 0.034)
NH_4*season3	0.081 (-0.055, 0.217)
NH_4*Ca	4.198 (2.215, 6.181)
CO*NH_4	-0.449 (-0.798, -0.099)

Figure 7.5: Distribution of daily backcast OP^{DTT} values by model for each year, Atlanta, GA, 1999-2013. Boxes represent the 25th through the 75th percentiles of daily OP^{DTT} values; median values are horizontal white lines within each box, and mean values are yellow dots. Whiskers extend to the most extreme points within 1.5 interquartile ranges of the box, while and outliers outside the whiskers are represented by colored dots.

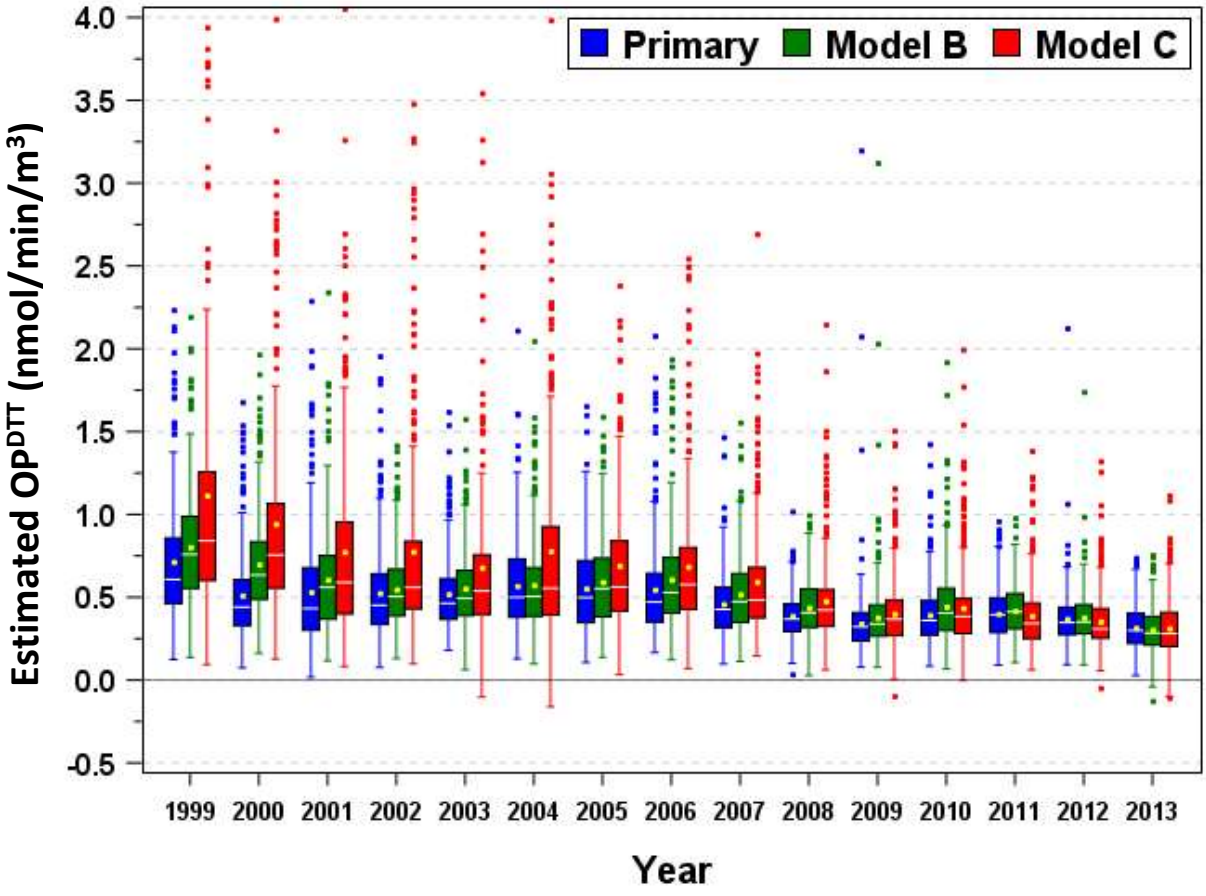
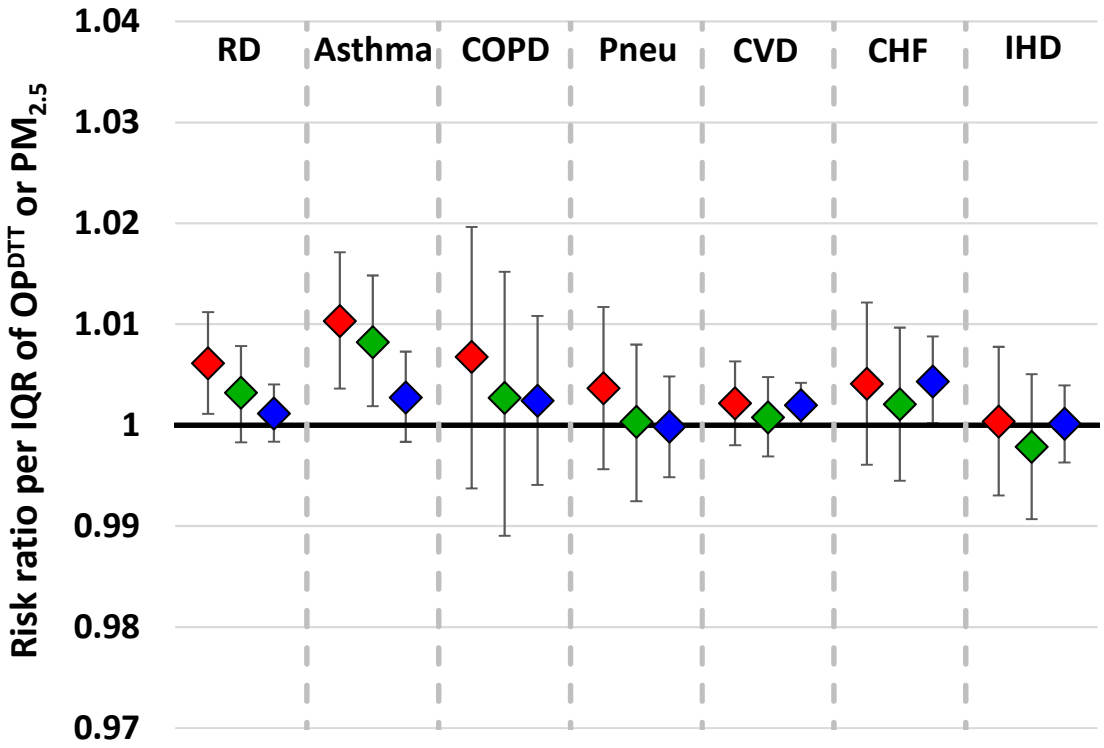


Figure 7.6: Associations between OP^{DTT} and cardiorespiratory ED visits for three models, per interquartile unit increase in OP^{DTT}, 5-county Atlanta metropolitan area, 1999-2013.



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8: AIM III: IMPACT OF AIR POLLUTION CONTROL POLICIES ON CARDIORESPIRATORY EMERGENCY DEPARTMENT VISITS, ATLANTA, GA, 1999-2013

8.1: Abstract

Background: Air pollution control policies linked to the 1990 Clean Air Act Amendments were aimed at reducing pollutant emissions, ambient concentrations, and ultimately negative health outcomes in the Atlanta, GA metropolitan area. We used a counterfactual study design to estimate the impact of these policies.

Methods: Six sets of pollution control policies were identified, and changes in emissions ratios were used to estimate emissions in the absence of pollution control policies. Regression modeling was performed to estimate daily counterfactual ambient pollutant concentrations from 1999-2013. Daily counts of cardiorespiratory emergency department (ED) visits were obtained from 42 Atlanta area hospitals. We assessed associations between pollutant levels and cardiorespiratory emergency department (ED) visits using a multipollutant Poisson time-series model, and these associations were used to estimate ED visits prevented due to pollution control policies.

Results: Pollution control policies were estimated to reduce all nine measured pollutant levels from 1999-2013. Emissions reductions from all selected pollution control policies led to an estimated 55,794 cardiorespiratory disease ED visits prevented, with greater proportions of visits prevented in later years as effects of policies became more fully realized. From 2012-2013, pollution control policies were estimated to prevent 5.9% of

ED visits due to respiratory disease (95% interval estimate: -0.4% to 12.3%); 16.5% of asthma ED visits (95% interval estimate: 7.5% to 25.1%); 2.3% of cardiovascular disease ED visits (95% interval estimate: -1.8% to 6.2%); and 2.6% of congestive heart failure ED visits (95% interval estimate: -6.3% to 10.4%).

