ANALYSIS OF AIR POLLUTION, HYPERTENSION AND NEIGHBORHOOD WALKABILITY

by

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DEDICATION

To my dear family, friends, as well as advisors
who gave me love, courage, and support which
made the completion of this dissertation possible.

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ABSTRACT

Introduction: Few studies have explored associations of long-term air pollution exposure with the prevalence and incidence of hypertension, or the joint relationships of neighborhood walkability, individual walking behavior, and social disadvantage.

Methods: Air pollution, hypertension, walkability, walking, and covariate data were assessed for >6,000 participants of the Multi-Ethnic Study of Atherosclerosis (MESA) between 2000 and 2007. These participants resided in six communities in the U.S and were aged 45 to 84 and without clinical cardiovascular disease at baseline. Particulate and gaseous air pollution levels ($PM_{2.5}$, $PM_{10-2.5}$, NO_x) from MESA-generated spatio-temporal models and walkability from the Walk Score Research Services were estimated at participant homes as well as on the census block group level. Census block groups in the six communities having low air pollution and high walk score levels, and the reverse, were classified as "sweet spot" and "sour spot", respectively. Population characteristics, including percent racial minority, low education level, and below poverty line at the census block group scale were collected from the American Community Survey. Logistic and Cox regressions were used to assess associations between air pollution and prevalent and incident of hypertension. Multinomial logistic regression was used to investigate associations between 1) population characteristics with the sweet/sour spot indicators, and 2) individual walking activity, neighborhood air pollution and walk score.

Results: Long-term exposure to ambient $PM_{2.5}$, NO_x, $PM_{10-2.5}$, and its composite chemicals were not associated with hypertension onset or prevalence at baseline. Geographical distributions of sweet- and sour-spot neighborhoods differed among the six communities. Socially deprived neighborhoods with lower education level populations were less likely to be sweet-spots. Finally, lower ambient $PM_{2.5}$ levels were associated with more walking for leisure whereas higher walk scores were associated with more walking for transport.

Conclusions: Long-term exposures to $PM_{2.5}$, $PM_{10-2.5}$ or NO_x were not a main contributor to

hypertension development in the MESA population, but in some communities, air pollution levels and walkability were associated with personal walking behavior. Socio-economic disadvantage in some communities was linked to higher likelihood of living in a more polluted and less walkable area, potentially contributing to health disparities.

CHAPTER I

Introduction

1.1 Background

The 2010 Global Burden of Disease Study reported that ischemic heart disease and stroke and other cerebrovascular diseases (CVD) are the top two leading causes of death in the world[1]. According to 2008 mortality rate data, about 150,000 persons died of CVD in the United States with one-third occurring before the age of 75 years[2]. High blood pressure is one of the main causes of ischemic heart disease and stroke, and is the leading cause of death and disability due to CVD and circulatory diseases worldwide[1]. Hypertension is also a serious public health issue in the United States which affects approximately one third of adults.

Previous research has indicated that a person's residential environment may relate to CVD. Some built-environment features such as transportation, sidewalks, land uses mix, street connectivity, and accessibility of recreational resources related to neighborhood walkability are associated with physical activity and personal walking which is related to changes in biological factors such as the elevation of blood pressure which is the primary risk factor for CVD. In addition, strong evidence from various studies has demonstrated that ambient particulate matter (PM) and traffic-related pollutants, often indicated by oxides of nitrogen (NOx), are related to increased risk of morbidity and mortality for CVD[3-8]. While associations between physical activity and hypertension are clearly established, associations between air pollution and hypertension are not well known. In addition, little is known about the co-occurrence patterns of air pollution and walkability in our neighborhoods and whether people modify their walking behaviors in a high-polluted environment.

Some recent epidemiological studies have indicated that PM may induce acute and chronic increases in blood pressure and even onset of hypertension[6,8-10]. Possible biological mechanisms by which PM could regulate the changes of blood pressure include the deposition of PM in the different regions of the respiratory tract, which may stimulate oxidative stress and inflammatory responses that in turn could trigger endothelial dysfunction and pro-coagulation effects[11,12]. In addition, PM could activate the autonomic nervous system imbalance and then lead to changes in arterial tone which are related to arterial vasoconstriction[13,14].

In the modern world, the major sources of air pollution are derived from human activities such as fossil fuel (e.g., coal, oil, and diesel) combustion by automobiles, power generation and industry, and from natural sources such as volcanos and forest fires. PM is a heterogeneous amalgam of compounds varying in size, chemical composition, surface area and sources of origins[15]. Due to the complexity of its physical and chemical characteristics, PM is broadly categorized and regulated by aerodynamic diameter. Ambient fine PM <2.5 μm in aerodynamic diameter ($PM_{2.5}$) has received the majority of attention in scientific research over the past few decades, in part, because it has been hypothesized that the small size and large surface area of $PM_{2.5}$ as well as the combustion-derived compounds contained in $PM_{2.5}$ could impose more toxicity to human health[3,15,16]. Coarse thoracic particles (2.5 μm < aerodynamic diameter ≤ 10 μm, $PM_{2.5\text{-}10}$) may also have health effects which are independent of those of $PM_{2.5}$, however, given differences in the physical, chemical, and toxic characteristics[15]. Yet little research has focused on the cardiovascular effects of $PM_{10\text{-}2.5}$ and existing findings are mixed[17]. Similarly, questions remain about the importance of different sources of PM, especially within the $PM_{10\text{-}2.5}$ fraction.

Emerging research on "environmental justice" indicates that more socially deprived neighborhoods, marked by a greater proportion of minority of race, low education level, and living in poverty are more likely to have higher levels of air pollution[18,19] and these socially disadvantaged residents are less likely to get recommended level of physical activity[20-23]. Physical inactivity is important as it is another key risk factor for CVD and recent reports showed that about one third of adults in U.S failed to meet minimum recommended levels of physical activity [24] [25]. Substantial questions about the interplay of air pollution and physical activity remain and in 2010, experts at a U.S. Centers for Disease Control and Prevention workshop suggested that more research was needed to clarify the relationship between physical activity and air pollution exposure[26], especially among vulnerable subpopulations such as children and elderly. Nevertheless, the most recent physical activity guidelines for Americans indicated that people should modify their physical activity time and location to reduce adverse health risks of ambient air pollution when ambient pollution is known to be high[25].

1.2 Research Objectives

The overall objective of this dissertation is first to explore the associations between various long-term ambient pollution concentrations of various particulate matter and gaseous air pollutants, including $PM_{2.5}$, $PM_{10-2.5}$, $PM_{10-2.5}$ chemical composition, and NO_x with the prevalence and the incidence of hypertension. The second objective is to understand the geographic distributions of neighborhood air pollution and walkability and how these relate with socially disadvantaged subgroups, and to clarify the independent and/or joint effects of two environmental health attributes, air pollution and walkability, on personal walking behavior in daily life. Five main aims, each with specific hypotheses, comprise the dissertation, as follows:

Aim 1 examines the cross-sectional and longitudinal associations between long-term ambient $PM_{2.5}$ and NO_x concentrations with the incidence and prevalence of hypertension, respectively. The hypothesis for this specific aim is that long-term exposure to ambient $PM_{2.5}$ and NO_x are positively associated with both hypertension outcomes.

Aim 2 investigates associations between chronic exposure to ambient $PM_{10-2.5}$ and four key components (copper, phosphorus, silicon, and zinc) with the risk of incident and the odds of prevalent hypertension. The hypothesis for this aim is that the total mass of $PM_{10-2.5}$ and chemicals indicative of traffic (copper and zinc) but not soil (phosphorous and silicon) are positively related to both hypertension outcomes.

Aim 3 displays spatial distributions of neighborhood air pollution and walkability to characterize “sweet-spot” (low air pollution, high walkability) and “sour-spot” (high air pollution, low walkability) area in six communities in the U.S.

Aim 4 explores if socially deprived neighborhoods, characterized by a greater proportion of population of minority of race, low education level, and living in poverty, are less likely to be “sweet-spot” neighborhoods. We hypothesize that more socially deprived neighborhoods will have lower odds of being sweet-spot neighborhoods.

Aim 5 investigates how and if neighborhood walkability and air pollution are associated with personal walking activity. The hypothesis is that neighborhoods with better walking environment and lower air pollution levels could promote personal walking activity for transport and for leisure.

1.3. Organization of Dissertation

This dissertation is composed of five chapters: Chapter 1 (this chapter) provides the background of this research and states specific objectives of this research and its related hypotheses. Chapters 2, 3 and 4 describe the detailed study design (data sources and analysis methods), results, and discussion for the research conducted to address corresponding aims. Chapter 5 briefly summarizes the findings of our research and the public health implications of these findings.

CHAPTER II

Traffic-related Air Pollution and Hypertension

2.1 Introduction

Numerous studies have demonstrated that both short- and long-term exposures to ambient air pollutants including fine particulate matter (≤ 2.5 micrometers in aerodynamic diameter, $PM_{2.5}$) and oxides of nitrogen (NO_x) are linked to increased hospital admissions, morbidity, and mortality for cardiovascular diseases[3-8]. Recently, several epidemiological studies have reported associations between air pollution, blood pressure, and hypertension[6-8,27-30]. As a primary risk factor of coronary heart disease and stroke, such findings suggest that hypertension may be implicated in the observed associations between air pollutants and cardiovascular events[31,32].

Inhalation of air pollutants may lead to elevated blood pressure and hypertension through several biological mechanisms[16]. First, the release of pro-oxidative and/or pro-inflammatory mediators such as cytokines from pulmonary tissues can result in systemic oxidative stress and inflammation, triggering endothelial dysfunction and vasoconstriction[11,12]. $PM_{2.5}$ and co-pollutants may also promote vascular dysfunction and arterial vasoconstriction in part through altering cardiovascular autonomic nervous system balance[13,14,33].

Several previous epidemiologic studies have found that 10 $\mu g/m^3$ higher short-term $PM_{2.5}$ concentrations were associated with 1 to 5 mm Hg higher systolic blood pressures [9,27,28,34-36] while other studies had inconsistent findings[37-39]. Most of these studies have focused on short-term associations with blood pressure, however, and increasing evidence shows that longer-term exposures may also promote the development of chronically elevated blood pressure, and even the onset of hypertension[27,29,30,40]. In fact, the few long-term studies published indicated that the associations with long-term exposure to particles with elevated blood pressure or hypertension were larger than those of short-term exposure[27,30]. Additionally, a few studies have shown that NO_x, a traffic-related air pollutant, was associated with higher blood pressure and hospital visits for hypertension[7,27,41]. This is consistent with other research that has demonstrated associations of traffic-related air pollution and road traffic noise with blood pressure and hypertension[27,29,42,43].

In this study, the availability of repeated blood pressure measurements from the prospective Multi-Ethnic Study of Atherosclerosis (MESA) cohort allowed us to investigate longitudinal associations of pollution exposure with incident hypertension. In addition, we explored cross-sectional associations between long-term $PM_{2.5}$ and NO_x concentrations and prevalent hypertension.

2.2 Material and Methods

2.2.1 Data

2.2.1.1 Study Participants

MESA is a population-based longitudinal cohort study designed to investigate predictors of subclinical cardiovascular disease[44]. Between July 2000 and September 2002, MESA recruited 6,814 men and women, aged 45 to 84 years, who were free of clinical cardiovascular disease from six U.S. communities (Winston Salem, North Carolina; New York City, New York; Baltimore City and Baltimore County, Maryland; St. Paul, Minnesota; Chicago, Illinois; and Los Angeles County, California). Institutional Review Boards from all of the participating institutions approved the study and study participants provided written informed consent. Additional details on study design and objectives have been published previously[44].

Participants with complete data for air pollution, hypertension, and key covariates were included in analysis for prevalent hypertension at baseline (sample size = 5,303). We further excluded those who were diagnosed as hypertensive at baseline (n = 2,530) for the analysis of incident hypertension, resulting in a sample size of 2,418.

2.2.1.2 Hypertension Outcomes

Systolic blood pressure (SBP) and diastolic blood pressure (DBP) were measured at each of the four MESA examinations conducted between 2000 and 2007. After resting for five minutes in the seated position, blood pressure was measured three times using an automated oscillometric sphygmomanometer (Dinamap Pro 100, GE Medical Systems Information Technologies, Inc., Milwaukee, Wisconsin), with an appropriate cuff size. The average of the second and third readings was used for analysis. Information about hypertension medication use was also collected via technician-administered questionnaire at each visit. Hypertension was defined as a SBP $\geq$ 140 mmHg, DBP $\geq$ 90 mmHg, use of any anti-hypertensive medication, or a self-reported previous diagnosis of hypertension.

2.2.1.3 Air Pollution Exposures

$PM_{2.5}$ and NO_x concentrations prior to each MESA examination were estimated for each subject's residential address using predictions from spatio-temporal models derived by the MESA Air Pollution study (MESA Air). These models are described elsewhere[45,46] but briefly, they utilize daily concentrations of $PM_{2.5}$ and NO_x collected from U.S. Environmental Protection Agency Air Quality System (AQS) along with two-week samples collected in the communities and at the homes of the MESA cohort. These data were combined with relevant geographic covariates such as home location addresses, land use data and distances to major roadways in a multistep procedure to assign individual estimates of long-term air pollution concentrations at each participant's residence while accounting for a complex spatio-temporal correlation structure[24,45,46]. Based on the availability of $PM_{2.5}$ measurements from the AQS, complete concentration estimates were available between 1999 and 2007. As such, annual average $PM_{2.5}$ and NO_x concentrations in the year prior to the baseline visit were used as long-term exposure measures for outcomes collected at the baseline exam. For outcomes collected at later clinical exams, round-year average concentrations were estimated for the period from baseline to each follow-up visit. In sensitivity analyses, we explored the impacts of different averaging periods for the pollutants including one year before each exam. We further explored relationship between ambient air pollution levels measured at the nearest AQS monitor and the impact of living near a major roadway as defined by participants' residential address locations within 100 meter of an interstate or U.S. highway (Census Feature Class Code A1 or A2) or within 50 meter of a state or county highway (Census Feature Class Code A3) at baseline examination. Residential addresses geocoding and distance calculations were on the basis of the Dynamap 2000 street network and geocoding database (Tele Atlas, Boston, Massachusetts) using ArcGIS 9.2 and 9.3 software (ESRI, Redlands, California).

2.2.1.4 Other Covariates

Detailed information on age, sex, race/ethnicity (white, black, Hispanic, and Chinese), tobacco smoke exposure, physical activity, education (high-school degree or under, some college or associate degree, or bachelors degree or higher), dietary sodium, calcium, and fiber intake, and medication use was collected using standardized questionnaires at baseline and/or follow-up visits. Tobacco smoke exposure was categorized into five groups: never-smoker without environmental tobacco smoke (ETS) exposure, never-smoker with ETS exposure, former smoker without ETS exposure, former smoker with ETS exposure, and current smoker. Physical activity was reported as total physical activity hours per day and it is categorized into quartiles of reported hours. Measurements of height and weight were collected during each of the clinical exams and body mass index (BMI) was calculated. Serum samples were also collected at baseline and follow-up exams and evaluated for fasting serum glucose, high-density lipoprotein cholesterol (HDL), and triglycerides. Glucose status was also measured and defined as normal (fasting glucose, $\leq$ 5.6 mmol/L), impaired fasting glucose (fasting glucose, 5.6-6.9 mmol/L without hypoglycemic medications), or diabetes (fasting glucose, $\geq$ 7 mmol/L or use of any hypoglycemic medication) based on the American Diabetes Association criteria[47]. For our hypertension incidence analysis, BMI, tobacco smoke exposure, physical activity, diabetes, HDL-C, triglycerides, and study site were included in the model as time-varying covariates while all other covariates were included as recorded at baseline.

2.2.2 Statistical Analysis

First, descriptive analyses were used to characterize the distribution of person-level characteristics among both groups of subjects who did and did not have prevalent hypertension at baseline visit. Then, logistic regression was used to assess the cross-sectional associations between pollution exposures and prevalent hypertension at baseline. Next, associations between pollution exposure and the risk of developing hypertension were then examined by using the Cox proportional hazards model. Since the occurrence of hypertension was only assessed at each exam, the onset date of new hypertension over the follow-up was assigned at the midpoint between the first reported date of hypertension and the date of the previous exam.

Covariates were selected *a priori* as potential confounders based on previously reported associations with blood pressure and/or the risk of hypertension. Since some of confounders may be on the causal pathway between air pollution and hypertension, we built our model in a staged fashion. First, we constructed the model adjusted for age, gender, and race/ethnicity. Next, BMI, smoke exposure, physical activity, education, dietary sodium, calcium, fiber, diabetes, HDL-C, and triglycerides were added into the previous model. We further examined associations after adjustment for site.

In sensitivity analysis, we examined the joint effects of $PM_{2.5}$, NO_x and living near roadways on the risk of hypertension in the same regression model. We additionally evaluated $PM_{2.5}$ and NO_x exposure using the concentrations reported at the nearest monitor to the MESA participants' residences, an exposure assessment method employed in other air pollution epidemiology research. We also explored heterogeneity in associations by site since fine particle composition and properties can vary greatly by geographic location[48,49] and modifying effect of community location has been observed on associations between exposures and hypertension[28]. Modifying effects of socioeconomic factors (education) on associations between air pollution and hypertension were also evaluated because vulnerability to air pollution associated blood pressure changes may be linked with socioeconomic position[28,50,51]. Modifying effects of demographic factors (age, sex, and race/ethnicity), tobacco smoke exposure, and diabetes mellitus were similarly investigated because vulnerability to incident hypertension relates to these risk factors[52-54]. All analyses were conducted using SAS software, version 9.2 (SAS Institute, Cary, North Carolina).

2.3 Results

Table II-1 showed the characteristics of the study participants by hypertension status at the baseline visit. The average age of participants at baseline was 62.1 years and 53.2% were women. Current smoking was reported by 12.2% of the subjects, and about half of the cohort (51.2%) reported never having smoked. At the baseline exam, 48% of participants had existing hypertension. Participants without prevalent hypertension had younger age, different racial composition, lower BMI, less diabetes, higher physical activity, higher education, and higher dietary intake of sodium, calcium and fiber than persons with hypertension at baseline. Little difference was observed between participants with and without prevalent hypertension at baseline for annual average concentrations of pollution. The overall mean annual average $PM_{2.5}$ and NO_x concentrations prior to baseline exam were 16.7 $\mu g/m^3$ and 49.1 ppb, respectively. The majority of participants (72.6%) were not living near roadways.

Exposure patterns of ambient $PM_{2.5}$ and NO_x differed significantly between different cities (**Table II-2**). Overall mean $PM_{2.5}$ level was the highest in Los Angeles (mean ± SD = 23.1 ± 1.9 $\mu g/m^3$) and the lowest in St. Paul (mean ± SD = 11.9 ± 1.0 $\mu g/m^3$). New York City had the highest mean NO_x level (mean ± SD = 84.2 ± 13.1 ppb) and Winston-Salem had the lowest (mean ± SD = 21.4 ± 6.9 ppb). Among 2,772 non-hypertensive members of the cohort at baseline, 878 individuals developed incident hypertension over the follow-up period at a rate of 82 new cases per 1,000 person-years. The lowest hypertension incidence rate (75 cases per 1,000 person-years) was observed in Chicago, and the highest (96 cases per 100 person-years) in Winston-Salem.

Table II-3 and **Table II-4** presented the associations of pollution exposures with the odds of hypertension prevalence and risk of incident hypertension. Mixed but non-significant associations were found for $PM_{2.5}$, NO_x, and living near a major roadway with hypertension prevalence and incidence. In sensitivity analyses, we found significant heterogeneity by gender in the association of hypertension prevalence with $PM_{2.5}$ and significant heterogeneity by education and diabetes status in the association between $PM_{2.5}$ and hypertension incidence. However, we did not find any significant associations between $PM_{2.5}$ and hypertension outcomes after stratification by these effect modifiers. In sensitivity analysis, we found similarly null associations between nearest-monitor measured $PM_{2.5}$ and both hypertension event outcomes in all models (data not shown).

Table II-1. The distribution of selected characteristics for subjects diagnosed as hypertensive or not at the baseline exam (n = 5,303); MESA 2000-2002

	Total	Hypertension at baseline		
	(n = 5,303)	No (n = 2,773)	Yes (n = 2,530)	*P* [b]
Age, years	62.1 (10.2)[a]	58.9 (9.7)	65.6 (9.5)	<0.0001
Female (%)	53.2	52.9	53.5	0.65
Race/ethnicity (%)				
White	40.2	43.5	36.6	<0.0001
Chinese	12.8	14.7	10.7	
Black	25.5	19.0	32.6	
Hispanic	21.5	22.8	20.1	
BMI[c], kg/m^2	28.2 (5.4)	27.2 (5.0)	29.2 (5.5)	<0.0001
Tobacco smoke exposure (%)				
Never-smoker without ETS	32.6	32.4	32.9	<0.0001
Never-smoker with ETS	18.6	19.5	17.6	
Former smoker without ETS	20.1	17.6	22.7	
Former smoker with ETS	16.6	16.4	16.8	
Current smoker	12.2	14.1	10.0	
Physical activity[d] (%)				
1st quartile	25.1	21.2	29.4	<0.0001
2nd quartile	25.4	25.6	25.1	
3rd quartile	25.0	26.8	23.0	
4th quartile	24.5	26.4	22.5	
Education (%)				
High-school degree or under	34.8	31.4	38.5	<0.0001
Some college or associate degree	28.1	27.4	28.8	
Bachelor degree or higher	37.2	41.2	32.8	
Dietary Sodium, mg	2352 (1406.1)	2450.2 (1420.1)	2244.4 (1382.9)	<0.0001
Dietary Calcium, mg	715.4 (528.2)	742.2 (536.8)	686.1 (517.1)	<0.0001
Dietary fiber, g	17.7 (9.3)	18.1 (9.5)	17.3 (9.1)	0.0023
Diabetes (%)				
No	74.8	82.9	65.9	<0.0001
Impaired glucose tolerance	13.5	10.7	16.5	
Diabetes	11.8	6.4	17.7	
High-density lipoprotein cholesterol (HDL-C), mg/dL	51.2 (14.9)	51.5 (15.1)	50.8 (14.7)	0.14
Triglycerides, mg/dL	131.5 (83.5)	127.1 (85.3)	136.4 (81.2)	<0.0001
Study site (%)				
Forsyth County, NC	15.6	12.6	18.8	<0.0001
New York City, NY	14.9	14.2	15.8	
Baltimore, MD	14.5	12.7	16.5	

St. Paul, MN	15.8	18.8	12.6	
Chicago, IL	19.0	21.1	16.7	
Los Angeles, CA	20.2	20.6	19.6	
Blood pressure, mm Hg				
Systolic blood pressure	125.9 (21.0)	114.7 (12.9)	138.2 (21.2)	<0.0001
Diastolic blood pressure	71.7 (10.1)	68.8 (8.7)	74.9 (10.7)	<0.0001
$PM_{2.5}$, µg/m^3	16.7 (3.8)	16.6 (3.8)	16.7 (3.7)	0.29
NO_x, ppb	49.1 (25.6)	49.1 (25.5)	49.1 (25.6)	0.83
Living near roadway[e]				
No	72.6	73.1	72.1	0.41
Yes	27.4	26.9	27.9	

[a]Mean (standard deviation).

[b]*P* Value from Kruskal-Wallis test and/or chi-square test.

[c]Body mass index = weight in kilograms / (height in meters)^2.

[d]Physical activity is characterized into four quartiles: 1st quartile, ≤ 8.8 hr/day; 2nd quartile, 8.8–11.9 hr/day; 3rd quartile, 11.9-15.3 hr/day; 4th quartile, > 15.3 hr/day.

[e]Living near roadway: Yes = location within 100m of an A1 or A2 road or 50m of an A3 road; No = otherwise.

Table II-2. Annual average air pollution exposure levels prior to baseline exam and hypertension prevalence and incidence rate by MESA enrollment site; MESA 2000-2002

		$PM_{2.5}$		NO_x			
Study site	**n**	**Mean (μg/m³)**	**s.d**[a]	**Mean (ppb)**	**s.d.**	**Prevalence (%)**	**Incidence rate**[b]
All	5,303	16.7	3.8	49.1	25.6	47.7	82
Forsyth County, NC	825	15.5	0.7	21.4	6.9	57.6	96
New York City, NY	792	15.4	0.8	84.2	13.1	50.4	85
Baltimore, MD	770	15.2	0.9	41.1	11.0	54.2	89
St. Paul, MN	840	11.9	1.0	24.1	5.6	38.0	79
Chicago, IL	1007	16.9	1.3	47.3	11.9	42.0	75
Los Angeles, CA	1069	23.1	1.9	71.4	17.0	46.5	80

[a]Standard deviation.

[b]Incidence rate = new case per 1000 person-years.

Table II-3. Estimated odds ratios (OR) for hypertension prevalence corresponding to each IQR increase in the level of $PM_{2.5}$ and NO_x, respectively, and living near roadway; MESA 2000-2002

	$PM_{2.5}$			NO_x			Living near roadway		
Model[a]	**OR**	**95% CI**		**OR**	**95% CI**		**OR**	**95% CI**	
Model 1	1.03	0.98	1.09	0.97	0.87	1.08	0.99	0.87	1.12
Model 2	1.03	0.98	1.09	1.00	0.89	1.12	1.00	0.87	1.14
Model 3	1.04	0.90	1.20	0.92	0.74	1.16	0.99	0.86	1.14
Model 4	1.12	0.93	1.36	0.82	0.60	1.11	1.02	0.87	1.19

[a]Model 1: $PM_{2.5}$ (NO_x or living near roadway) + age, sex, and race/ethnicity;

Model 2: Model 2 + BMI, smoke exposure, physical activity, education, dietary sodium, calcium, fiber, diabetes, HDL-C, and triglycerides;

Model 3: Model 2 + study site;

Model 4: Model 3 + all other pollution covariates

Table II-4. Estimated hazard ratios (HR) for hypertension incidence rate corresponding to each IQR increase in the level of $PM_{2.5}$ and NO_x, respectively, and living near roadway; MESA 2000-2007

	$PM_{2.5}$			NO_x			Living near roadway		
Model[a]	**HR**	**95% CI**		**HR**	**95% CI**		**HR**	**95% CI**	
Model 1	0.99	0.94	1.05	0.96	0.85	1.09	0.98	0.85	1.14
Model 2	0.99	0.91	1.06	0.99	0.83	1.17	0.99	0.82	1.20
Model 3	1.00	0.80	1.24	1.07	0.76	1.50	0.99	0.80	1.21
Model 4	0.95	0.72	1.25	1.14	0.73	1.79	0.96	0.77	1.20

[a]Model 1 $PM_{2.5}$ (or NO_x or living near roadway) + adjustment for age, sex, and race/ethnicity;

Model 2: Model 2 + BMI, smoke exposure, physical activity, education, dietary sodium, calcium, fiber, diabetes, HDL-C, and triglycerides;

Model 3: Model 2 + study site;

Model 4: Model 3 + all other pollution covariates

2.4 Discussion

In a prospective cohort of middle-aged participants with no clinical cardiovascular disease at baseline, we found that long-term exposure to ambient $PM_{2.5}$ and NO_x were not significantly associated with increased prevalence or incidence of hypertension after adjustment for selected confounders. As such, this work does not support the hypothesis from controlled human and animal experiments, which suggest a plausible biological mechanism by which exposure to air pollution could regulate changes of blood pressure and promote the development of chronic hypertension.

Several epidemiological studies have similarly demonstrated that recent exposure to air pollution was associated with increased emergency department visits for hypertension[6,7,41] and elevations in blood pressure[27,28]. However, few previous studies have explored the associations between long-term air pollution with hypertension onset, and results were inconsistent[8,10,40]. For hypertension prevalence, a study explored the relationship between $PM_{2.5}$ and the prevalence of self-reported hypertension using data from the National Health Interview Survey (NHIS). They found a positive association between annual average $PM_{2.5}$ and prevalent hypertension in non-Hispanic white adults, but not in non-Hispanic black or Hispanic adults[40]. For hypertension incidence, a study conducted in a cohort of black women living in Los Angeles found that annual average NO_x exposure was positively associated with the incidence of hypertension while $PM_{2.5}$ was not[8]. However, a study on the association between long-term NO_x with hypertension prevalence and incidence outcomes among a Danish population-based cohort, reported a small inverse association in the cross-sectional analysis of self-reported hypertension at baseline, whereas NO_x was not associated with incident self-reported hypertension during follow-up[10].

The strength of this study included investigating the longitudinal associations between hypertension incidence and time-varying air pollution levels in a large population-based cohort through repeated blood pressure measurements and detailed information on various potential confounders. Included in these possible confounders was living near a major roadway as an indicator of traffic-related noise, which has been linked to hypertension outcomes[42,55]. This study also represents a substantial improvement with respect to exposure assessment from most previous epidemiology studies of air pollution and blood pressure effects that have relied on central site monitoring or city-average concentrations. Levels of $PM_{2.5}$ and NO_x in our study were estimated for each subject's location using extensive project-specific measurements and city-specific models that considered various spatial and temporal factors[45,46]. Nevertheless, measurement error of air pollution remains a concern due the possibility of prediction error due to use of a model-derived exposures as well as a failure to account for indoor and personal exposures. Assuming that this error was non-differential with respect to hypertension, we would expect bias towards the null.

Selection bias could also be an important factor in this study, which could bias estimated effects of air pollution on prevalent hypertension towards null. Because the eligiblity criteria for the recruitment of the MESA cohort includes a restriction to be without any cardiovascular diseases at enrollment, this makes these samples for analysis may have healthier status than general population and this may limit the generalizability of these findings. Another possible explanation for null associations between long-term air pollution exposures with incidence of hypertension is attrition bias from death or other loss-to-follow-up[56]. Attrition bias is a concern in all longitudinal studies of aging-related outcomes and may be an issue in our study because air pollution exposure and hypertension events are strongly related to morbidity for other cardiovascular diseases and mortality after study enrollment[16,32,57]

Conclusions

In summary, results from this study did not provide conclusive evidence to support the hypothesis that long-term exposure to ambient air pollutants and traffic proximity may contribute to the onset of hypertension. An important challenge of this prospective study is addressing selection bias from loss to follow-up due to death or withdrawal during the follow-up period.

CHAPTER III

Ambient Coarse Particulate Matter and Hypertension Events

3.1 Introduction

Numerous studies have revealed the strong evidence that both short and long term exposures to fine particulate matter (aerodynamic diameter < 2.5 micrometer, $PM_{2.5}$) are positively related to the mortality and morbidity of cardiovascular diseases[3,4,58-60]. Although it has historically been believed that larger thoracic coarse particles (2.5 to 10 micrometers, $PM_{10-2.5}$) are less important, suggestive evidence of the cardiovascular and pulmonary health effects of $PM_{10-2.5}$ is now emerging[17,61]. Most studies to date have focused on the impacts of short-term exposures and very limited information about the chronic health effects of $PM_{10-2.5}$ exist. As such, the U.S. Environmental Protection Agency (EPA) recently concluded that the evidence from these studies was still inadequate and that further research on the cardiovascular effects of coarse thoracic particles was needed[62].