Conclusion: Air pollution control policies resulted in substantial reductions in pollutant concentrations and cardiorespiratory ED visits in the Atlanta area.

8.2: Introduction

Ambient air pollution is a substantial contributor to cardiovascular and respiratory morbidity, and federal policies aimed at limiting air pollution cost over $80 billion per year.(1) As efforts to improve air quality have grown in scope and sophistication, more attention has turned to evaluating the effectiveness of these policies. Accountability research aims to quantify the impact of pollution control policies on ambient pollutant levels and human health endpoints.

Many accountability studies utilize a pre-post study design, which compares outcomes before and after an intervention is implemented. This approach has been used to measure health effects of distinct events such as the closure of a steel mill, government regulations to reduce fuel sulfur levels, and short-term traffic restrictions during the Olympics and the Asian Games.(2-5) Some pre-post studies additionally employ distinct geographic locations unexposed to an intervention as control populations, comparing changes in the target area after the intervention to those in the control area.(6-8) Pre-post studies can suffer from temporal confounding, as the difference between outcomes before and after an intervention could possibly be due to many known or unknown factors other than the intervention. Potential for temporal confounding can increase with study length, therefore pre-post studies are best suited for short-term events with distinct target and control periods.

Assessing the impact of pollution control policies presents many challenges. One primary consideration is that the ultimate goal is generally to improve health outcomes, but the policies act upon sources of pollutant emissions. Studies aimed at capturing the complete consequences of pollution control policies therefore are tasked with quantifying

the effect of policies on emissions, then assessing downstream effects of emissions reductions on ambient pollutant levels, which are then used to estimate impacts on public health.(9) These types of studies require collection of substantial amounts of data as well as complex modeling to link changes at each outcome level.

Consequently, few accountability studies have attempted to assess impacts of pollution control policies on all three outcome levels of emissions, ambient pollutant concentrations, and health endpoints. The US Environmental Protection Agency compiled estimated impacts of the Clean Air Act from 1970-1990 on emissions and ambient pollutant concentrations, ultimately using estimates from previous studies to estimate health impacts.(10) Study of rapid improvement of pollution control in Erfurt, Germany described decreases in pollutant concentrations and mortality linked to emissions reductions.(11) Both these studies demonstrate net health benefits of comprehensive pollution control efforts, but fall short of describing the impacts of individual policies. These studies utilized single-pollutant or bipollutant models to estimate health impacts.

In our current study, we determined the effect of pollution control policies in Atlanta, Georgia, which were largely implemented in order to bring the metropolitan area into compliance with the National Ambient Air Quality Standards (NAAQS) set by the 1990 Clean Air Act Amendments. We utilized a counterfactual study design, in which outcomes after an intervention were compared to outcomes during the same time period and in the same geographic location but in the absence of the intervention; all external factors are held constant. This study assessed the impact of numerous overlapping pollution control policies which take full effect over long time periods, such that there are

no clear-cut reference or intervention periods. The counterfactual design used for this study modeled continuous changes to emissions, ambient pollutant levels, and health outcomes, and was therefore able to more accurately quantify the impacts of these policies.

In addition to assessing impacts of all combined pollution control policies, we estimated the impact of individual interventions, which is vital for determining the relative effectiveness of different types of regulatory programs. We also used multipollutant modeling in order to more fully capture the joint effects of pollutant mixtures on public health. Altogether, the thorough methodologies and extensive datasets utilized contribute to make this the most comprehensive air pollution accountability study to date.

8.3: Methods

Air quality modeling

Methods for modeling of air quality levels have been previously described.(12) Briefly, this involves three primary steps: 1) identifying relevant pollution control policies, 2) estimating counterfactual emissions in the absence of pollution control policies, and 3) evaluating relationships between emissions and ambient pollutant levels in order to estimate counterfactual ambient pollutant levels in the absence of pollution control policies.

Pollution control policies

Through conversations with air pollution stakeholders (i.e. government policy-makers and persons involved in regulatory implementations), we identified six sets of pollution control policies which affected emissions in the Atlanta area.(12) Overarching policies were considered in tandem with the specific state or local regulatory rules employed to meet the appropriate standards. Three sets of policies regulated emissions from electricity-generating units (EGUs):

- Acid Rain Program (ARP) and the Georgia Rules for Air Quality Control state program yy ($GRAQC_{yy}$)
- NO_x Budget Trading Program (NBP) and associated State Implementation Plan (SIP) Call and $GRAQC_{jjj}$
- Clean Air Interstate Rule (CAIR) and $GRAQC_{ss}$

Three additional sets of policies regulated emissions from mobile sources:

- Inspection and Maintenance programs
- Tier 2 Gasoline Program and Georgia Gasoline Marketing Rule ($GRAQC_{bbb}$)
- Heavy Duty Diesel Rule

Counterfactual analyses were performed for nine scenarios: the six scenarios representing the non-implementation of a single set of policies; the non-implementation of all EGU pollution control policies; the non-implementation of all mobile pollution control policies; and the non-implementation of all selected pollution control policies.

Impacts of pollution control policies on EGU emissions

Continuous Emissions Monitoring (CEM) data, required under the Acid Rain Program, were downloaded from EPA's Air Markets Database (U.S. EPA 2016a) for EGUs from seven southeastern states (Alabama, Georgia, Mississippi, North Carolina, South Carolina, and Tennessee) that have been shown to be major contributors to air quality issues for the Atlanta area.(13) EGU emissions data were obtained for nitrogen oxides (NO_x) and sulfur dioxide (SO_2), and were split into local EGUs (those within the 20-county Atlanta non-attainment area, or ANAA) and those outside the ANAA.

Average annual emissions ratios(14) were defined for base years predating the implementation of the selected EGU pollution control policies:

$$ER_{y^*} = \left[\sum_{d=1}^{365} \frac{E_{(d,y^*)}}{L_{(d,y^*)}}\right]/(365)$$

Where ER_{y^*} is the emissions ratio for base year y^* (defined as 1995 for EGUs within the ANAA and 1997 for regional EGUs outside the ANAA), $E_{(d,y^*)}$ is the emissions on day d for year y^*, and $L_{(d,y^*)}$ is the gross load (MW-h) on day d for year y^*. Daily counterfactual emissions were calculated for 1999-2013 by assuming that, in the absence of all selected EGU pollution control policies, daily load would remain unaffected but be subject to base year emissions ratios:

$$E_{d,y}^{CFACT} = \left(L_{(d,y)}\right)\left(ER_{y^*}\right)$$

The impact of the three separate sets of EGU pollution control policies was determined by matching up known dates of regulatory compliance with observed trends in daily emissions data, and dividing observed emissions reductions accordingly.

Impacts of pollution control policies on mobile emissions

EPA's MOVES2010b software was used to estimate daily mobile emissions based on inputs specific to the 20-county ANAA. Mobile emissions data was estimated for fine particulate matter ($PM_{2.5}$), NO_x, volatile organic carbons (VOCs), SO_2, elemental carbon (EC), and organic carbon (OC). Data for vehicle population, speed distribution fuel formulation, road type distribution, and vehicle type age distribution were obtained from the Georgia Environmental Protection Division, and estimated average annual vehicle miles traveled were obtained from the Georgia Department of Transportation web database.(15) Counterfactual emissions under the non-implementation of the inspection and maintenance policy were estimated by running MOVES without the inspection and maintenance table, effectively eliminating relevant emissions reductions. For the gasoline and diesel programs, emissions ratios for pollutants were determined based on fuel type, process type, source type, month, day, and vehicle age for a base year (1993) prior to selected pollution control policies. Counterfactual emissions were estimated by applying those 1993 emissions ratios to applicable vehicle data from 1999-2013.

Estimation of counterfactual air quality data

Data on air quality and meteorology were obtained from the Southern Aerosol Research and Characterization Study (SEARCH) site at Jefferson Street, roughly 2 miles northwest of downtown Atlanta; details on their measurement have been previously reported.(16-18) Hourly data were converted to daily values using previously established metrics.(12, 19) For periods of missing meteorological data, observations from Hartsfield-Jackson International Airport (roughly 10 miles south of Jefferson Street) were used.