Inhaled particles are hypothesized to induce cardiovascular diseases including stroke and myocardial infarction through oxidative stress and inflammatory responses, which may trigger endothelial dysfunction and pro-coagulation effects[11,12]. PM may also activate autonomic nervous system balance and consequent changes in arterial tone, which may result in arterial vasoconstriction[13,14]. As each of these mechanisms involves changes to the vasculature, it is likely that exposures to pollution may also lead to alterations in blood pressure. A limited literature has investigated associations between $PM_{2.5}$ and blood pressure with inconclusive findings[9]. In addition, since $PM_{10-2.5}$ has different deposition and clearance patterns in the respiratory tract[15], it is likely that these particles may have different relationships with blood pressure than $PM_{2.5}$. Different composition chemicals of $PM_{10-2.5}$ from various sources may also have different oxidative potential and thus toxicity. No investigations, however, have yet explored associations between $PM_{10-2.5}$ and blood pressure nor has there been data on indicators of different sources and blood pressure.

The Multi-Ethnic Study of Atherosclerosis and Coarse Particle Study (MESA Coarse) characterized $PM_{10-2.5}$ mass and key indicators of different sources throughout three U.S. communities. This allows us to examine relationships between long-term exposure to ambient coarse particles and the risk of incident hypertension and odds of prevalent hypertension. We hypothesize that elevated ambient $PM_{10-2.5}$ levels, especially from traffic sources, are positively associated with both incident and prevalent hypertension.

3.2 Material and Methods

3.2.1 Data

3.2.1.1 Study Participants

MESA is a population-based prospective cohort study designed to investigate the risk factors of subclinical cardiovascular disease[44]. The MESA cohort comprised 6,814 elderly adults, aged 45 to 84 years, who were free of clinical cardiovascular disease at enrollment and were recruited from six U.S. cities (Forsyth County, North Carolina; northern Manhattan and the Bronx, New York; Baltimore City and Baltimore County, Maryland; St. Paul, Minnesota; Chicago, Illinois; and Los Angeles County, California). Participants of the MESA Coarse project included those participants residing in Chicago, Winston-Salem, and St. Paul. These participants with hypertensive status data at the baseline exam (n = 2,580) were included in the analysis of prevalent hypertension. For incident hypertension analysis, we only included participants without prevalent hypertension and complete data on hypertensive status and other covariates over the following-up period from 2000 to 2007 (n = 1,394). All procedures were approved by the relevant institutional review board, and all participants gave informed consent.

3.2.1.2 Hypertension Outcomes

Systolic blood pressure (SBP) and diastolic blood pressure (DBP) were measured at each of the four MESA examinations conducted between 2000 and 2007. After resting for five minutes in the seated position, blood pressure was measured three times using an automated oscillometric sphygmomanometer (Dinamap Pro 100, GE Medical Systems Information Technologies, Inc., Milwaukee, Wisconsin), with an appropriate cuff size. The average of the second and third readings was used for analysis. Information about hypertension medication use was also collected via technician-administered questionnaire at each visit. Hypertension was defined as a SBP ≥ 140 mmHg, DBP ≥ 90 mmHg, use of any anti-hypertensive medication, or a self-reported previous diagnosis of hypertension.

3.2.1.3 Coarse Particulate Matter Exposures

Estimated concentrations of $PM_{10\text{-}2.5}$ were predicted for MESA Air participants' addresses using cohort-specific measurements and city-specific land-use regression models. Details of the exposure assessment are presented elsewhere but briefly, long-term concentrations were estimated using two-week "snapshots" of $PM_{10\text{-}2.5}$ in which approximately 40 samples were collected simultaneously outside of participants' home and fixed site locations during the summer and winter of each city[63]. Geographic predictors including land use, roadway, and vegetation were used to estimate fine spatial scale gradients in concentrations for $PM_{10\text{-}2.5}$ mass and four key chemical components (copper, silicon, phosphorus, and zinc). These components were identified from positive matrix factorization as indicator species of brake wear (copper), tire wear (zinc), fertilized soil (phosphorous), and soil (silicon)[64]. Five-year average of predicted concentrations prior to the baseline visit was calculated as long-term exposure metrics.

3.2.1.4 Other Covariates

Participant's age, sex, race/ethnicity tobacco smoke exposure (never-smoker without environmental tobacco smoke (ETS) exposure, never-smoker ETS exposure, former smoker without ETS exposure, former smoker with ETS exposure, and current smoker), physical activity (the quartile of total physical activity hours per day), attained education (High-school degree or under, some college or associate degree, or Bachelor degree or higher), dietary sodium, calcium, and fiber intake were collected using a standardized questionnaire at the baseline examination. Body mass index (BMI) was calculated based on measurements of height and weight collected at each examination. Serum samples were evaluated for fasting serum glucose, high-density lipoprotein cholesterol, and triglycerides. Glucose status is defined as normal (fasting glucose, <5.6 mmol/L), impaired fasting glucose (fasting glucose, 5.6–6.9 mmol/L without hypoglycemic medications), or diabetes (fasting glucose, ≥7 mmol/L or use of any hypoglycemic medication).

3.2.2 Statistical Analysis

Descriptive analyses were used to characterize the distribution of baseline characteristics of overall MESA Coarse participants, ambient concentrations of $PM_{10-2.5}$ and composition chemicals, and the crude prevalence and incidence rates of hypertension for each study site. Logistic regression models were then constructed to assess the associations with the prevalence of hypertension at baseline. A Cox proportional hazards model with random subject effects was used to estimate associations with incident hypertension. Since blood pressure and medication use data were only collected at the MESA clinical exams, we defined the follow-up time for incident hypertension as the midpoint between the first examination when they were diagnosed as incident hypertension and the previous examination.

Covariates were selected as a priori as potential confounders based on the previous review of references and all models were constructed in a staged fashion to assess sensitivity of our results to control for different potential confounders. Minimally adjusted models included baseline age, gender, and race/ethnicity. Next, baseline dietary sodium, calcium, fiber and time-varying BMI, smoke exposure, physical activity, education, diabetes, HDL-C, and triglycerides were added in the previous model. We further controlled for site and, in analyses of chemical components, adjusted for $PM_{10-2.5}$ mass. Finally, we added $PM_{2.5}$ for sensitivity analyses. All covariates were assessed at baseline, except BMI, tobacco smoke exposure, physical activity, diabetes, HDL-C, triglycerides, and study site, which were explored as time-varying covariates in our models for incident hypertension.

In secondary analysis, we examined effect modification by age, gender, race, education, tobacco smoke exposure, diabetes mellitus, and site by including the corresponding interaction term in the fully adjusted model. We furthermore restricted participants to the subset of participants who reported that they did not change residence during the follow-up period as baseline exposures were utilized as our primary exposure metric. We performed all analyses using SAS statistical package (version 9.2.1; SAS Institute, Cary, North Carolina).

3.3 Results

Table III-1 shows the selected demographic and clinical characteristics of the study participants (n = 2,580) at the baseline examination. The mean age of the sample was 61.8 years and just more than half were female. A little more than half of the sample's race/ethnicity was white. Overall hypertension prevalence was 45.9 %. During the follow-up period (median = 4.6 years), 433 persons were newly classified as developing hypertension with an incidence rate of 81 new cases per 1,000 person-years.

Table III-2 illustrates the overall mean of concentrations of $PM_{10-2.5}$ mass and chemical composition prior to baseline examination and hypertension prevalence and incidence rate by study site. Exposure patterns of ambient $PM_{10-2.5}$ and its chemical composition were all significantly different between different study sites ($p < 0.0001$). Chicago had the highest ambient concentrations of $PM_{10-2.5}$, copper, and zinc (mean = 5.6 μg/m^3, 7.3 ng/m^3, and 19.9 ng/m^3, respectively) and Winston-Salem had the lowest levels for these three air pollutants (mean = 3.7, 2.4, and 3.2 μg/m^3, respectively). Overall, the mean phosphorus level was the highest in Winston-Salem and the lowest in St. Paul (mean = 19.8 and 12.9 μg/m^3, respectively) and the highest and the lowest silicon level were observed in St. Paul and Winston-Salem (mean = 0.51 and 0.37 μg/m^3, respectively).

The adjusted odds of having prevalent hypertension associated with each interquartile (IQR) increase in $PM_{10-2.5}$ and composition chemicals are shown in **Table III-3**. We found that the higher levels of $PM_{10-2.5}$, silicon, and zinc were associated with lower prevalence of hypertension in models without adjustment for site. In contrast, we found an increased odds of prevalent hypertension per IQR unit increase in phosphorous but again these could not distinguished from no association after control for study site. No associations were identified between any of the pollutants and incident hypertension before or after adjustment for site (**Table III-4)**.

In sensitivity analysis, we found similar results among non-moving participants for the associations of air pollutants with hypertension incidence. In addition, while we found some evidence of heterogeneity by education on the associations of silicon with incident hypertension, there were no consistent trends across multiple analyses.

Table III-1. Demographic and clinical characteristics of participants included in the analyses (n=2,580); MESA 2000–2002

Characteristics	Mean (s.d) or percent
Age, years	61.8 (10.1)
Female (%)	53.8
Race/ethnicity (%)	
White	54.2
Chinese	10.1
Black	23.6
Hispanic	12.5
BMI[a], kg/m^2	28.2 (5.3)
Tobacco smoke exposure (%)	
Never-smoker without second hand smoke exposure	25.9
Never-smoker with second hand smoke exposure	22.1
Former smoker without second hand smoke exposure	18.4
Former smoker with second hand smoke exposure	21.1
Current smoker	12.5
Education (%)	
High-school degree or under	26.5
Some college or associate degree	30.0
Bachelor degree or higher	43.5
Diabetes (%)	
No	78.1
Impaired glucose tolerance	11.9
Diabetes	10.0
High-density lipoprotein cholesterol (HDL-C), mg/dL	51.6 (15.3)
Triglycerides, mg/dL	132.3 (87.8)
Study site (%)	
Forsyth County, NC	30.7
St. Paul, MN	31.3
Chicago, IL	38.0

[a]Body mass index = weight in kilograms / (height in meters)^2

Table III-2. Five-year average $PM_{10-2.5}$ and composition chemicals prior to baseline exam and hypertension prevalence and incidence rate by MESA enrolment site

	Total	Winston-Salem, NC	St. Paul, MN	Chicago, IL
$PM_{10-2.5}$, μg/m^3	5.0 (1.6) [a]	3.7 (1.1)	5.4 (1.8)	5.6 (1.2)
Cu, ng/m^3	4.6 (2.6)	2.4 (0.8)	3.4 (0.8)	7.3 (2.3)
P, ng/m^3	16.1 (3.6)	19.8 (2.2)	12.9 (1.9)	15.7 (2.8)
Si, μg/m^3	0.4 (0.1)	0.4 (0.04)	0.5 (0.07)	0.4 (0.1)
Zn, ng/m^3	10.3 (11.0)	3.2 (1.6)	5.2 (1.5)	19.9 (12.4)
Prevalence (%)	45.9	56.9	39.3	42.5
Incidence rate[b]	80.6	96.6	76.6	75.1

[a]Mean (standard deviation).

[b]Incidence rate = new case per 1000 person-years.

Table III-3. Adjusted odds ratio (OR) for hypertension prevalence associated with per IQR unit increase in 5-year average $PM_{10-2.5}$ and composition chemicals at baseline (n = 2,580); MESA 2000-2002

	Model 1[a]			Model 2			Model 3			Model 4			Model 5		
Exposure	**OR**	**95% CI[b]**		**OR**	**95% CI**		**OR**	**95% CI**		**OR**	**95% CI**		**OR**	**95% CI**	
$PM_{10-2.5}$	0.89	0.80	1.00	0.86	0.77	0.97	0.95	0.83	1.09	0.94	0.82	1.09		-	
Cu	0.87	0.77	0.98	0.90	0.80	1.02	1.07	0.88	1.32	1.06	0.83	1.35	1.11	0.89	1.40
P	1.19	1.03	1.36	1.23	1.07	1.42	1.09	0.88	1.34	1.05	0.83	1.33	1.13	0.90	1.43
Si	0.93	0.81	1.07	0.85	0.74	0.99	0.90	0.76	1.06	0.85	0.71	1.03	0.88	0.72	1.08
Zn	0.87	0.79	0.96	0.88	0.79	0.97	0.92	0.81	1.06	0.90	0.77	1.04	0.93	0.80	1.07

[a]Model 1: $PM_{10-2.5}$ (Cu, P, Si, or Zn) + age, sex, and race/ethnicity;

Model 2: Model 2 + BMI, smoke exposure, physical activity, education, dietary sodium, calcium, fiber, diabetes, HDL-C, and triglycerides;

Model 3: Model 2 + study sites;

Model 4: Model 3 + $PM_{2.5}$

Model 5: Model 3 + $PM_{10-2.5}$

[b]95% confidence interval

Table III-4. Adjusted hazard ratio (HR) for hypertension incidence associated with per IQR unit increase in 5-year average $PM_{10-2.5}$ and composition chemicals over follow-up period; MESA 2000-2007

	Model 1[a]			Model 2			Model 3			Model 4			Model 5		
Exposure	HR	95% CI[b]		HR	95% CI		HR	95% CI		HR	95% CI		HR	95% CI	
$PM_{10-2.5}$	1.01	0.89	1.14	0.92	0.79	1.08	0.89	0.74	1.08	0.91	0.75	1.12		-	
Cu	0.92	0.80	1.05	1.00	0.83	1.20	0.81	0.61	1.06	0.82	0.59	1.15	0.84	0.62	1.15
P	1.02	0.87	1.21	0.93	0.75	1.15	0.74	0.54	1.01	0.76	0.54	1.07	0.76	0.54	1.07
Si	0.99	0.85	1.16	0.87	0.71	1.06	0.92	0.73	1.16	0.98	0.76	1.26	0.99	0.76	1.30
Zn	0.99	0.89	1.11	0.98	0.85	1.14	0.90	0.74	1.09	0.94	0.76	1.16	0.93	0.75	1.14

[a]Model 1: $PM_{10-2.5}$ (Cu, P, Si, or Zn) + age, sex, and race/ethnicity;

Model 2: Model 2 + BMI, smoke exposure, physical activity, education, dietary sodium, calcium, fiber, diabetes, HDL-C, and triglycerides;

Model 3: Model 2 + study sites;

Model 4: Model 3 + $PM_{2.5}$

Model 5: Model 3 + $PM_{10-2.5}$

[b]95% confidence interval

3.4 Discussion

In this population-based prospective study, we failed to find evidence that long-term exposure to $PM_{10-2.5}$ and four key chemical components were associated with prevalent or incident hypertension over a seven-year follow-up period. In models that were not controlled for study site, there was a decreased prevalence of hypertension with $PM_{10-2.5}$ mass, silicon, and zinc, whereas long-term exposure to phosphorous was positively associated with the prevalence of hypertension. However, these associations were not statistically significant after further adjustment for site and other air pollutants. In addition, higher long-term exposures to $PM_{10-2.5}$ and its chemical components were associated with lower risks of incident hypertension during the follow-up period though none of these associations were statistically different from no association.

To our knowledge, this is the first study to examine associations of long-term $PM_{10-2.5}$ and its chemical composition with the prevalence and the incidence of hypertension. Although we found no evidence of an association, this work is from a high quality population-based cohort with repeated blood pressure measurements and detailed information on time-varying potential confounders. Since $PM_{10-2.5}$ are more spatially heterogeneous than $PM_{2.5}$ due to shorter residence time in the atmosphere, a major advantage of our study is that extensive air pollution monitoring and land-use regression models specific to this project provided better long-term concentrations of coarse PM at each subject's home location. This substantially improves on previous epidemiology studies, which have relied solely on the limited spatial information from regulatory monitors. In addition, chemical composition data were available, allowing us to explore the differential effects of several air pollution sources on hypertension outcomes. Specifically, we examined the effects of composition chemicals of $PM_{10-2.5}$ including phosphorous, silicon, copper, and zinc from fertilized soil, windblown soil, brake wear, and tire wear, respectively on the development of hypertension. With suggestive results of positive relations for phosphorous with the prevalence of hypertension but inverse associations with copper, silicon, and zinc, our findings may provide supportive evidence that exposure to different sources may have differential impacts on cardiovascular outcomes, in this case hypertension.

Only one other study has investigated associations between $PM_{10-2.5}$ and blood pressure. Ebelt et al. conducted a panel study in Vancouver, British Columbia to investigate the relative impact of ambient and non-ambient exposures to $PM_{2.5}$, PM_{10}, and $PM_{10-2.5}$ on various health outcomes including blood pressure changes. Results showed that decreased SBP was associated with ambient exposures to each PM size fraction[65].

In spite of our null findings, there was reason to hypothesize that these associations could be important since inhalation of PM is thought to promote oxidative stress and inflammatory responses, which could trigger endothelial dysfunction and elevated blood pressure[11,12]. This pathway may be especially important for $PM_{10-2.5}$ since these particles are enriched in endotoxin as compared to $PM_{2.5}$ and endotoxin has been linked to *in vitro* cytokine production and promotion of inflammatory response. In fact, a toxicological study conducted by Becker et al. showed that human lung macrophages were more likely to be stimulated to produce inflammatory responses by $PM_{10-2.5}$ than by $PM_{2.5}$, and that it was related to bacterial endotoxin content[66]. Not all studies show clear links between $PM_{10-2.5}$ and inflammation in humans, however. Delfino et al. reported that 24-hour mean mass concentrations of $PM_{10-2.5}$ were not associated with plasma C-reactive protein, a biomarker of systemic inflammation, among elderly subjects with a history of coronary artery disease living in the Los Angeles, California[67].

In our study, we did not see evidence of increasing $PM_{10-2.5}$ concentrations with increasing prevalent or incident of hypertension. Two sources of bias are plausibly important factors which may have contributed to our findings. First, the MESA cohort was restricted to middle-aged and elderly population without any clinical cardiovascular diseases at enrollment. This could result in a far healthier sample of the population than the general population and a selection of individuals who were insensitive to the influences of air pollution on cardiovascular disease. Secondly, attrition bias usually caused by loss to follow-up due to death, withdraw or nonresponse in the longitudinal study if it regards to both the risk factor and the outcome[56]. This selective attrition could be an important concern in our study if those who remain in the study are healthier and have different air pollution levels than those who drop out.

3.5 Conclusions

Results from this study indicated that long-term exposure to $PM_{10-2.5}$ was inversely associated with the prevalence of hypertension before adjustment for study site, whereas it was not associated with the incidence of hypertension. Phosphorus, one composition chemical of coarse particles, was positively associated with the prevalence of hypertension before adjustment for study site. Our results suggested that different composition chemicals of coarse PM with different characteristics from different sources may have differential effects on the onset of hypertension. Further epidemiological study and animal and human experiments are needed to clarify relations between exposure to coarse PM and its constituents and changes in blood pressure and the chronic development of hypertension.

CHAPTER IV

Air Pollution and Walking

4.1 Introduction

Previous studies have clearly indicated that participating in regular physical activity is beneficial to both physical and mental health, including lowering risks of mortality, obesity, cardiovascular diseases, type 2 diabetes, metabolic syndrome, and some cancers as well as improving mental health and mood[25]. Despite the known health benefits of physical activity, about one third of U.S. adults failed to meet minimum levels of physical activity as defined by the 2008 guidelines[24]. In addition, many individuals who exercise do so in environments that can be detrimental to health for reasons such as safety or exposure to environmental hazards.

Since exposure to traffic-related air pollution including fine particulate matter ($PM_{2.5}$) and oxides of nitrogen (NO_x) has been associated with adverse cardiovascular and respiratory health, [16,68] the health benefits of physical activity may be detracted from and even adverse health effects may occur, when doing outdoor physical activities in neighborhoods with high ambient air pollution concentrations. Given this issue, the 2008 Physical Activity Guidelines for Americans indicated that people should modify the location or time of exercise to reduce adverse health risks of air pollution exposure, specifically by exercising away from heavy traffic and industrial sites, especially during rush hour or times when pollution is known to be high[25]. However, questions remain about the balance between health benefits versus costs of walking in highly polluted environments[69].

An important, related issue addressed in the environmental justice literature is whether disadvantaged and vulnerable populations have a disproportionate exposure to and burden of harmful environmental conditions, including air pollution, and decreased opportunities for physical activity. More socially deprived neighborhoods, marked by a greater proportion of residents who have low income, low education level, and/or are people of color, are often more likely to have higher levels of traffic-related pollution[18,19]. These same individuals often live in areas with poor neighborhood safety, which has also been shown to serve as a barrier to regular physical activity[23,70]. In fact, people from certain racial groups (e.g., African Americans and Hispanics) and those who are socioeconomically disadvantaged (lower family income and education levels) are less likely to get recommended levels of physical activity and experience disproportionately higher rates of chronic diseases associated with physical inactivity[20-23].

A study in metropolitan Vancouver, British Columbia, Canada found that spatial patterns of ozone and nitrogen oxides (NO_x) concentrations and walkability scores were patterned by the income of the neighborhoods. This study indicated that walkable built environment characteristics can offer health benefits but may also come with health costs for people with different socioeconomic status when exposure to high air pollution exposure is considered[71]. Few studies have also explored how neighborhood air pollution levels may relate to walking environment and/or individual physical activities[71-74]. Lawrence et al. found that neighborhoods with better indices of walkability were characterized by increased time spent in physically active travel, fewer grams of NO_x and volatile organic compounds emitted and decreased levels of ambient air pollution[75]. Holmes et al. also showed that changes in trail use could vary with air quality and suggested that reducing levels of outdoor air pollution will likely lead to an increase in physical activity[76]. However, more needs to be understood about how neighborhood air pollution level is correlated with people's walking activities.

A principal limitation from previous studies is the ability to simultaneously access neighborhood-scale air pollution and walkability data and reported individual walking activity. The present study is carried out in the context of the Multi-Ethnic Study of Atherosclerosis (MESA), which allows linkage of data on neighborhood walkability and actual reported walking time of MESA participants with concurrent measures of air pollution concentrations in six communities in the U.S. This manuscript addresses three different aims: first, we explore spatial distributions and spatial intersections of air pollution and a walkability index to characterize "sweet spots" (low air pollution, high walkability) and "sour spots" (high air pollution, low walkability) in the six MESA communities. Then, we explore the associations between neighborhood social advantages with the odds of being sweet-spot neighborhoods at census block group scale. Finally, we examine how and if neighborhood walkability and air pollution level are independently and/or jointly associated with different types of personal walking activities among MESA participants.

4.2 Material and Methods

4.2.1 Data

4.2.1.1 Study Region and Population

The regions for investigating the spatial distributions of neighborhood sweet and sour spots corresponded to the six major U.S. metropolitan areas of the MESA cohort: Los Angeles, CA; New York, NY; Chicago, IL; Minneapolis-St. Paul, MN; Winston-Salem, NC; and Baltimore, MD. MESA is a longitudinal study of progression of cardiovascular disease among adults aged 45–84 years in six communities in the U.S. MESA participants were recruited between July 2000 and September 2002 and were free of clinical cardiovascular disease at baseline[44]. The study was approved by the relevant Institutional Review Boards and all participants gave written informed consent. Analyses are conducted for the MESA participants for whom air pollution, walking activity, and other covariate data were complete at Exam 5, occurring between 2010 and 2012.

4.2.1.2 Walkability index

Walk score is a measure of "walkability" created by Walk Score Research Services (http://www.walkscore.com/, Front Seat Management, LLC) that combines the distances to a number of different destinations (grocery, restaurants, shopping, coffee, banks, parks, schools, books, entertainment) and is weighted based on pedestrian-friendly street characteristics (intersection density, block length). We purchased 9,915 lattice points of Walk Score data that covered geographic space across the six MESA communities as well as at all participant residential addresses at Exam 5 (n=3,661). These measurements were both reflective of walkability in 2012. To generate a gradient map of neighborhood walk score in each community, we conducted spatial interpolation using kriging in ArcGIS v9.3.1 (ESRI, Redlands, CA).

4.2.1.3 Walking Activity

We used cross-sectional measurements of walking activities for each participant reported at

Exam 5. Walking activity data was collected using a self-administered questionnaire adapted from the Cross-Cultural Activity Participation Study, which included reports of all forms of physical activity, including leisure, household, work, and transportation activities[77,78]. Time spent in minutes on walking for transport (e.g., walking to get places such as to the bus, work, or store) and for leisure (e.g., walking for exercise, pleasure, social reasons, during work breaks, walking the dog) were reported independent of their location for a typical week in the past month preceding their clinical examination. Walking time for transport, walking time for leisure, and total walking time (the sum of walking time for transport and leisure) were used as dependent variables in different models separately. Based on previous research in this cohort[79], we examined this variable as an ordinal variable by categorizing each type of walking into three levels for each study site: no walking, walking time less than the median of non-zero data in the specific city, and walking time greater than or equal to the median of non-zero data in the specific city.

4.2.1.4 Air Pollution Exposure

Concentrations of $PM_{2.5}$ and NO_x were predicted at the homes and in the communities of the MESA participants using a spatio-temporal modeling methodology developed by the MESA and Air Pollution study (MESA Air)[45,46,80]. These models utilized two-week average concentrations of $PM_{2.5}$ and NO_x collected from the Environmental Protection Agency's (EPA's) Air Quality System (AQS) repository of ambient monitoring data and supplemental monitoring stations specific to this project. We assigned the annual average of the air pollution concentration for the year 2012 at all lattice points falling within each census block group as an approximation of subjects' neighborhood air pollution exposures. In addition, since reported walking activities were for a typical week in the past month, one-month average $PM_{2.5}$ and NO_x concentrations prior to Exam 5 were estimated for each subject at their home residence. .

4.2.1.5 Sweet Spot and Sour Spot Covariates

To understand the co-occurrence of walkability and air pollution, we categorized both the census block groups and the individual participant addresses into two levels by the site-specific median of air pollution concentrations and walk score in each study site: low level (< median) and high level (≥ median). A census block group having a low air pollution level and a high walk score level was assigned as a "sweet-spot" whereas a block group having a high air pollution level and low walk score level was classified as a "sour spot".

4.2.1.6 Social Disadvantage Covariates

Neighborhood demographic and socioeconomic characteristics data at the census block groups scale were obtained from the data product published for the American Community Survey (ACS), conducted by the U.S. Census Bureau[30]. We used the 2006-2010 ACS five-year estimates for legal areas which are based on boundaries reported to the Census Bureau as of January 1, 2010. We then evaluated the following covariates for each census block group in the analysis of the association with higher probability of being a sweet- or sour-spot census block groups: 1) percentage of total population who meet the U.S. EPA Office of Environmental Justice's definition of minority of race, i.e., Hispanics, Asian-Americans, and Pacific Islanders, African-Americans, and American Indians and Alaskan Natives; 2) percentage of population 25 years and over with less than high school education; and 3) proportion of population living below the poverty line.

4.2.1.7 Other Covariates

Person-level data on variables including age, gender, body mass index, asthma status, and emphysema or chronic obstructive pulmonary disease (COPD) were also collected at MESA Exam 5. These covariates were selected a priori as potential confounders based on the previously reported associations with walking activity. Neighborhood safety score data was collected via telephone questionnaire through an ancillary study[81]. Respondents indicated agreement with three items using a five-point Likert scale: 1) I feel safe walking in my neighborhood, day or night; 2) violence is not a problem in my neighborhood; and 3) my neighborhood is safe from crime. These individual survey responses were then aggregated to estimate the perceived safety for the neighborhoods within a mile of the MESA participants' homes. Neighborhoods with higher safety scores are considered "safer" neighborhoods.

4.2.2 Analysis

First, we generated a thematic map to illustrate spatial distributions of sweet and sour spots in each study site. For this purpose, we interpolated predicted values for cells in a raster by kriging from predicted air pollution and walk score data points with the same latitude and longitude. We then reclassified the air pollution and walk scores into two levels (low and high) defined as above and below the site-specific median value for each grid cell. Finally, we overlaid the categorized air pollution level raster and walk score level raster to create a sweet- and sour-spot map. All geographical procedures were done using geographic information system (GIS) mapping software (ArcGIS; ESRI, Redlands, CA, USA).

After we created the grid cell raster-scale map, we evaluated the census-block group level air pollution concentrations and walk scores created by averaging all lattice point data within each block group. Spearman correlations between the air pollution concentrations and the walk scores at the census block group were calculated by study site. Next, we characterized the distributions of neighborhood air pollution concentrations, walk score, race/ethnicity and socioeconomic status (SES) at census block group level by study sites. Descriptive statistics were also computed for participants' personal characteristics, air pollution levels, and walk score near their residences by three levels of walking time for each walking activity by MESA site. Multinomial logistic regression models were then constructed to investigate % of minority race, % of population over 25 years with less than a high school education, and % below poverty line at the census block group level, individually and then together, as predictors of the census block group sweet/sour spot indicators. The above statistical analyses were stratified by study site.

Multinomial logistic regression models were then constructed to investigate the associations between each MESA participant's walking activity for leisure and transportation with air pollution and walk score at their home addresses before and/or after adjustment for other characteristics, including age, gender, race/ethnicity, body mass index, income, education, asthma status, emphysema or COPD, safety, and study site. Models also included adjustment for season since the pollution and walking data were resolved to a one-month time frame and this may introduce confounding by seasonality. In addition, we examined all associations stratified by study sites. In secondary analysis, we examined joint effects of air pollutants and walk score on each walking activity outcome by adding interaction terms in the model. We also included both $PM_{2.5}$ and NO_x in the same model and explored the possible heterogeneity in associations between air pollution and walking activity by participant's health status (asthma and COPD). All statistical analyses were performed using SAS statistical package (version 9.3; SAS Institute, Cary, North Carolina).

4.2.3 Results

Demographic and clinical characteristics for the entire MESA sample, grouped by walking activity levels are presented in **Table IV-1**. The mean age of study participants in 2010-2012 was 69.7 years and just more than half of the sample (53.8%) was female. The composition of non-Hispanic whites, non-Hispanic blacks, Hispanics, and Chinese in our samples is 40.6%, 27.5%, 19.8%, and 12.1% of participants, respectively. Participants who reported higher levels of walking for transport were more likely to be younger, female, white, more highly educated, with higher family income, and living in a neighborhood with: lower safety score; higher walk score; and higher $PM_{2.5}$ and NO_x concentrations. Participants reporting higher levels of walking for leisure were more likely to be younger, male, white, with lower BMI, higher education levels, higher family incomes, and living in a neighborhood with: higher safety score and lower $PM_{2.5}$ and NO_x concentrations.

Sweet spot and sour spots

The summary statistics of air pollution concentrations, walk scores, social disadvantages, and sweet and sour spots at the census bock group scale in different study sites are presented in **Table IV-2**. In total, we included 4,826 census block groups with one or more lattice points with data on air pollution and walk score in the analysis across six study sites. Overall means of $PM_{2.5}$ and NO_x concentrations were 11.1 μg/m^3 and 28.9 ppb, respectively. $PM_{2.5}$ concentrations ranged from 9.2 μg/m^3 in St. Paul to 11.8 μg/m^3 in Chicago, and NO_x concentrations ranged from 12.6 μg/m^3 in Forsyth County to 43.7 μg/m^3 in New York City. The highest average percentage of minority of race (59.6%) and proportion of population living below the poverty line (20.2%) were in Chicago and the highest average proportion with less than a high school education (23.8%) was in Los Angeles.