Observed concentrations were obtained for nine pollutants of interest: ozone (O_3), nitrogen dioxide (NO_2), sulfur dioxide (SO_2), carbon monoxide (CO), total fine particulate matter mass ($PM_{2.5}$), and the following $PM_{2.5}$ components: sulfate (SO_4), nitrate (NO_3), organic carbon (OC), and elemental carbon (EC). Relationships between daily emissions and daily pollutant concentrations were estimated using the following regression model:

$$C_i = \beta_0 + \beta_E(\boldsymbol{E}) + \beta_{E*PS}(\boldsymbol{E} * PS) + \beta_{E*k}(\boldsymbol{E} * k) + \beta_M(\boldsymbol{M}) + \epsilon$$

Here, C_i represents concentration of pollutant, $\boldsymbol{E}$ is the matrix of emission variables, $\boldsymbol{M}$ is the matrix of meteorology variables, the β's represent vectors of relevant regression coefficients, and $\in$ is the vector of model residuals. Photo-oxidative state (PS), which was captured by meteorological detrending (19) of O_3, was included in interaction terms in order to capture atmospheric conditions affecting chemical transformation of pollutants. The ammonium nitrate dissociation term (k) was included to account for enhanced nitrate at only the coldest temperatures.

Emissions variables available for inclusion were estimated actual (non-counterfactual) values determined from earlier study steps, with emissions from ANAA EGUs, regional EGUs, and mobile sources considered as separate variables. Initial emissions variables and interaction terms included for each pollutant model were selected based on literature results describing potentially contributing factors.(20-24) Backwards selection was used to remove terms that were not statistically significant ($p<0.05$), though in some cases, terms which were considered *a priori* to be important were maintained in pollutant models. All models included four meteorology variables (wind speed,

temperature, relative humidity, and rainfall), selected based on earlier results of detrending analyses.

Regression coefficients were obtained for each pollutant model. Counterfactual pollutant levels were estimated by substituting counterfactual emissions under each of the nine scenarios.

Health impact analysis

A key objective of this study was to contrast daily observed levels of pollutants with their corresponding counterfactual levels to estimate the number and percentage of cardiorespiratory emergency department (ED) visits that were prevented due to pollution control policies. Below we describe the methods used to estimate ED visits prevented in the 5-county Atlanta metropolitan area from 1999-2013.

Hospital emergency department dataset

Data were collected from 42 acute care hospitals on emergency department (ED) visits for the people living in the Atlanta, GA metropolitan area between January 1, 1999 and December 31, 2013. Computerized billing records for patient-level data were pulled. Patient variables included date of admission, the primary International Classification of Diseases 9th Revision (ICD-9) diagnostic code, patient date of birth, sex, race, and 5-digit residential ZIP code. ED visits were included if the patient ZIP code was located wholly or partially within the 5 primary urban counties of metropolitan Atlanta (Fulton, DeKalb, Gwinnett, Cobb, Clayton).

Daily counts of ED visits were calculated for four cardiorespiratory outcome categories, based on primary ICD-9 codes, shown to be associated with pollution levels

in previous studies using the same Atlanta ED data.(25-29) We used daily counts of ED visits for all respiratory diseases (RD) (ICD-9 codes 460-465, 466.0, 466.1, 466.11, 466.19, 477, 480-486, 491-493, 496, 786.07) as well as the RD subcategory of asthma ED visits (ICD-9 codes 493, 786.07). We also used daily counts of ED visits for all cardiovascular diseases (CVD) (ICD-9 codes 410-414, 427, 428, 433-437, 440, 443-445, 451-453) as well as the CVD subcategory of congestive heart failure (CHF) (ICD-9 code 428).

Multipollutant health impact model

We used Poisson generalized linear regression models accounting for overdispersion in order to estimate the joint effect of multiple pollutants on ED visits in a time-series framework. Seven pollutants were included in the model: $PM_{2.5}$, O_3, CO, SO_2, NO_2, OC, and NO_3. EC and SO_4 were not included due to concerns of collinearity: daily EC levels were highly correlated with OC (r=0.80) while SO_4 was highly correlated with $PM_{2.5}$ (r=0.79), and we removed the pollutant that did not contribute to the model. To account for potential nonlinear relationships and effect modification through pollutant mixtures, we used cubic polynomials for each pollutant along with first-order interactions between all linear pollutant terms.

To maintain consistent methodology with previous research that showed more delayed effects of respiratory outcomes, 3-day moving averages (average of pollutant levels same-day, 1 day prior, and 2 days prior, or lag 0-2) were chosen a priori as the relevant exposure values for RD and asthma ED visits.(28-31) For CVD and CHF ED visits, same-day pollutant values (lag 0) were used as had been done in previous studies.(26, 32)

Prior studies have analyzed the association between EPA criteria pollutants and ED visits using the same Atlanta ED data.(25-30, 33-40) These studies identified important covariates and model parameterizations that were necessary in order to provide optimal control of potential temporal confounders. All covariates described below were included a priori based on findings from the time series models used in these previous analyses.

We utilized a quasi case-crossover formulation to control for long-term as well as seasonal trends, including terms for year, month, and weekday (with holidays separate) all as categorical variables, as well as the interaction terms year*month and month*weekday. Meteorology covariates included temperature (cubic polynomial of the daily maximum temperature and the cubic polynomial of the lag 1-2 daily minimum temperature), dew point (cubic polynomial of the lag 0-2 moving average of daily mean dew point), and interaction terms between the same-day maximum temperature cubic polynomials and season. Indicator variables for periods of hospital data contribution were included, as well as for other dates which may have unique pollutant or ED profiles (day after Thanksgiving, day after Christmas, dates of Christmas/Thanksgiving/Veteran's Day/New Year's Day when different from date of federal holiday).

Initial analyses showed that there were stronger observed associations between pollutants and ED visits in the first half of the study period (roughly 1999-2005) compared to the latter half. If the change in associations between pollutants and ED visits over the study period is in any way attributable to regulatory actions, then the true impact of pollution control policies is best estimated using associations from the early study period, so we used 1999-2005 data to fit the health impact model.

Generating daily risk ratios

The counterfactual model formulation allowed us to estimate outcomes if only pollutant levels changed but all other factors (e.g. meteorology, temporal trends) remained the same. For each pollution control scenario, we took the difference between daily counterfactual and daily observed pollutant levels then multiplied by the appropriate parameter coefficient. These values were all summed up, then exponentiated to produce daily risk ratios (RR) for each scenario for each outcome. The risk ratio represents the daily observed risk of ED visits compared to the daily risk of ED visits in counterfactual scenarios: risk ratios below 1 describe protective effects of pollution control policies.

To obtain estimates for daily counts of counterfactual ED visits, we divided the daily observed number of ED visits by these daily risk ratios; observed daily ED visits were then subtracted in order to produce estimates for daily number of ED visits prevented. These daily numbers of ED visits prevented were then aggregated to produce estimates for ED visits prevented by season, by year, and for the entire study period. We added together the observed ED visits and prevented ED visits to get estimate of all ED visits which would have occurred in the absence of pollution control policies, then divided this number from ED visits prevented to get the percent of ED visits prevented.

Accounting for uncertainty

Typically, when accounting for uncertainty of air pollution health effects (i.e., constructing interval estimates), that uncertainty solely results from the uncertainty in the estimation of the model parameters representing the health effects. For the health

analyses here, we consider two broad layers of uncertainty: the uncertainty in the estimation of the model parameters representing the health effects and the uncertainty in the estimation of the counterfactual daily time series for each pollutant. We used Monte Carlo simulations to account for the overall uncertainty in the health analyses.

Daily counterfactual EGU emissions were estimated by using the mean base year emissions ratios, therefore we accounted for uncertainty by sampling from a normal distribution with the mean and variance of measured daily emissions ratios during the base year. For daily counterfactual mobile emissions uncertainty, we utilized the established approach of sampling from a uniform distribution between ±50% estimated change in emissions due to pollution control policies.(41) For uncertainty in linking emissions to pollutant concentrations, we sampled from a multivariate normal distribution of regression coefficients based on the estimated variance-covariance structure. Similarly, for uncertainty in linking concentrations with health outcomes, we sampled from a multivariate normal distribution of regression coefficients based on the estimated variance-covariance structure. These samples were used to generate daily risk ratios and daily numbers of ED visits prevented, which were then aggregated to produce overall estimates of ED visits prevented through pollution control policies. We obtained 5,000 samples at each step, and took the 2.5th and 97.5th percentiles of ED visits prevented to represent the 95% interval estimate which incorporates both the uncertainty in the health impact model parameters and the uncertainty in the estimation of the counterfactual air pollution time series for each pollutant in the health model.