In **Figure IV-1** to **Figure IV-12,** the spatial distributions of sweet spots and sour spots based on $PM_{2.5}$ and NO_x were quite different within most study sites but similar spatial distribution patterns were found in Los Angeles and New York City. In **Table IV-2**, we found that both $PM_{2.5}$-walkscore and NO_x-walk score correlations were positive and strong in New York City. In Chicago, we found the highest prevalence of sweet- and sour-spot census block groups based on the $PM_{2.5}$ level and walk score level, and the only negative $PM_{2.5}$-walkscore correlation. In Los Angeles, both $PM_{2.5}$-walkscore and NO_x-walk score correlations were positive and weak, and the prevalence of sweet- and sour-spot census block groups based on the NO_x level and walk score level were the highest.

Results from univariate and multivariate analyses of associations of sweet spot census block groups with social disadvantage, stratified by study sites, are shown in **Table IV-3a and Table IV-3b.** We found inconsistent associations between minority of race and sweet-spots at the census block group level among different study sites. Negative associations between a neighborhood having higher proportion of people of minority of race and being a sweet-spot (low $PM_{2.5}$/NO_x level and high walk score level) compared to being a sour-spot were found in Chicago and Los Angeles, whereas positive associations were found in Baltimore. In contrast, lower odds of being a sweet-spot neighborhood were consistently associated with higher proportion of people having less than a high school education in most study sites. In addition, we found negative associations between neighborhoods with a greater proportion of population living below the poverty line and being a sweet-spot neighborhood in univariate analysis, but the associations turned inverse after adjustment for all other social disadvantage characteristics in some study sites, e.g., Los Angeles.

MESA participant analysis: Walking for transport

Adjusted associations of the one-month averages of $PM_{2.5}$ and NO_x prior to MESA Exam 5, and walk score with walking for transport are shown in **Table IV-4a**. A higher walk score was associated with higher levels of walking for transport even after adjustment for all covariates and air pollutants. While $PM_{2.5}$ was not associated with walking for transport, lower levels of NO_x were associated with higher levels of walking for transport, but significant associations were attenuated towards null after adjustment for other confounders. In sensitivity analyses for heterogeneity by selected covariates, the walk score-by-site interaction term was statistically significant in the model which included $PM_{2.5}$, walk score, and other confounders. Patterns of positive associations between walk score and walking for transport were generally consistent in different study sites, with dose-response relationships across all sites and significantly positive associations in Baltimore, Chicago, and New York (**Table IV-4b**).

MESA participant analysis: Walking for leisure

Higher $PM_{2.5}$ concentrations were negatively associated with higher levels of walking for leisure after adjustment for other confounders as well as NO_x levels (**Table IV-4a**). In addition, we found that higher walk score was positively associated with higher odds of having the highest level of walking for leisure compared to no walking after adjustment for $PM_{2.5}$, NO_x, and all other confounders. In sensitivity analyses for heterogeneity by selected covariates, walk score-by-$PM_{2.5}$ and $PM_{2.5}$-by-asthma interaction terms were significant. After stratifying by categorical $PM_{2.5}$ level, the positive association between walk score and the most walking for leisure was slightly stronger in the higher $PM_{2.5}$ group than that in the lower group, but associations were not statistically significant in either group. After stratifying by asthma status, $PM_{2.5}$ was negatively associated with higher levels of walking for leisure among participants without asthma, while associations were positive among participants with asthma. After stratification by study sites, we found that higher level $PM_{2.5}$ exposure was negatively associated with higher level of walking for leisure in Forsyth County and St. Paul. We also found negative associations between NO_x with walking for leisure in Forsyth County. In addition, we only found a positive association between walk score and walking for leisure in Baltimore (**Table IV-4c**).

Table IV-1. Distributions of participants' selected characteristics by walking activity levels; MESA 2010

		Walking for transport (minutes/week)			Walking for leisure (minutes/week)		
	Total	**Level 1[a]**	**Level 2**	**Level 3**	**Level 1**	**Level 2**	**Level 3**
n	3661	781	1409	1471	1320	1139	1220
Age, years	69.7 (9.4)[b]	70.7 (9.6)	69.9 (9.4)	68.9 (9.1)	71.2 (9.5)	68.7 (9.4)	69.0 (9.0)
Female (%)	53.8	50.1	52.5	56.7	58.3	52	50.5
Race/ethnicity (%)							
non-Hispanic white	40.6	34.6	41.1	43.4	35.5	41.9	45.0
Chinese	12.1	11.8	14.9	9.6	9.6	13.2	13.9
non-Hispanic black	27.5	27.8	26.1	28.6	29.7	26.6	25.8
Hispanic	19.8	25.9	18	18.4	25.2	18.4	15.3
BMI[c], kg/m^2	28.4 (5.7)	28.8 (5.8)	28.20 (5.6)	28.5 (5.7)	29.2 (6.1)	28.3 (5.4)	27.7 (5.3)
Education (%)							
High-school degree or under	31.4	37.1	31.9	27.8	39.9	28.4	25.0
Some college or associate degree	28.7	29.2	26.3	30.6	28.9	27.8	29.2
Bachelor degree or higher	40.0	33.7	41.7	41.6	31.3	43.8	45.8
Income (%)							
< $30,000	32.5	38.4	32.8	29.0	39.5	29.1	28.1
$30,000 to $75,000	39.4	37.8	38.2	41.4	39.3	39.8	39.1
> $75,000	28.1	23.8	29.0	29.6	21.2	31.2	32.8
Study site (%)							
Forsyth County, NC	16.7	21.5	15.8	15.2	15.4	18.1	17.0
New York City, NY	18.0	6.3	21.4	20.9	19.4	17.6	16.9
Baltimore, MD	14.3	15.2	13.3	14.7	16.3	13.3	13.1
St. Paul, MN	14.6	17.3	14.0	13.7	14.9	14.1	14.7
Chicago, IL	19.5	11.4	21.7	21.8	16.0	20.5	22.4
Los Angeles, CA	16.9	28.3	13.8	13.8	18.1	16.5	16.0
Safety score, mean (s.d.)	3.7 (0.5)	3.7 (0.5)	3.6 (0.5)	3.6 (0.5)	3.6 (0.5)	3.7 (0.5)	3.7 (0.5)
Asthma (%)	3.3	2.8	3.6	3.1	3.9	2.8	2.9
Emphysema or COPD (%)	2.1	2.1	2.5	1.7	2.7	1.4	2.1
Walk score, mean (s.d.)	61.5 (27.3)	51.4 (24.0)	63.4 (27.0)	65.1 (27.8)	61.4 (26.0)	60.9 (27.7)	62.2 (28.1)
Air Pollution[d]							
$PM_{2.5}$, μg/m^3	10.8 (2.6)	10.5 (2.4)	11.0 (2.7)	10.8 (2.7)	11.0 (2.6)	10.7 (2.6)	10.8 (2.6)
NO_X, ppb	24.5 (17.8)	22.1 (17.1)	25.6 (18.7)	24.6 (17.2)	25.7 (18.0)	24.1 (18.1)	23.4 (17.3)

[a]Walking for transport and walking for leisure measures categorized into level 1: no walking; level 2: walking time < median of nonzero data; level 3: walking time ≥ median of nonzero data.

[b]Mean (standard deviation).

[c]Body mass index = weight in kilograms / (height in meters)^2.

[d]Annual average of air pollutants prior to MESA baseline exam.

Table IV-2. Social disadvantages, air pollution concentrations, walk score, and sweet and sour spots and correlations between air pollution and walk score at census block groups level by study sites; MESA 2010

	All six sites		Forsyth County, NC		New York City, NY		Baltimore, MD		St. Paul, MN		Chicago, IL		Los Angeles, CA	
n[a]	4,886		431		751		682		506		885		1,631	
Population characteristics	**Mean**	**s.d.[b]**	**Mean**	**s.d.**	**Mean**	**s.d.**	**Mean**	**s.d.**	**Mean**	**s.d.**	**Mean**	**s.d.**	**Mean**	**s.d.**
Minority of race (%)	47.2	31.4	39.6	30.4	49.3	32.9	48.5	36.0	25.5	21.8	59.4	35.4	47.9	24.5
< High school education (%)	19.0	17.1	13.5	11.9	20.3	16.8	15.3	13.6	10.8	11.2	19.4	14.7	23.8	20.5
Living below poverty line (%)	16.3	15.7	16.6	16.9	18.0	16.5	13.4	15.5	15.1	16.2	20.1	16.4	15.0	13.9
Air pollution[c]														
$PM_{2.5}$, $\mu g/m^3$	11.1	1.3	10.6	0.3	11.6	1.6	10.7	0.6	9.2	0.6	11.8	0.5	11.4	1.33
NO_x, ppb	28.8	13.8	12.6	5.5	42.6	17.6	19.0	7.3	18.0	5.0	26.7	6.3	35.3	9.5
Walk score	60.1	22.7	31.2	20.6	79.8	20.5	49.8	22.2	51.5	19.8	65.3	16.1	62.7	17.0
Sweet spot (%)														
Low $PM_{2.5}$ and high walkscore	22.4		17.6		13.5		21.0		21.3		28.5		25.3	
Low NO_X and high walkscore	19.1		10.4		13.7		16.0		14.0		22.6		25.0	
Sour spot (%)														
High $PM_{2.5}$ and low walkscore	20.3		17.6		8.8		18.3		20.8		27.3		23.3	
High NO_X and low walkscore	17.1		10.2		9.1		13.3		13.4		21.6		22.9	
Correlation coefficient[b]														
$PM_{2.5}$ and walk score	0.45193[d]	(<.0001)	0.413	(<.0001)	0.751	(<.0001)	0.404	(<.0001)	0.094	(0.035)	-0.073	(0.030)	0.112	(<.0001)
NO_x and walk score	0.595	(<.0001)	0.724	(<.0001)	0.755	(<.0001)	0.616	(<.0001)	0.640	(<.0001)	0.175	<.0001	0.106	(<.0001)

[a]Sample sizes of census block groups with one or more lattice points.

[b]Standard deviation.

[c]Annual average of air pollutants in 2010.

[d]Spearman's rank correlation coefficient (*P* Value).

Table IV-3a. Estimated odds ratio (95% CI) of being sweet spot (low $PM_{2.5}$ level and high walk score level) associated with social disadvantages at census block groups scale; MESA 2010

	Forsyth County, NC						New York City, NY						Baltimore, MD					
	Sweet Spot vs. Sour Spot						Sweet Spot vs. Sour Spot						Sweet Spot vs. Sour Spot					
Population Characteristic	Crude OR[a]	95% CI		Adjusted OR[b]	95% CI		Crude OR	95% CI		Adjusted OR	95% CI		Crude OR	95% CI		Adjusted OR	95% CI	
Minority of race	1.15	1.03	1.28	1.15	0.99	1.34	1.02	0.93	1.13	1.11	0.99	1.26	0.61	0.56	0.65	1.22	1.13	1.32
< High school education	1.17	0.89	1.54	0.85	0.58	1.27	0.85	0.72	1.01	0.65	0.49	0.85	0.91	0.75	1.10	0.71	0.55	0.91
Living below poverty line	1.23	0.99	1.52	1.12	0.82	1.54	0.99	0.83	1.18	1.24	0.95	1.62	1.05	0.88	1.25	1.02	0.82	1.27
	St. Paul, MN						**Chicago, IL**						**Los Angeles, CA**					
	Sweet Spot vs. Sour Spot						Sweet Spot vs. Sour Spot						Sweet Spot vs. Sour Spot					
Population Characteristic	Crude OR	95% CI		Adjusted OR	95% CI		Crude OR	95% CI		Adjusted OR	95% CI		Crude OR	95% CI		Adjusted OR	95% CI	
Minority of race	0.90	0.78	1.03	0.97	0.80	1.17	0.61	0.56	0.65	0.61	0.56	0.66	0.70	0.65	0.74	0.77	0.72	0.83
< High school education	0.69	0.52	0.92	0.63	0.43	0.92	0.74	0.65	0.84	0.90	0.77	1.05	0.59	0.55	0.65	0.59	0.53	0.66
Living below poverty line	0.97	0.80	1.17	1.18	0.92	1.51	0.59	0.52	0.67	1.01	0.86	1.19	0.73	0.65	0.81	1.29	1.12	1.49

[a]Model includes one of the population characteristics variables.

[b]Model includes all population characteristics variables.

Table IV-3b. Estimated odds ratio (95% CI) of being sweet spot (low NO_x level and high walk score level) associated with social disadvantages at census block groups scale; MESA 2010

	Forsyth County, NC Sweet Spot vs. Sour Spot						New York City, NY Sweet Spot vs. Sour Spot						Baltimore, MD Sweet Spot vs. Sour Spot					
Population Characteristic	Crude OR[a]	95% CI		Adjusted OR[b]	95% CI		Crude OR	95% CI		Adjusted OR	95% CI		Crude OR	95% CI		Adjusted OR	95% CI	
Minority of race	0.65	0.61	0.70	0.74	0.60	0.92	0.94	0.86	1.04	0.94	0.83	1.06	1.05	0.97	1.13	1.10	1.01	1.20
< High school education	0.50	0.33	0.77	0.56	0.32	1.00	0.96	0.81	1.13	1.01	0.77	1.32	0.79	0.64	0.98	0.73	0.56	0.96
Living below poverty line	0.81	0.62	1.05	1.45	0.99	2.13	0.96	0.81	1.14	1.01	0.78	1.31	0.91	0.76	1.09	0.98	0.78	1.23

	St. Paul, MN Sweet Spot vs. Sour Spot						Chicago, IL Sweet Spot vs. Sour Spot						Los Angeles, CA Sweet Spot vs. Sour Spot					
Population Characteristic	Crude OR	95% CI		Adjusted OR	95% CI		Crude OR	95% CI		Adjusted OR	95% CI		Crude OR	95% CI		Adjusted OR	95% CI	
Minority of race	0.86	0.71	1.03	1.09	0.85	1.40	0.70	0.65	0.75	0.70	0.65	0.77	0.65	0.61	0.70	0.74	0.69	0.79
< High school education	0.56	0.37	0.84	0.61	0.36	1.02	0.56	0.47	0.65	0.61	0.51	0.73	0.49	0.44	0.54	0.48	0.43	0.54
Living below poverty line	0.67	0.50	0.90	0.75	0.53	1.06	0.67	0.59	0.76	1.12	0.95	1.32	0.64	0.57	0.72	1.35	1.16	1.57

[a]Model includes one of the population characteristics variables.

[b]Model includes all population characteristics variables.