Sensitivity analyses

To assess the influence of modeling choices on estimated ED visits prevented, we conducted several separate sensitivity analyses. First, we ran the health impact model using the entire 1999-2013 dataset to fit regression coefficients. Also, instead of using cubic polynomials and interaction terms, we ran the health impact model with only linear pollutant terms, with cubic polynomials but no interaction terms, and with linear terms and interaction terms. We additionally ran models with different pollutants included: a full model with all nine pollutants; a single pollutant model with $PM_{2.5}$, since this pollutant measure is a mixture affected by a number of different sources and was strongly associated with cardiorespiratory outcomes in our data; and a model with the five EPA criteria pollutants included in this study ($PM_{2.5}$, O_3, CO, SO_2, and NO_2). Finally, we tested expansion of the outcome to include ED visits prevented in the full 20-county ANAA.

Statistical programs utilized

All analyses in the health impact modeling were performed through SAS version 9.3 (SAS Institute, Cary, NC) and R version 3.01 (The R Foundation for Statistical Computing, 2013) using the data.table, MASS, and Cairo packages.

8.4: Results

Observed concentrations fell for all measured pollutants from 1999-2013 (Figure 8.1a). The greatest drop was for SO_2, with 2013 concentrations being only 9.2% of 1999 levels, while O_3 changed the least with 2013 concentrations being 82.6% of 1999 levels. For all other pollutants, 2013 concentrations ranged from 27.8% - 53.8% of 1999 levels.

Counterfactual 2013 concentrations under the non-implementation of all pollution control policies ranged from 77.2% - 125.3% of observed 1999 levels (Figure 8.1b). In all instances, observed concentrations from 2000-2013 were lower than counterfactual levels during those periods, demonstrating the effect of pollution control policies on ambient pollutant levels.

There were 16,191,785 total emergency department (ED) visits recorded in the 5-county Atlanta metropolitan area from 1999-2013, an average of roughly 1.08 million ED visits per year. There were 1,637,338 ED visits for respiratory disease (RD), 374,126 ED visits for asthma, 416,392 ED visits for cardiovascular disease (CVD), and 105,561 ED visits for congestive heart disease (CHF).

The percent of ED visits prevented by all selected pollution control policies is shown in Figure 8.2. These percentages gradually increased over time as the impacts of pollution control policies became more fully realized. Estimated RD ED visits prevented increased from 2.5% in 1999 to 6.1% in 2013, estimated asthma ED visits increased from 2.0% in 1999 to 17.0% in 2013, estimated CVD ED visits prevented increased from 0.2% in 1999 to 2.5% in 2013, and estimated CHF ED visits prevented increased from 0.9% in 1999 to 3.0% in 2013. To describe the full effect of all selected pollution control policies, subsequent results are presented for ED visits prevented over the last two years of the study (2012-2013), which captures the period of greatest impact of these policies.

From 2012-2013, there were 260,018 recorded RD ED visits in the 5-county Atlanta metropolitan area and all selected pollution control policies prevented an estimated 16,315 visits, or 5.9% of all RD ED visits which would have occurred in the absence of these policies (95% interval estimate: -0.4% to 12.3%) (Figure 8.3). There

were 60,731 recorded asthma ED visits and pollution control policies prevented an estimated 11,985 visits (16.5%; 95% interval estimate: 7.5% to 25.1%). There were 69,910 recorded CVD ED visits and pollution control policies prevented an estimated 1,662 visits (2.3%; 95% interval estimate: -1.8% to 6.2%). There were 18,129 recorded CHF ED visits and pollution control policies prevented an estimated 477 visits (2.6%; 95% interval estimate: -6.3% to 10.4%). Using traditional interval estimates which describe uncertainty in the associations between pollutants and health outcomes, the 95% interval estimates for percent ED visits prevented is 0.6 to 11.0% for RD, 8.6% to 24.0% for asthma, -1.2% to 5.9% for CVD, and -5.1% to 9.9% for CHF. These interval estimates are only slightly smaller than the interval estimates which incorporate uncertainty at multiple stages of the model, indicating that uncertainty in the health impact model parameters is much greater than uncertainty in modeling counterfactual ambient pollutant levels.

Percent ED visits prevented by pollution control scenario are shown in Figure 8.4 A-D. EGU policies were generally estimated to have a greater health impact than mobile policies for preventing RD ED visits, especially the NO_x Budget Trading program and the Acid Rain program. Those patterns were also similar for asthma ED visits. For CVD ED visits, the Clean Air Interstate Rule/multipollutant program was estimated to have the largest impact of any set of policies. For all outcomes, there was considerable overlap in the interval estimates for the majority of pollution control scenarios, and particular caution in comparing the relative effectiveness of these policies is advised.

In sensitivity analyses, estimates for ED visits prevented were lower for all four outcomes when using the entire 1999-2013 period to fit parameter estimates (Figure 8.5).

The inclusion of cubic polynomial terms and interaction terms substantially increased estimates of ED visits prevented for RD and asthma, but results for CVD and CHF were less affected (Figure 8.6). The 1-pollutant, 5-pollutant, and 9-pollutant models all estimated fewer ED visits prevented than the primary 7-pollutant model, though all models showed significant reduction in asthma ED visits due to pollution control policies (Figure 8.7). Assessing results over the 20-county ANAA generally resulted in slightly smaller percentage of ED visits prevented (Figure 8.8).

8.5: Discussion

The current study represents a vast undertaking which constitutes a significant step forward in terms of air pollution accountability studies. We combined proven methodologies to link pollution control policies to emissions levels, ambient pollutant levels, and health outcomes. Meetings with relevant stakeholders proved to be an important aspect of this study for linking pollution control policies to the implementation of specific controls that reduced emissions. These counterfactual emissions estimates were then integrated with extensive air quality and hospital datasets which provided daily data over a long-term, 15-year study period. The health data were aggregated from 42 different hospitals capturing daily counts of ED visits over a large metropolitan area, and this substantial dataset allowed for the partitioning of ED data to assess daily counts of several different health outcomes.

The use of the counterfactual study design was important, as this study did not compare between well-defined case vs. control time periods or geographic locations.

Rather, this study evaluated the health impacts of six different overlapping sets of pollution control policies which took place over a 15-year period. Many of these policies included in this study were gradually implemented over long periods of time. For example, engine emissions standards were phased in over several years; they applied to new cars, and vehicle fleet turnover is a constant occurrence; and car manufacturers, while required to meet standards by set dates, may not all reach those standards all at the same point in time. The impacts of these types of policies would have been difficult to accurately estimate using traditional pre-post analyses. Additionally, pre-post analyses for this study could have been susceptible to many potential temporal confounding issues from long-term changes (e.g. population demographics and ED usage) or specific events (e.g. reduced energy consumption during the Great Recession, unique climate events).

The purpose of this study was not to evaluate the associations between individual pollutants and health outcomes; rather, it was to assess how changes to broader air quality profiles due to pollution control policies may have reduced adverse health outcomes. Therefore, we used multipollutant analyses to determine the joint effect of changes in ambient pollutant levels to best account for multipollutant covariation. These models accounted for nonlinear relationships between pollutants and health outcomes, as well as interaction between different pollutants. The models drew upon previous studies with the same Atlanta ED data that had identified model parameterizations and covariates critical for addressing potential temporal confounding.

In order to limit concerns over multiple comparisons or data fishing, we used *a priori* choices for key modeling properties. We used set covariates, which had been determined through previous studies, including the particular formulation of

meteorological terms. We used *a priori* lag structures, with lag 0-2 used for RD and asthma and lag 0 used for CVD and CHF, decisions also based on previous research. The 1-, 5-, and 9-pollutant models were chosen *a priori*, and the 7-pollutant model reduced concerns about collinearity. We did try models with or without cubic polynomials and interaction terms since we were not sure if those factors would affect model results. However, to avoid picking and choosing convenient results, we did decide *a priori* to either use cubic polynomials for all pollutants or none, and to either include interactions between all pollutants or none.