Table IV-4a. Estimated odds ratio (95% CI) of higher level of walking for transport and walking for leisure associated with per IQR unit increase in air pollution and walk score; MESA 2010

		Walking for Transport						Walking for Leisure					
		Level 2 vs. Level 1[b]			Level 3 vs. Level 1			Level 2 vs. Level 1			Level 3 vs. Level 1		
Exposure	Model number[a]	OR	95% CI		OR	95% CI		OR	95% CI		OR	95% CI	
$PM_{2.5}$	Model 1a	1.09	0.93	1.27	0.99	0.85	1.15	0.80	0.70	0.92	0.83	0.73	0.95
	Model 2a	1.03	0.86	1.23	0.95	0.80	1.14	0.77	0.66	0.90	0.85	0.73	0.99
	Model 3a	1.04	0.87	1.25	0.98	0.81	1.18	0.75	0.64	0.88	0.84	0.72	0.98
Walk score	Model 1a	1.17	1.13	1.21	1.20	1.16	1.24	1.01	0.98	1.04	1.02	0.99	1.05
	Model 2a	1.13	1.07	1.20	1.21	1.14	1.28	1.04	0.98	1.09	1.07	1.02	1.13
	Model 3a	1.13	1.07	1.20	1.22	1.15	1.29	1.03	0.98	1.09	1.07	1.01	1.12
NO_x	Model 1b	0.84	0.73	0.97	0.74	0.64	0.86	0.87	0.77	0.99	0.79	0.70	0.90
	Model 2b	0.97	0.78	1.19	0.88	0.71	1.09	1.02	0.86	1.23	0.99	0.83	1.19
	Model 3b	0.95	0.77	1.19	0.88	0.71	1.10	1.13	0.94	1.36	1.05	0.87	1.27
Walk score	Model 1b	1.21	1.16	1.26	1.26	1.21	1.32	1.02	0.98	1.06	1.05	1.01	1.09
	Model 2b	1.13	1.07	1.20	1.22	1.15	1.29	1.03	0.97	1.08	1.07	1.01	1.12
	Model 3b	1.13	1.07	1.20	1.22	1.15	1.29	1.03	0.98	1.09	1.07	1.01	1.12

[a]

Model 1a: $PM_{2.5}$ + Walk score + season;

Model 2a: Model 1 + age, gender, BMI, race, education, income, asthma, emphysema or COPD, neighborhood safety score, and site;

Model 3a: Model 2 + NO_x

Model 1b: NO_x + Walkscore + season;

Model 2b: Model 1 + age, gender, BMI, race, education, income, asthma, emphysema or COPD, neighborhood safety score, and site;

Model 3b: Model 2 + $PM_{2.5}$

[b]Walking for transport and walking for leisure measures categorized into level 1: no walking; level 2: walking time < median of nonzero data; level 3: walking time ≥ median of nonzero data.

Table IV-4b. Estimated odds ratio (95% CI) of higher level of walking for transport associated with per IQR unit increase in air pollution and walk score by study sites; MESA 2010

	Forsyth County, NC						New York City, NY						Baltimore, MD					
	Level 2 vs. Level 1[a]			Level 3 vs. Level 1			Level 2 vs. Level 1			Level 3 vs. Level 1			Level 2 vs. Level 1			Level 3 vs. Level 1		
	OR	95% CI		OR	95% CI		OR	95% CI		OR	95% CI		OR	95% CI		OR	95% CI	
Model 1[b]																		
$PM_{2.5}$	0.63	0.32	1.23	0.79	0.40	1.54	1.03	0.65	1.65	0.98	0.61	1.56	1.03	0.65	1.64	0.79	0.50	1.26
Walkscore	1.01	0.90	1.14	0.96	0.85	1.08	1.40	0.95	2.08	1.79	1.18	2.70	1.21	1.06	1.39	1.33	1.16	1.53
Model 2																		
NO_x	0.92	0.24	3.55	2.17	0.57	8.27	1.21	0.72	2.05	0.89	0.52	1.52	1.90	0.91	3.97	1.63	0.79	3.35
Walkscore	1.01	0.88	1.15	0.93	0.81	1.05	1.34	0.89	2.01	1.84	1.20	2.81	1.16	1.01	1.34	1.28	1.11	1.47

	St. Paul, MN						Chicago, IL						Los Angeles, CA					
	Level 2 vs. Level 1			Level 3 vs. Level 1			Level 2 vs. Level 1			Level 3 vs. Level 1			Level 2 vs. Level 1			Level 3 vs. Level 1		
	OR	95% CI		OR	95% CI		OR	95% CI		OR	95% CI		OR	95% CI		OR	95% CI	
Model 1[b]																		
$PM_{2.5}$	1.59	0.68	3.73	0.59	0.25	1.37	1.43	0.76	2.68	0.96	0.50	1.83	0.67	0.39	1.15	0.67	0.40	1.14
Walkscore	1.10	0.94	1.29	1.14	0.97	1.32	1.23	1.06	1.42	1.47	1.26	1.72	1.07	0.94	1.23	1.08	0.95	1.23
Model 2																		
NO_x	1.17	0.34	4.07	1.41	0.42	4.78	0.55	0.26	1.18	0.64	0.29	1.39	0.78	0.53	1.14	0.69	0.47	1.01
Walkscore	1.11	0.94	1.30	1.11	0.95	1.30	1.28	1.10	1.48	1.50	1.28	1.76	1.09	0.95	1.25	1.11	0.97	1.26

[a]Walking for transport measure was categorized into level 1: no walking; level 2: walking time < median of nonzero data; level 3: walking time ≥ median of nonzero data.

[b]

Model 1: $PM_{2.5}$ + walk score + season, age, gender, BMI, race, education, income, asthma, emphysema or COPD, and safety score.

Model 2: NO_x + walk score + season, age, gender, BMI, race, education, income, asthma, emphysema or COPD, and safety score.

Table IV-4c. Estimated odds ratio (95% CI) of higher level of walking for leisure associated with per IQR unit increase in air pollution and walk score by study sites; MESA 2010

	Forsyth County, NC						New York City, NY						Baltimore, MD					
	Level 2 vs. Level 1[a]			Level 3 vs. Level 1			Level 2 vs. Level 1			Level 3 vs. Level 1			Level 2 vs. Level 1			Level 3 vs. Level 1		
	OR	95% CI		OR	95% CI		OR	95% CI		OR	95% CI		OR	95% CI		OR	95% CI	
Model 1[b]																		
$PM_{2.5}$	0.48	0.25	0.93	0.46	0.24	0.90	0.79	0.60	1.06	0.88	0.66	1.18	0.80	0.53	1.23	1.13	0.75	1.72
Walkscore	1.01	0.89	1.13	1.01	0.90	1.14	1.14	0.86	1.50	1.15	0.86	1.54	0.98	0.87	1.11	1.16	1.03	1.31
Model 2																		
NO_x	0.41	0.11	1.48	0.18	0.04	0.72	1.13	0.82	1.56	1.18	0.85	1.64	0.98	0.53	1.82	0.98	0.54	1.76
Walkscore	1.05	0.81	1.37	1.06	0.93	1.21	1.09	0.60	1.97	1.06	0.79	1.43	0.95	0.72	1.24	1.17	1.03	1.33

	St. Paul, MN						Chicago, IL						Los Angeles, CA					
	Level 2 vs. Level 1			Level 3 vs. Level 1			Level 2 vs. Level 1			Level 3 vs. Level 1			Level 2 vs. Level 1			Level 3 vs. Level 1		
	OR	95% CI		OR	95% CI		OR	95% CI		OR	95% CI		OR	95% CI		OR	95% CI	
Model 1[b]																		
$PM_{2.5}$	0.74	0.33	1.68	0.30	0.13	0.71	0.67	0.41	1.11	0.83	0.52	1.33	1.05	0.63	1.74	0.81	0.48	1.37
Walkscore	0.95	0.82	1.11	0.93	0.80	1.08	1.07	0.94	1.21	1.10	0.97	1.25	1.03	0.91	1.17	1.08	0.94	1.23
Model 2																		
NO_x	1.10	0.35	3.48	0.49	0.15	1.61	0.99	0.51	1.91	1.06	0.56	2.01	0.89	0.62	1.28	0.85	0.58	1.25
Walkscore	0.89	0.65	1.23	0.94	0.80	1.09	1.12	0.85	1.47	1.10	0.96	1.25	1.08	0.83	1.41	1.09	0.95	1.24

[a] Walking for leisure measure was categorized into level 1: no walking; level 2: walking time < median of nonzero data; level 3: walking time ≥ median of nonzero data.

[b]

Model 1: $PM_{2.5}$ + walk score + season, age, gender, BMI, race, education, income, asthma, emphysema or COPD, and safety score.

Model 2: NO_x + walk score + season, age, gender, BMI, race, education, income, asthma, emphysema or COPD, and safety score.

Figure IV-1. Spatial distributions of sweet- and sour-spot neighborhoods for $PM_{2.5}$/walk score level in Los Angeles, California.

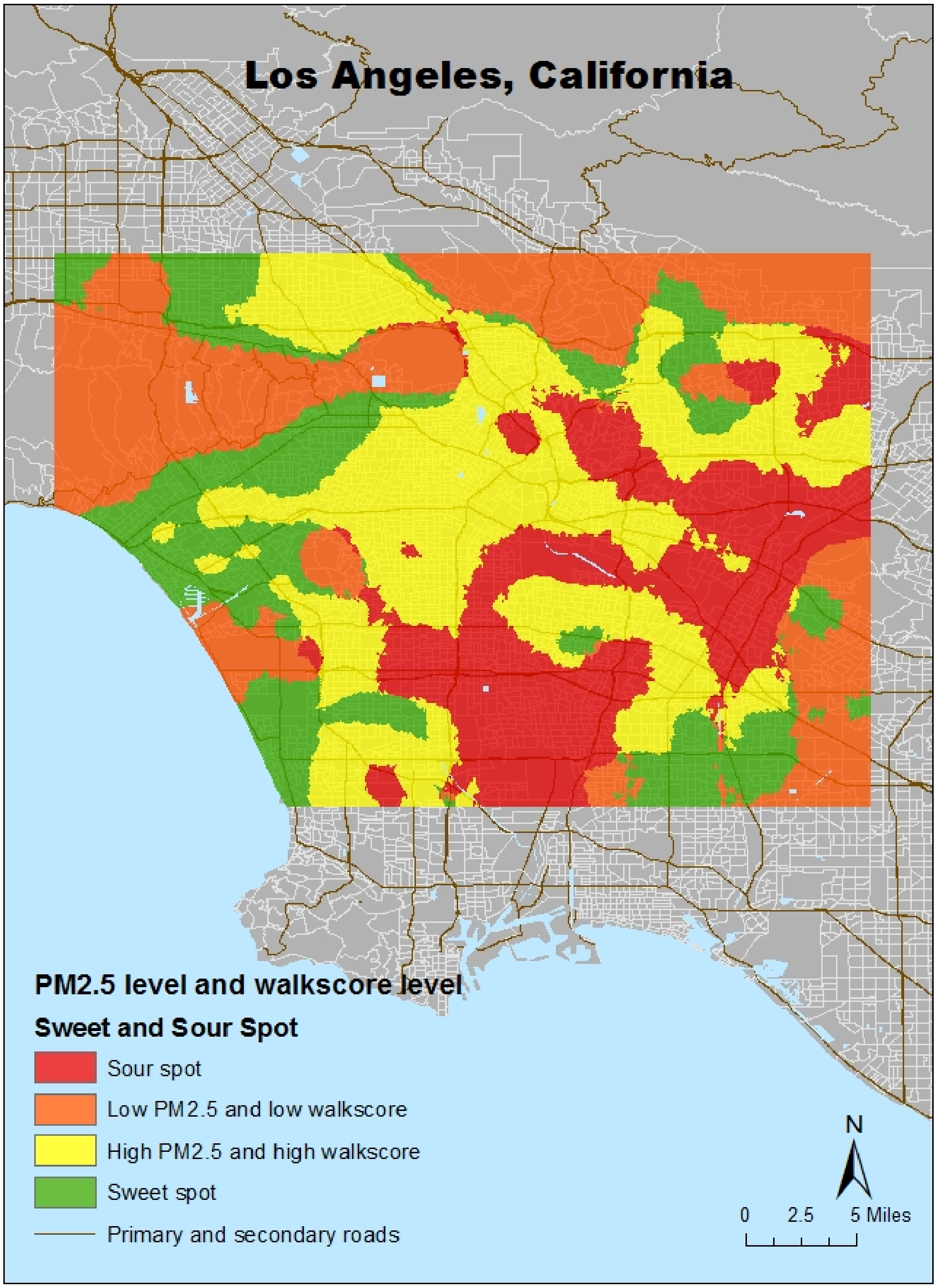


Figure IV-2. Spatial distributions of sweet- and sour-spot neighborhoods for NO_x/walk score level in Los Angeles, California.

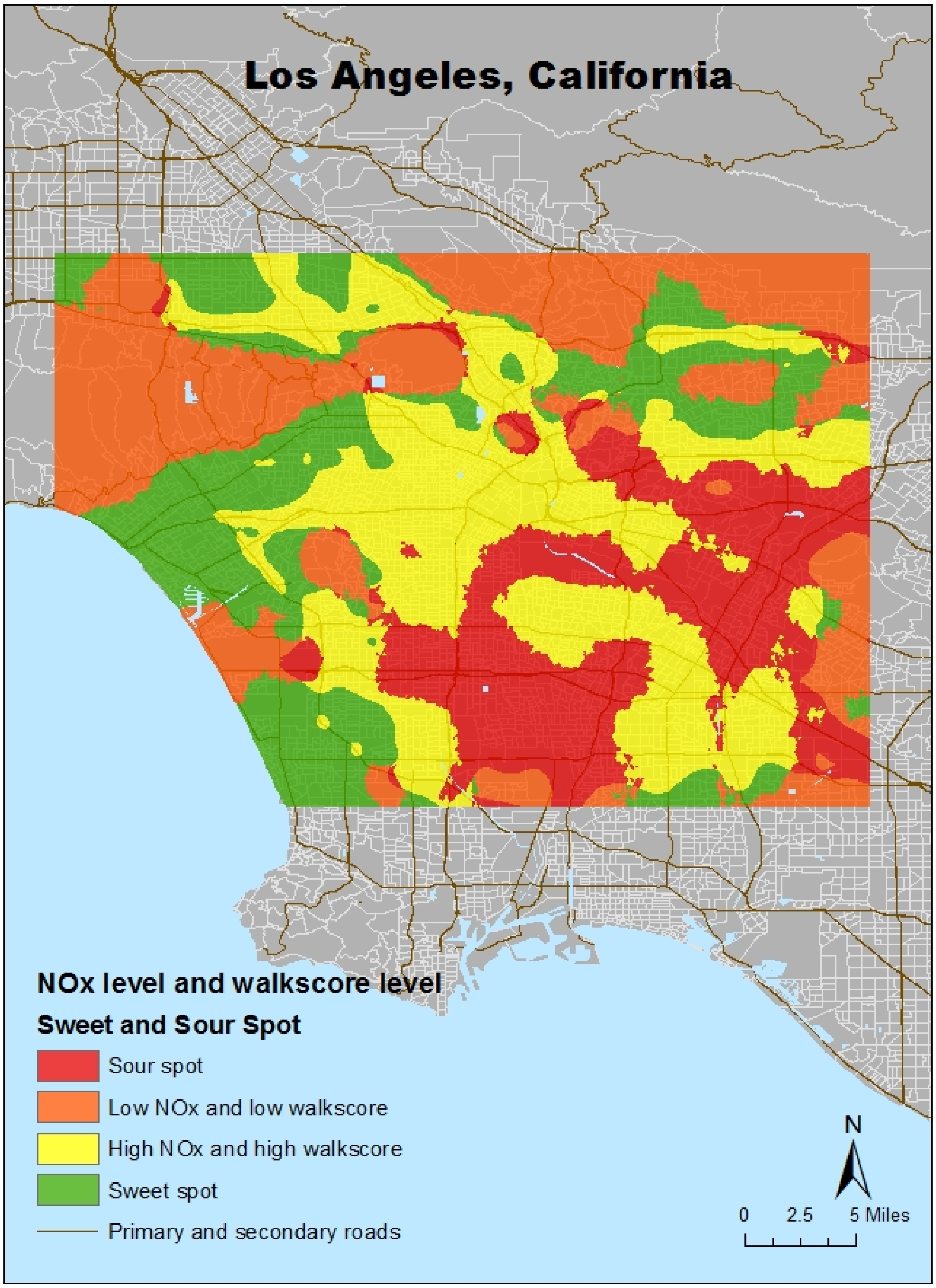


Figure IV-3. Spatial distributions of sweet- and sour-spot neighborhoods for $PM_{2.5}$/walk score level in Chicago, Illinois.

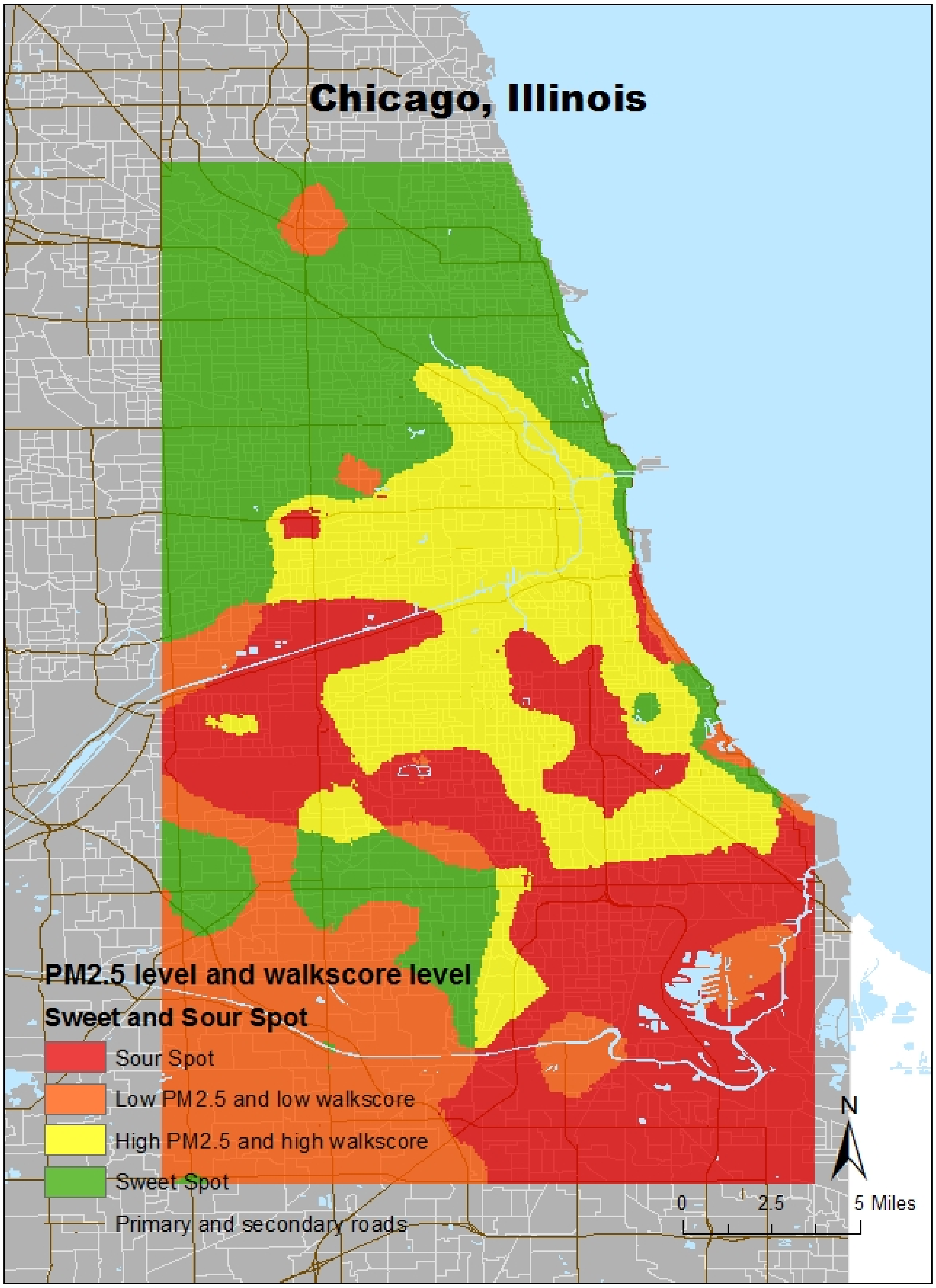


Figure IV-4. Spatial distributions of sweet- and sour-spot neighborhoods for NO_x/walk score level in Chicago, Illinois.

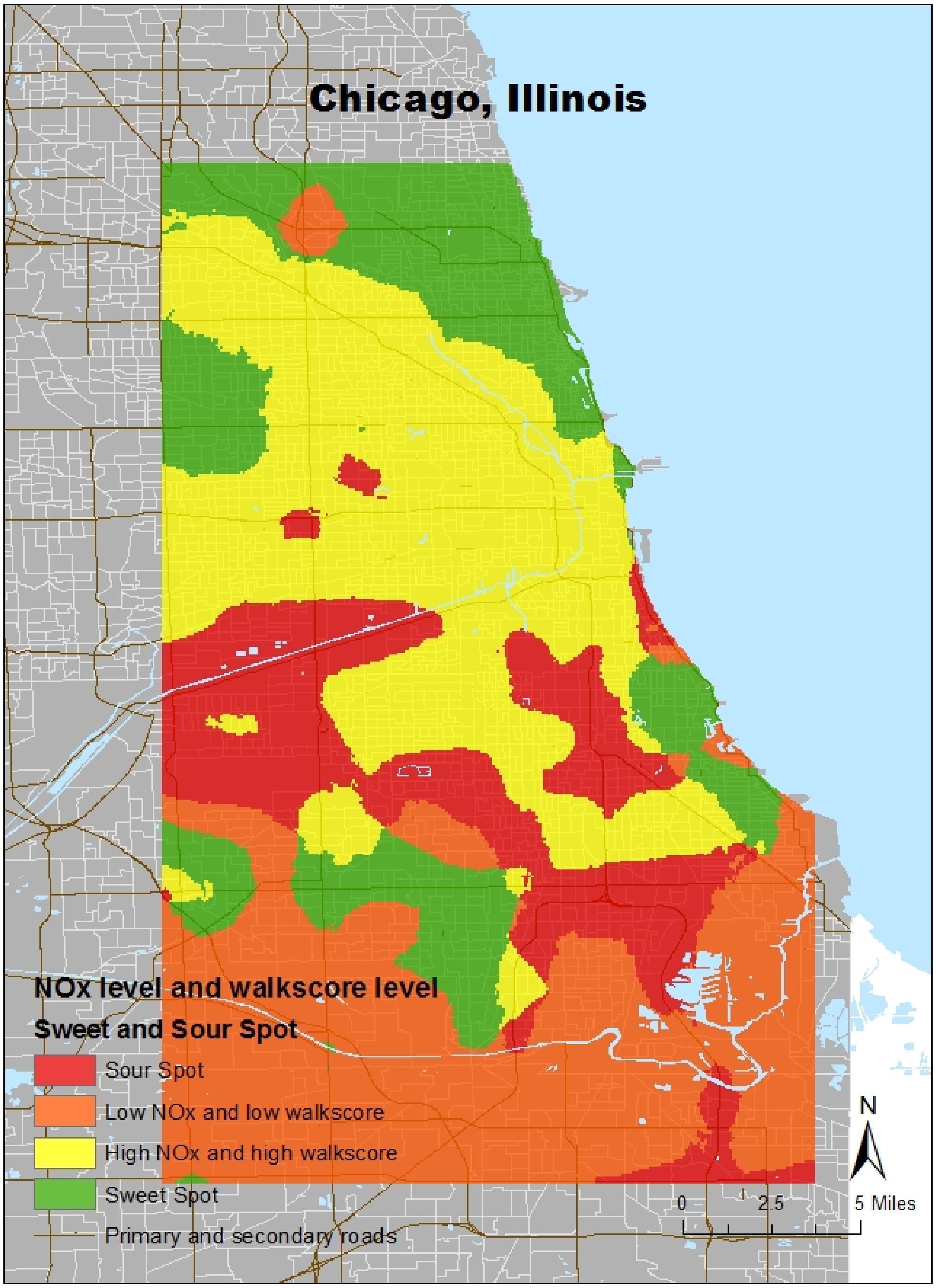


Figure IV-5. Spatial distributions of sweet- and sour-spot neighborhoods for $PM_{2.5}$/walk score level in Baltimore, Maryland.

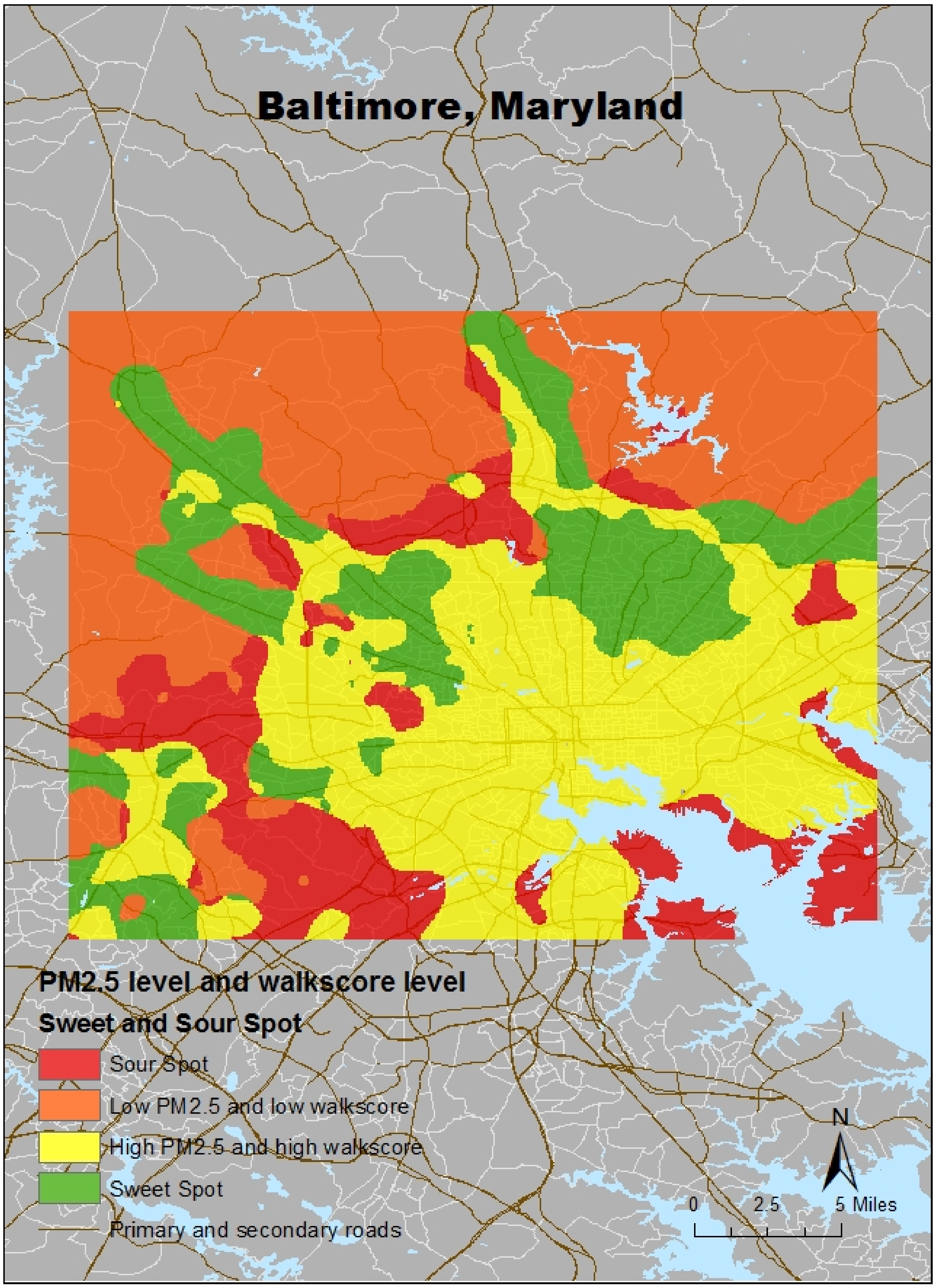


Figure IV-6. Spatial distributions of sweet- and sour-spot neighborhoods for NO_x/walk score level in Baltimore, Maryland.

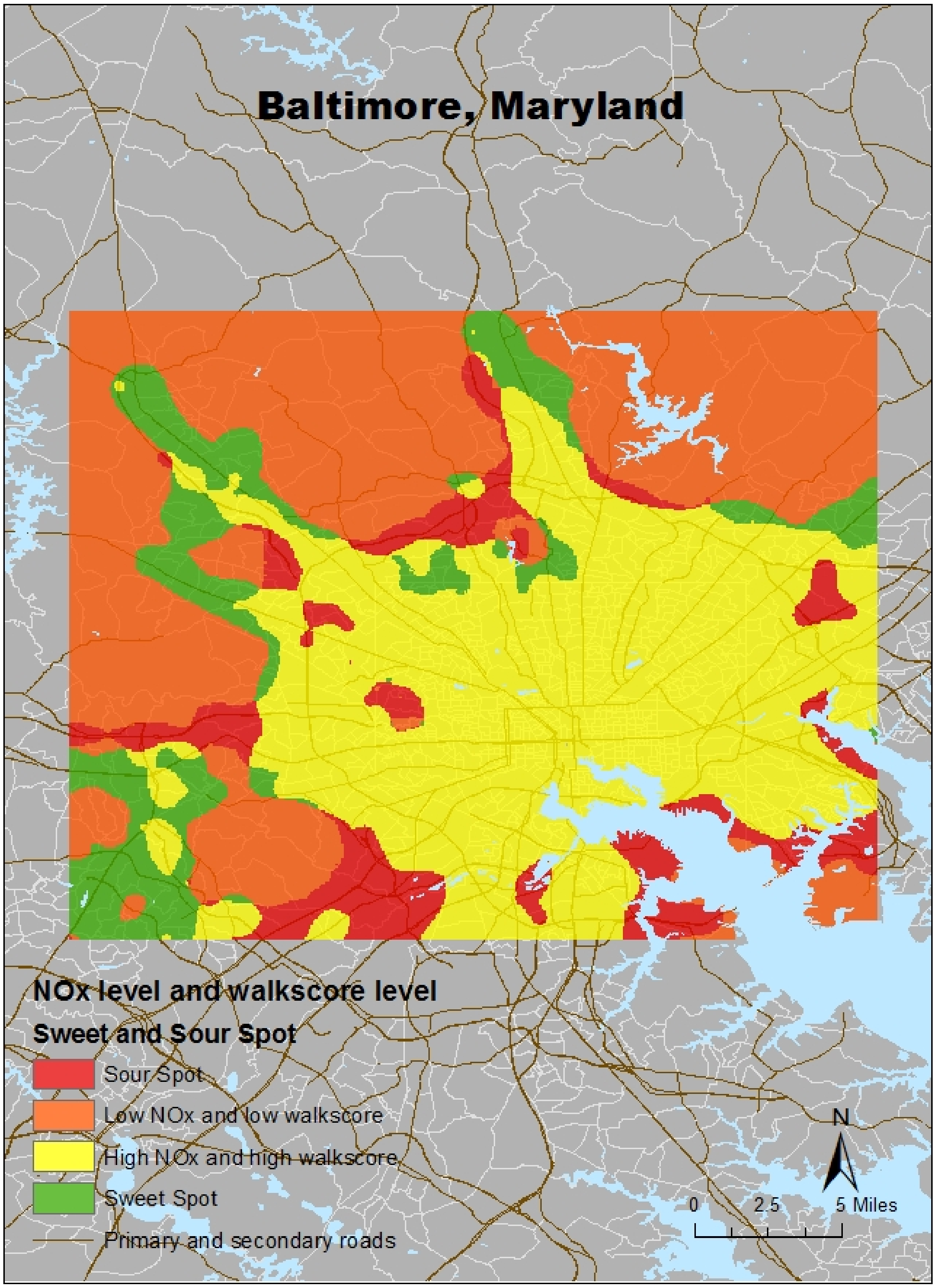


Figure IV-7. Spatial distributions of sweet- and sour-spot neighborhoods for $PM_{2.5}$ /walk score level in St. Paul, Minnesota.