There were other modeling decisions in which we were guided at least partially by results, but this was only done when these choices were appropriate and consistently applied. After early testing showed that 7-pollutant models, models with cubic polynomials, and models with interaction terms consistently captured more of the health impact of pollution control policies, we used those model parameterizations for the primary model results. These modeling choices resulted in consistently stronger results for all outcomes, suggesting that the difference may be due to a decrease in model misspecification as opposed to simply random noise. Pollutants were generally more predictive of ED visits in the first half of the study period. Increased concentrations and daily variability of pollutants in earlier years could have led to more accurately measured associations with ED visits, potentially contributing to this result. The 7- pollutant model incorporated the most information on overall air quality without the larger collinearity issues of the 9-pollutant model, and the cubic polynomials and interaction terms additionally added to a more refined model of the associations between pollutants and ED visits.

We used results from a single central monitor to predict ED visits across the 5-county Atlanta metropolitan area. This could be a potential study limitation, as pollutant levels measured at the monitor may differ substantially from pollutant levels experience by the study population. Exposure measurement error for time-series analyses was assessed in a previous study in the Atlanta metropolitan area; this study found that the use of measurements from urban monitors (within 20 miles of the city center) located different distances from geographic subpopulations produced similar associations between pollutants and health outcomes.(35) This suggests that even if measured pollutant levels differed from ambient pollution levels where individuals are located, daily trends in these measures were correlated enough so that measurements from a single central monitor could reproduce valid health associations. Another study using simulated time-series pollutant data showed that, using Poisson generalized linear models similar to those used in this study, associations between pollutants and health outcomes were biased toward the null.(42) If measured concentrations differ meaningfully from population average exposures, this can create biased associations with the direction most likely toward null effects.(43) The sensitivity analyses using 20-county ED data are consistent with this hypothesis: the population of the 20-county area includes people even further from the central monitor and whose individual exposure to ambient pollutant levels is likely quite different, which may explain the reduced estimates of ED visits prevented. If exposure measurement error resulted in a bias toward the null for this study, the true impacts of pollution control policies may be greater than those estimated for the 5-county analysis.

Hospital ED visits represent serious adverse health outcomes: patients are suffering distress which is drastic and severe enough to seek immediate, potentially life-saving medical care. Such outcomes would be relatively uncommon compared to more moderate health effects of ambient air pollution, such as mild respiratory distress or minor irritation of the eyes and throat. Additionally, this study only assessed impacts of pollution control policies on cardiorespiratory outcomes; ambient air pollution has also been linked to other health problems such as urinary dysfunction, nervous system damage, digestive issues, and developmental disorders.(44) Finally, this study only captured acute effects of daily increases in pollutants. Long-term exposure to ambient air pollution can lead to cumulative harm and ultimately increased rates of mortality, especially from cardiovascular disease, stroke, or lung cancer.(45-49) While this study estimated that tens of thousands of ED visits in the Atlanta metropolitan area had been prevented by pollution control policies, this result is only the tip of the iceberg for the overall impact of these policies. Furthermore, the policies described in this study continue to be implemented, so similar quantities of dramatic health impacts should still be occurring every year.

8.6: Conclusion

Pollution control policies in the Atlanta area were effective in reducing ambient pollutant levels and cardiorespiratory ED visits, and these impacts were stronger in later years after all pollution control policies had been more fully implemented. The results describing the effectiveness of specific policies may help inform future pollution control strategies.

Figure 8.1: Annual mean ambient levels for nine pollutants, relative to observed 1999 levels, A) observed and B) counterfactual scenario of non-implementation of all selected pollution control policies

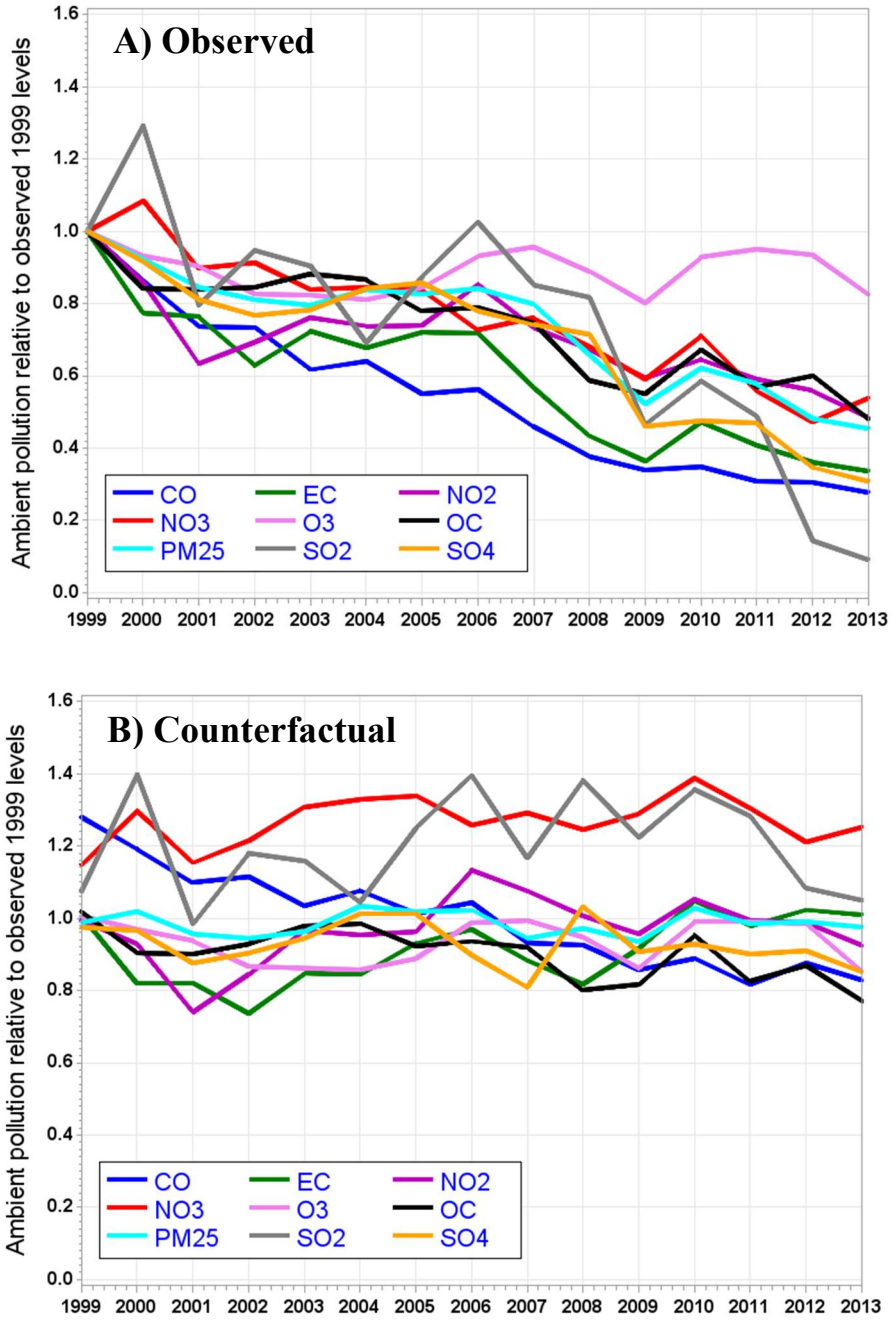


Figure 8.2: Percent emergency department (ED) visits prevented by all selected pollution control policies by outcome and year in the 5-county Atlanta metropolitan area, 1999-2013.

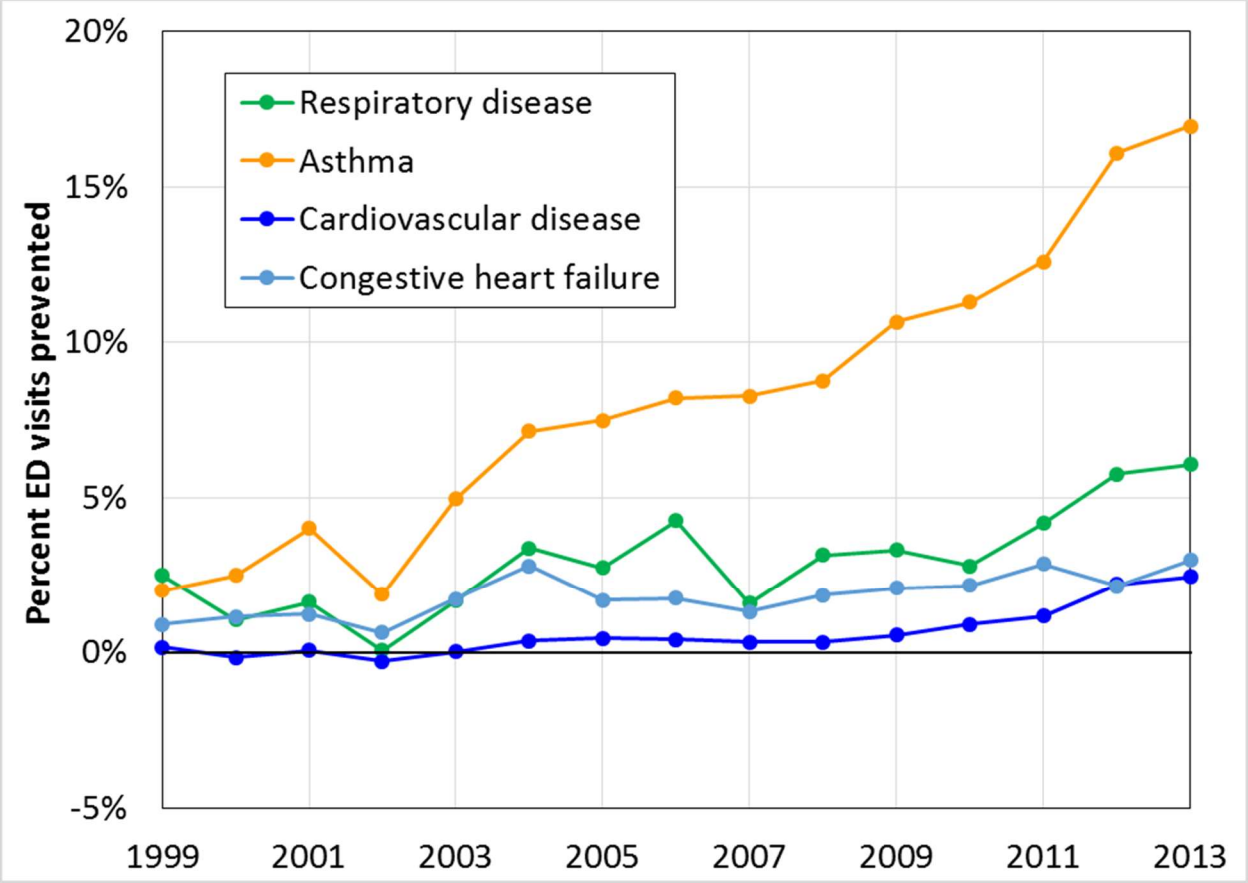


Figure 8.3: Percent emergency department visits (ED) prevented by all selected pollution control policies by outcome, 5-county Atlanta metropolitan area, 2012-2013.

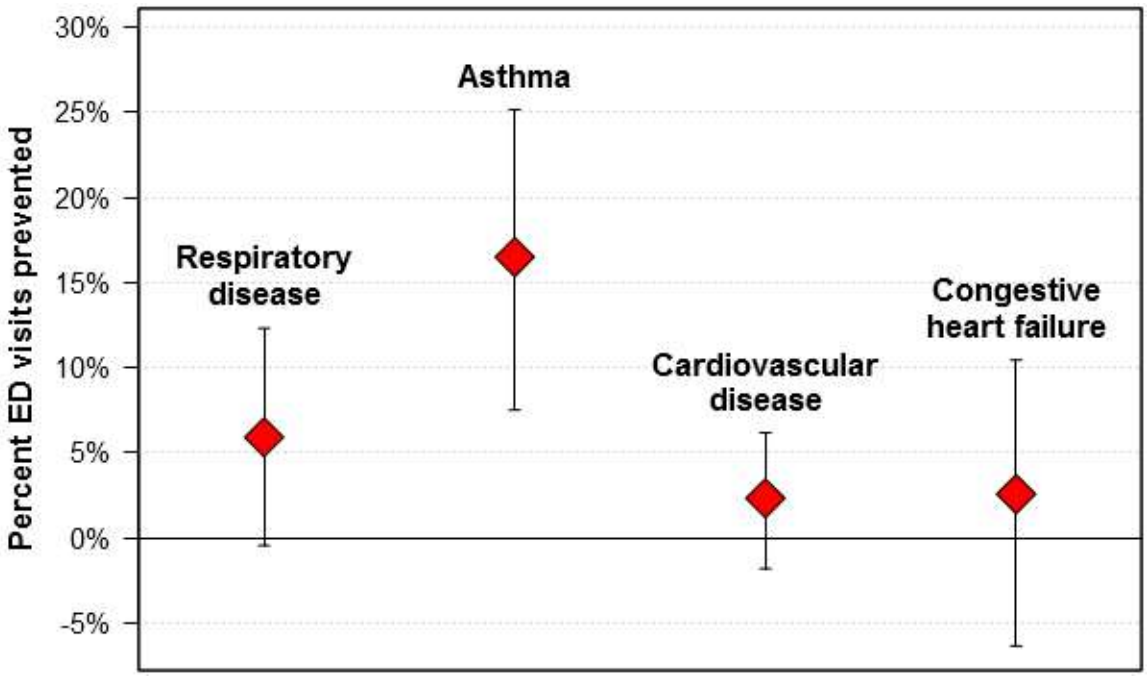


Figure 8.4: Percent emergency department visits prevented by pollution control scenario, 5-county Atlanta metropolitan area, 2012-2013, for A) respiratory disease, B) asthma, C) cardiovascular disease, and D) congestive heart failure. Abbreviations for pollution control scenarios: All=all pollution control policies; EGU=all electricity generating unit policies; ARP=Acid Rain Program; NBP=NO_x Budget Trading program; CAIR=Clean Air Interstate Rule/multipollutant rule; MOB=all mobile policies; GSP=gasoline programs; DSP=diesel programs; IM=inspection and maintenance programs. Policies regulating EGU emissions are shown in green; policies regulating mobile emissions are shown in purple. Confidence intervals with all uncertainty included were calculated for all pollution control policies, all EGU policies, and all mobile policies, but not for the individual sets of policies.

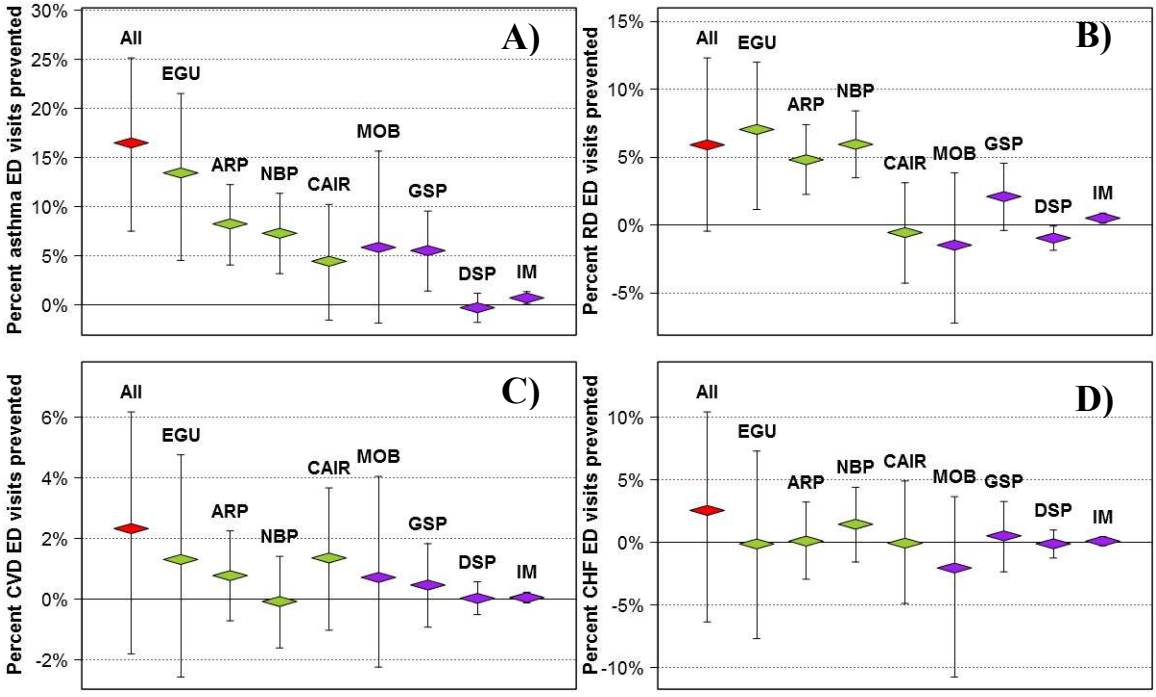


Figure 8.5: Percent emergency department (ED) visits prevented by all selected pollution control policies by outcome, 2012-2013, comparing results using parameter estimates fit from 1999-2005 (red) with results using parameter estimates fit from the 1999-2013 time period (green).

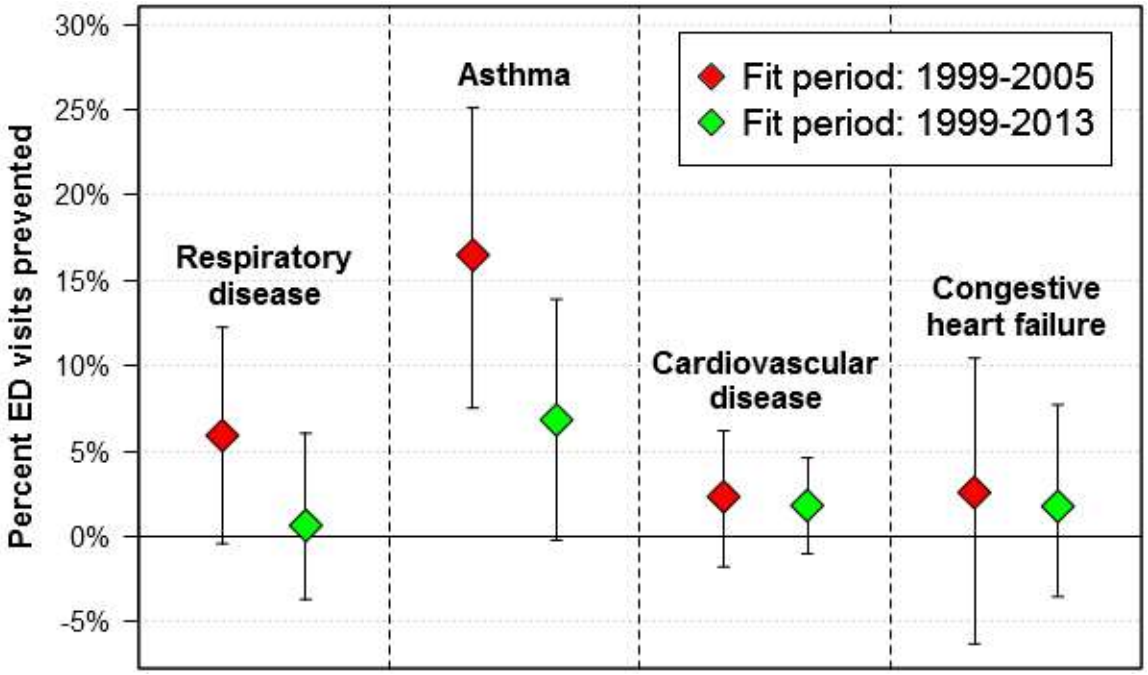


Figure 8.6: Percent emergency department visits prevented by all selected pollution control policies by outcome, 5-county Atlanta metropolitan area, 2012-2013, comparing models with linear pollutant terms, models including cubic polynomial pollutant terms, and models including first-order interactions between linear pollutant terms. Model group 1 (light gray) only has linear pollutant terms. Model group 2 (medium gray) has cubic polynomial pollutant terms. Model group 3 (dark gray) has linear pollutant terms with all first-order interaction terms. Model group 4 (red) has cubic polynomial pollutant terms along with first-order interactions between linear terms.

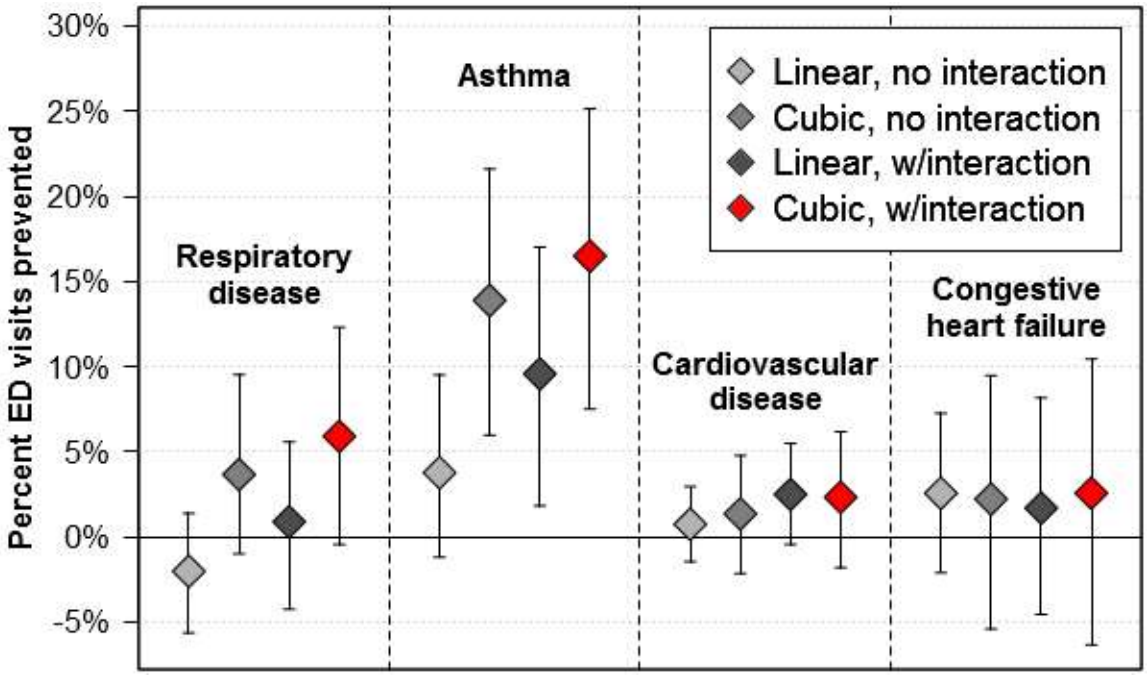


Figure 8.7: Percent emergency department visits prevented by all selected pollution control policies by outcome, 5-county Atlanta metropolitan area, 2012-2013, comparing models with different multipollutant formulations. The 1-pollutant model reflects ED visits prevented due to the effect of policies on ambient $PM_{2.5}$; the 5-pollutant model included the effects of policies on PM2.5, CO, O_3, NO_2, and SO_2; the 7-pollutant model included the effects of policies on PM2.5, CO, O_3, NO_2, SO_2, OC, and NO_3; the 9-pollutant model included the effects of policies on PM2.5, CO, O_3, NO_2, SO_2, OC, NO_3, EC, and SO_4.

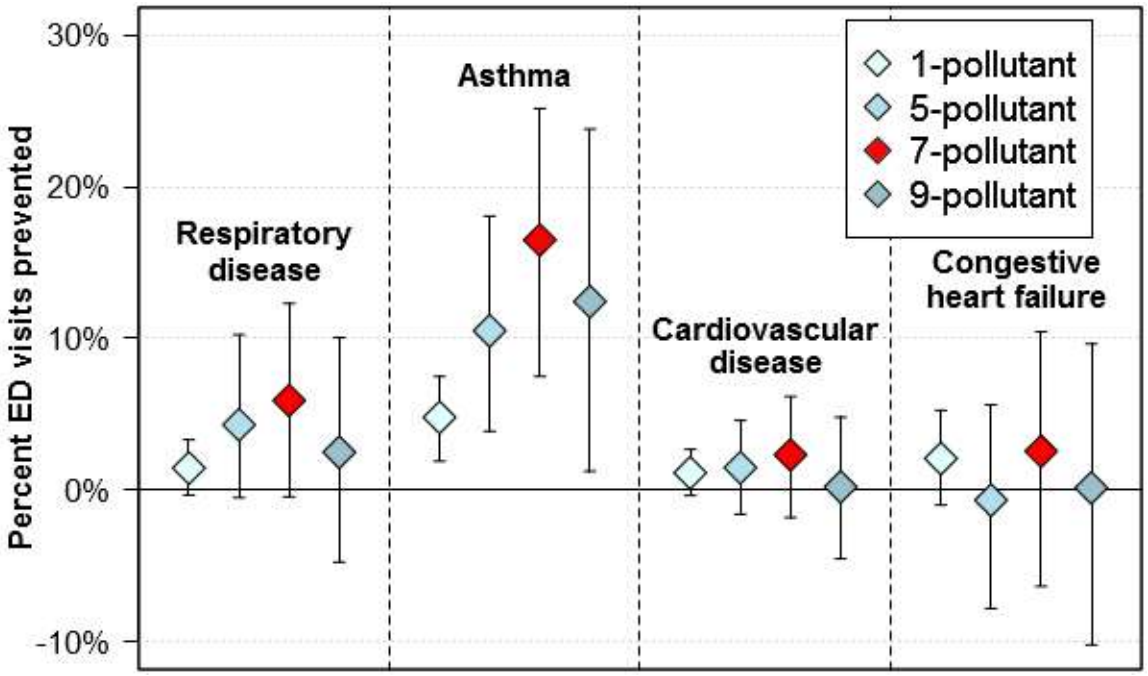
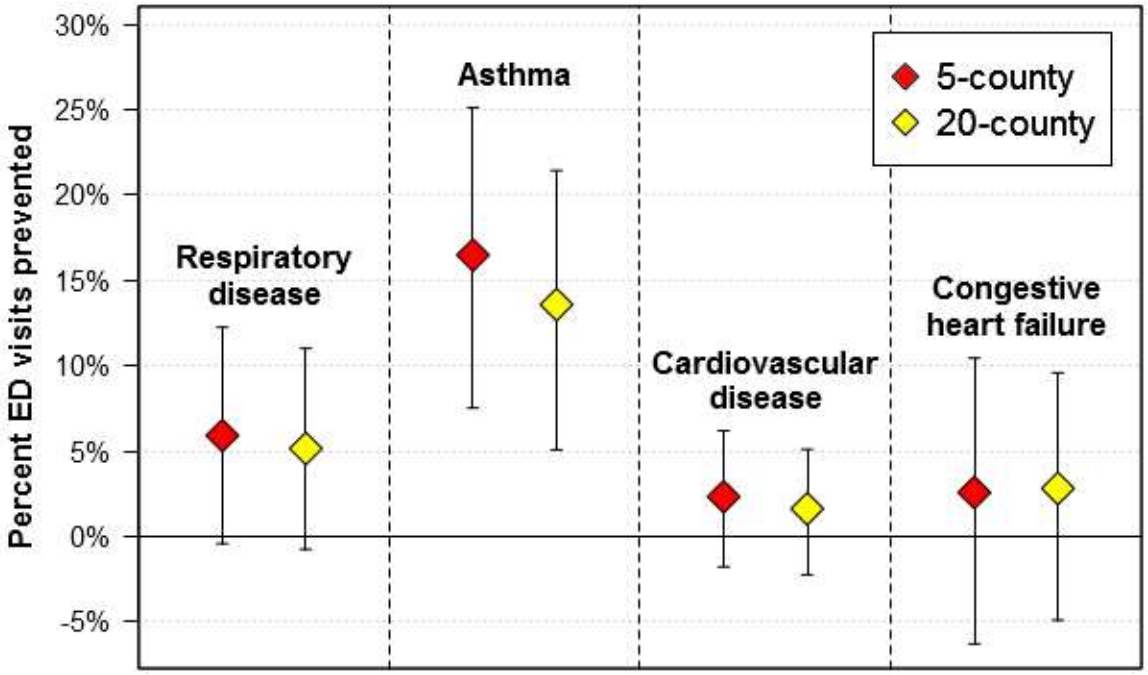


Figure 8.8: Percent emergency department (ED) visits prevented by all selected pollution control policies by outcome, 2012-2013, comparing results for the 5-county Atlanta metropolitan area (red) with results for the 20-county Atlanta metropolitan area (yellow).



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9: OVERALL CONCLUSIONS

This dissertation was able to address important research questions in order to make meaningful contributions to air pollution research. The first research question asked: What are the effects of the oxidative potential of ambient particulate matter on human health? In Aim I, we utilized a time series approach to estimate associations between directly measured OP^{DTT} and cardiorespiratory ED visits. This study was the first to evaluate population-level effects of directly measured OP. Measured OP^{DTT} was significantly associated with ED visits for respiratory disease, asthma, and ischemic heart disease. We expanded upon these results in Aim II by developing a predictive model for OP^{DTT}, which was selected prior to assessing health effects in order to deter any preferential selection of positive results. This model was used to backcast daily OP^{DTT} values over a 15-year time period, and associations between this modeled OP^{DTT} time series and ED visits were estimated. Modeled OP^{DTT} was significantly associated with ED visits for respiratory disease and asthma. For both regression analyses with measured OP^{DTT} and regression analyses with modeled OP^{DTT}, we assessed bipollutant models; in these models, effects of OP^{DTT} were largely not attenuated. Taken together, all these results provide additional support for OP^{DTT} and oxidative potential in general being strong independent predictors of human health effects of ambient particulate matter.

The second study question asked: What are the health benefits of air pollution control policies? In Aim III, we leveraged collaborations with researchers at the Georgia Institute of Technology to conduct an accountability study of the impact of six sets of air pollution control policies which affected emissions in the Atlanta metropolitan area. We

developed a multipollutant model to estimate the combined effect of pollutant mixtures. We then incorporated observed and counterfactual ambient pollutant levels in order to estimate cardiorespiratory ED visits prevented by pollution control policies. We found that substantial numbers of cardiorespiratory ED visits had been prevented due to pollution control policies, and the percent ED visits prevented increased in later years as impacts of these policies were more fully realized. These results were important for validating the protective effects of pollution control policies, and analyses conducted for individual policies may help inform future pollution control efforts.

These studies were able to make use of extensive long-term exposure and outcome datasets providing daily data over a 15-year period. We utilized a large hospital database capturing ED data from 42 Atlanta area hospitals. We had access to detailed patient-level data, which were converted into daily counts for a 15-year period for several cardiorespiratory outcomes. There were over 16 million ED visits recorded in this database from 1999-2013, and the considerable study size (both in ED visit counts and in length of the study) allowed for assessment of a variety of outcomes, model parameterizations, and pollution control scenarios. In addition, the large suite of air quality variables that were continuously measured on a daily basis over the 15-year period allowed for assessment of various different multipollutant model formulations. The OP^{DTT} measurements, while made over a shorter time period, still provided more measurements than other comparable measurements of PM oxidative potential.

Both study questions utilized modeled air quality data, and health effects were estimated through additional regression modeling. Relying on multiple layers of modeling can be potentially problematic, especially without reliable ways of validating

modeled exposure data. We addressed these concerns in multiple ways. The first approach was to make primarily *a priori* choices for model parameterizations. This included covariate control and model formulations developed in time series models from previous studies using the same Atlanta ED data. We also used *a priori* decisions about lag structures, variables for model inclusion, and outcome groups. However, for situations in which we utilized a more exploratory approach for modeling choices, we conducted sensitivity analyses to assess the impact of different model formulations. This included number of terms included in models, cubic polynomial and interaction terms, and period of model fit. These analyses helped to describe how sensitive results were to modeling parameterizations. Regardless of modeling decisions, random error in estimation can also play an important role in the modeling of exposure data. Instead of assuming that modeled air quality data were fixed, as most modeling studies do, we utilized Monte Carlo simulation to generate large numbers of possible pollutant time series. These were generated from sampling coefficient values from multinormal distributions using the observed variance-covariance matrix of the regression models used for air quality modeling. Similarly, we sampled from distributions of possible coefficient values describing associations between pollutants and ED visits. The iterations of pollutant time series were combined with the iterations of health effect estimates to produce simulated confidence intervals that incorporated uncertainty in the modeling of both air quality data and health effects of these pollutants.

In conclusion, these studies provided valuable information about the measurement and mitigation of health effects of ambient air pollution. These results are an important

contribution to the field of air pollution research and will help inform future efforts to address this critical public health issue.