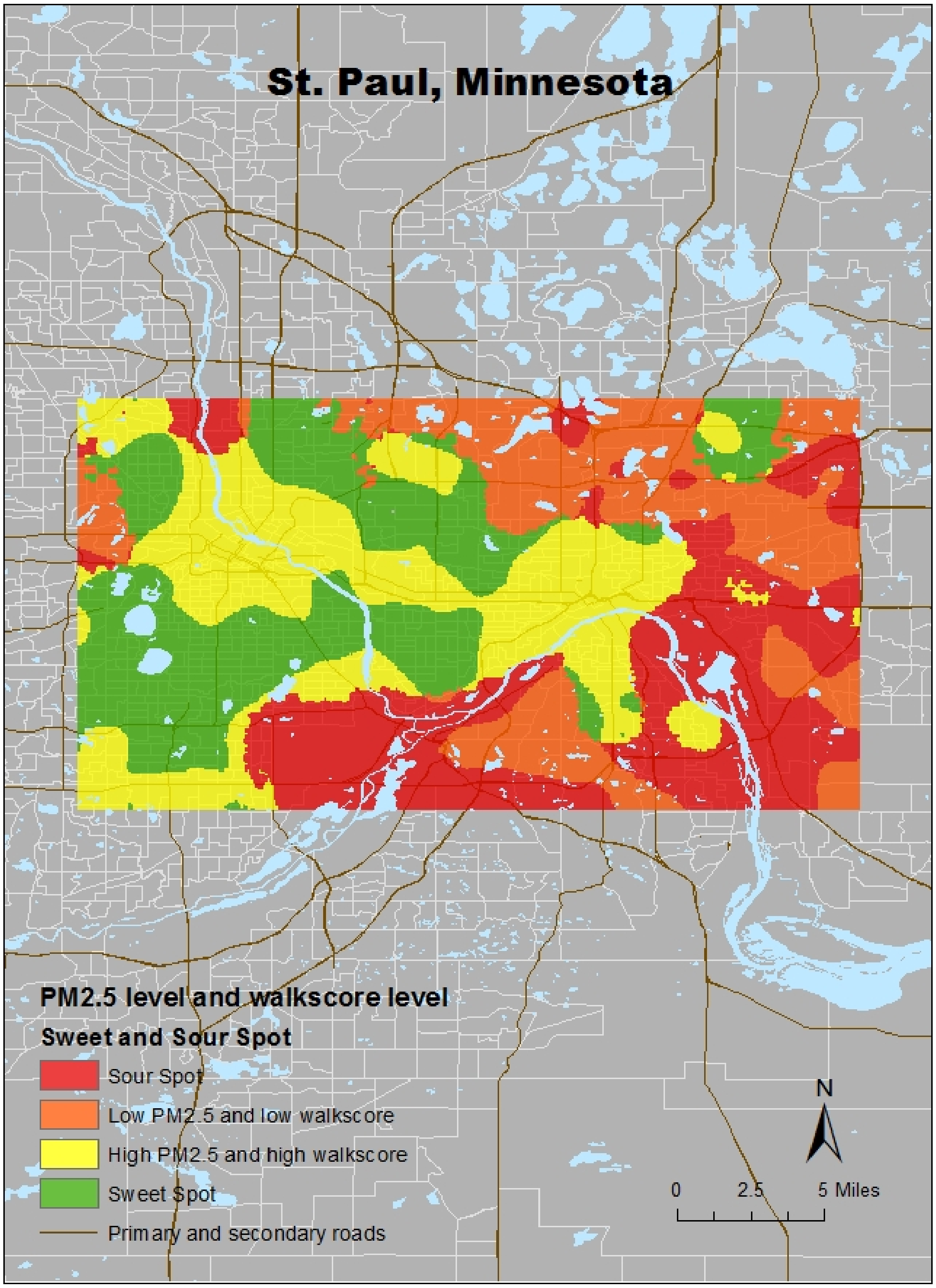


Figure IV-8. Spatial distributions of sweet- and sour-spot neighborhoods for NO_x/walk score level in St. Paul, Minnesota.

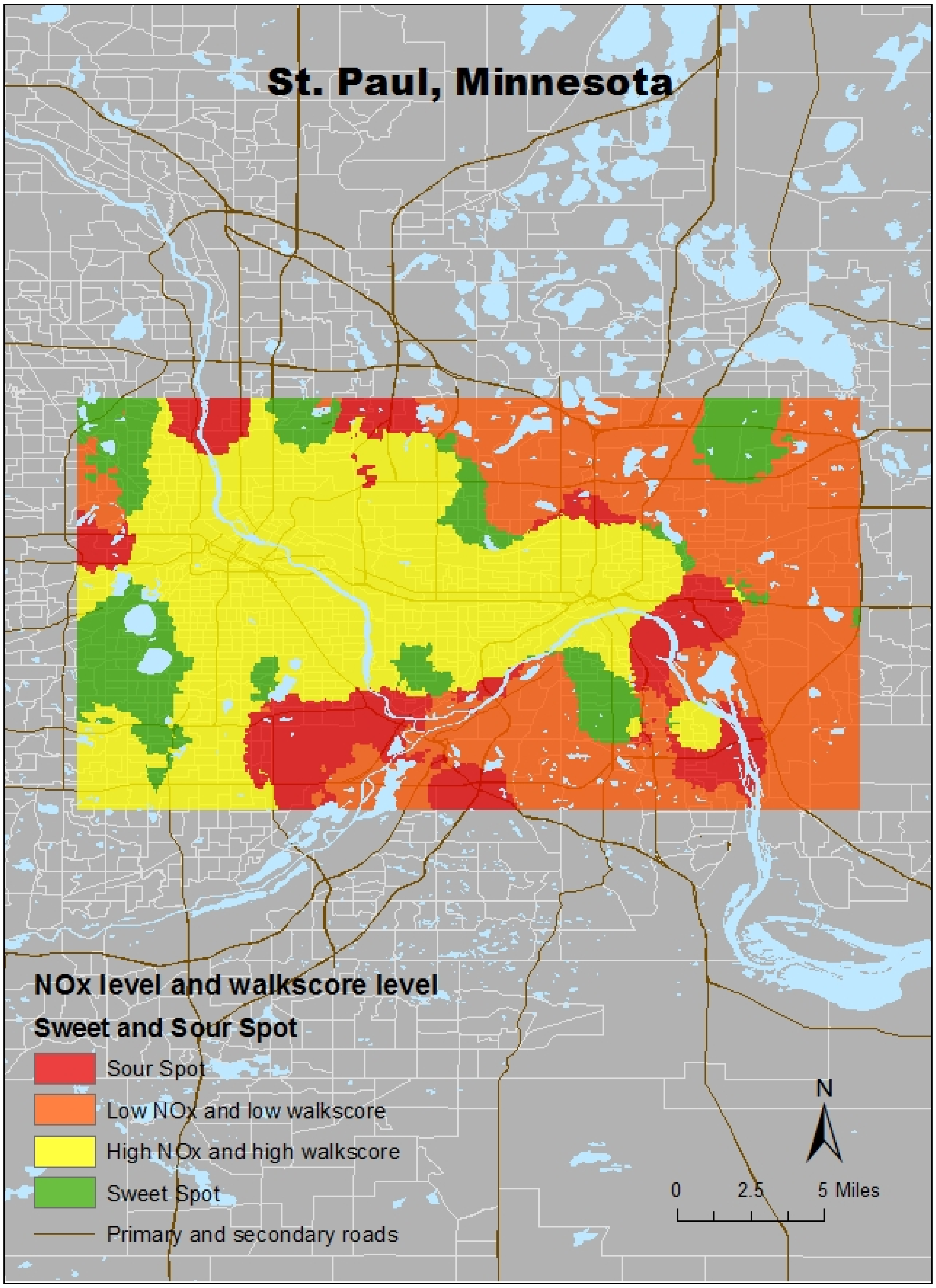


Figure IV-9. Spatial distributions of sweet- and sour-spot neighborhoods for $PM_{2.5}$/walk score level in Forsyth County, North Carolina.

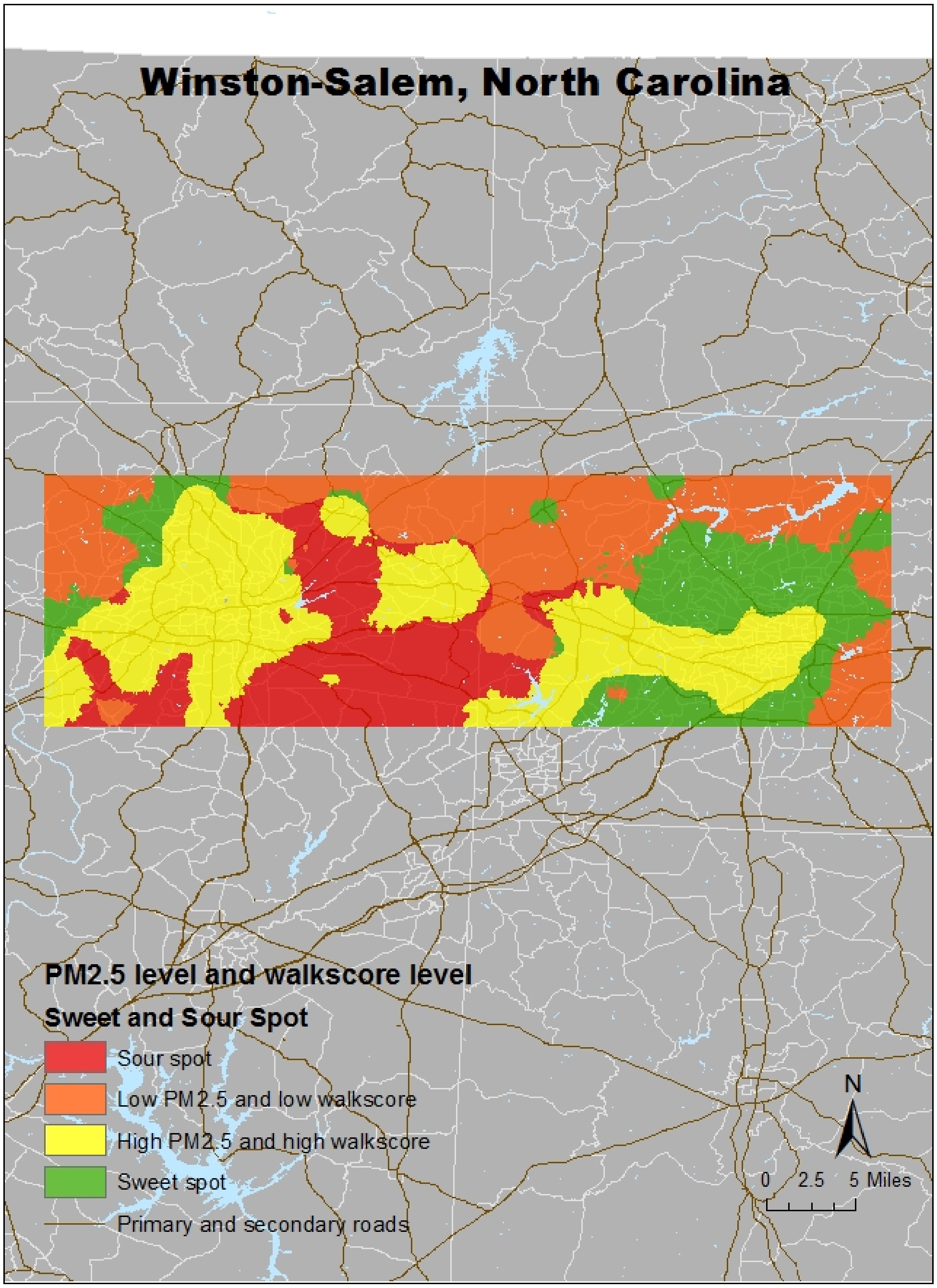


Figure IV-10. Spatial distributions of sweet- and sour-spot neighborhoods for NO_x/walk score level in Forsyth County, North Carolina.

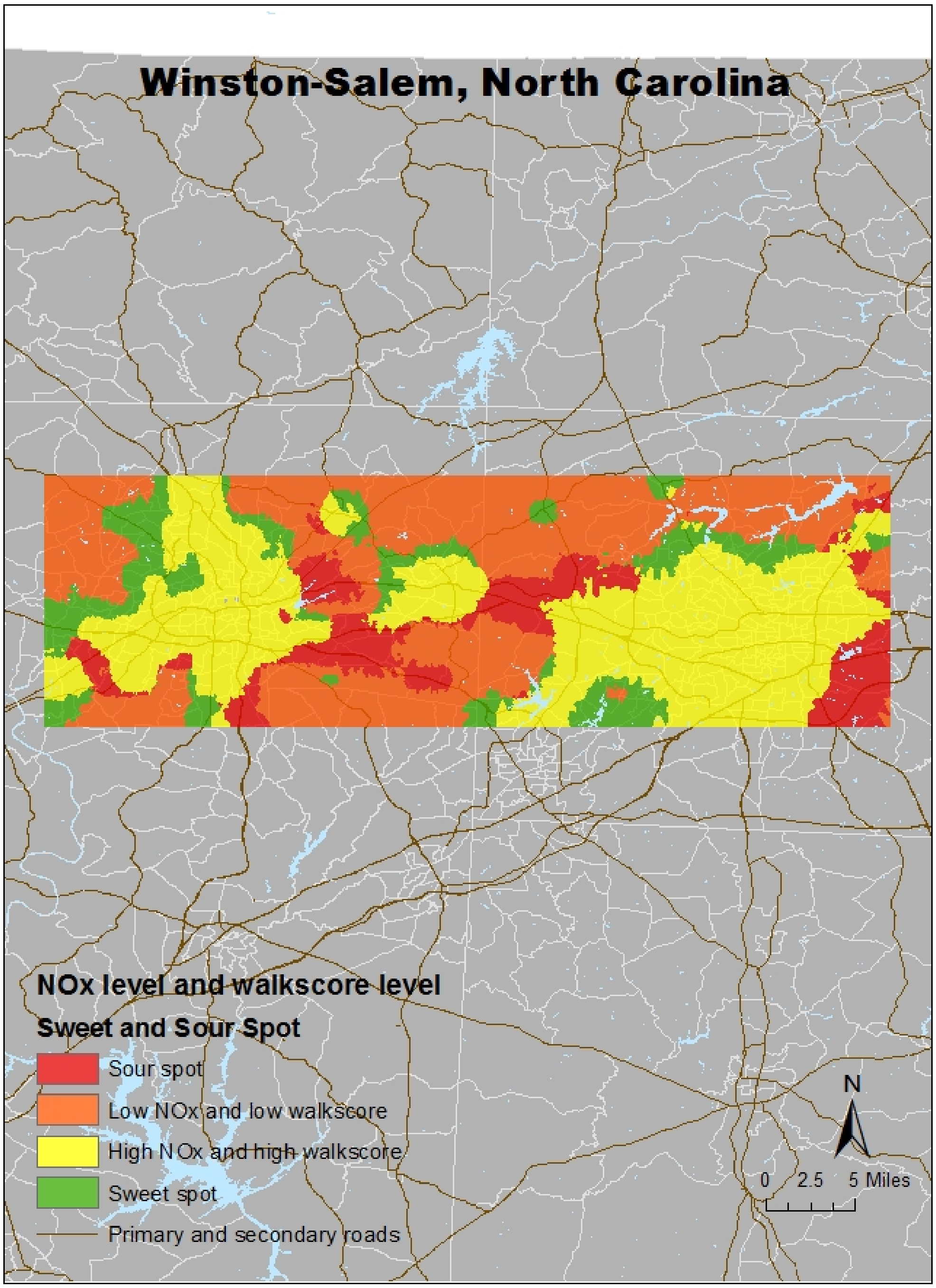


Figure IV-11. Spatial distributions of sweet- and sour-spot neighborhoods for $PM_{2.5}$/walk score level in New York City, New York.

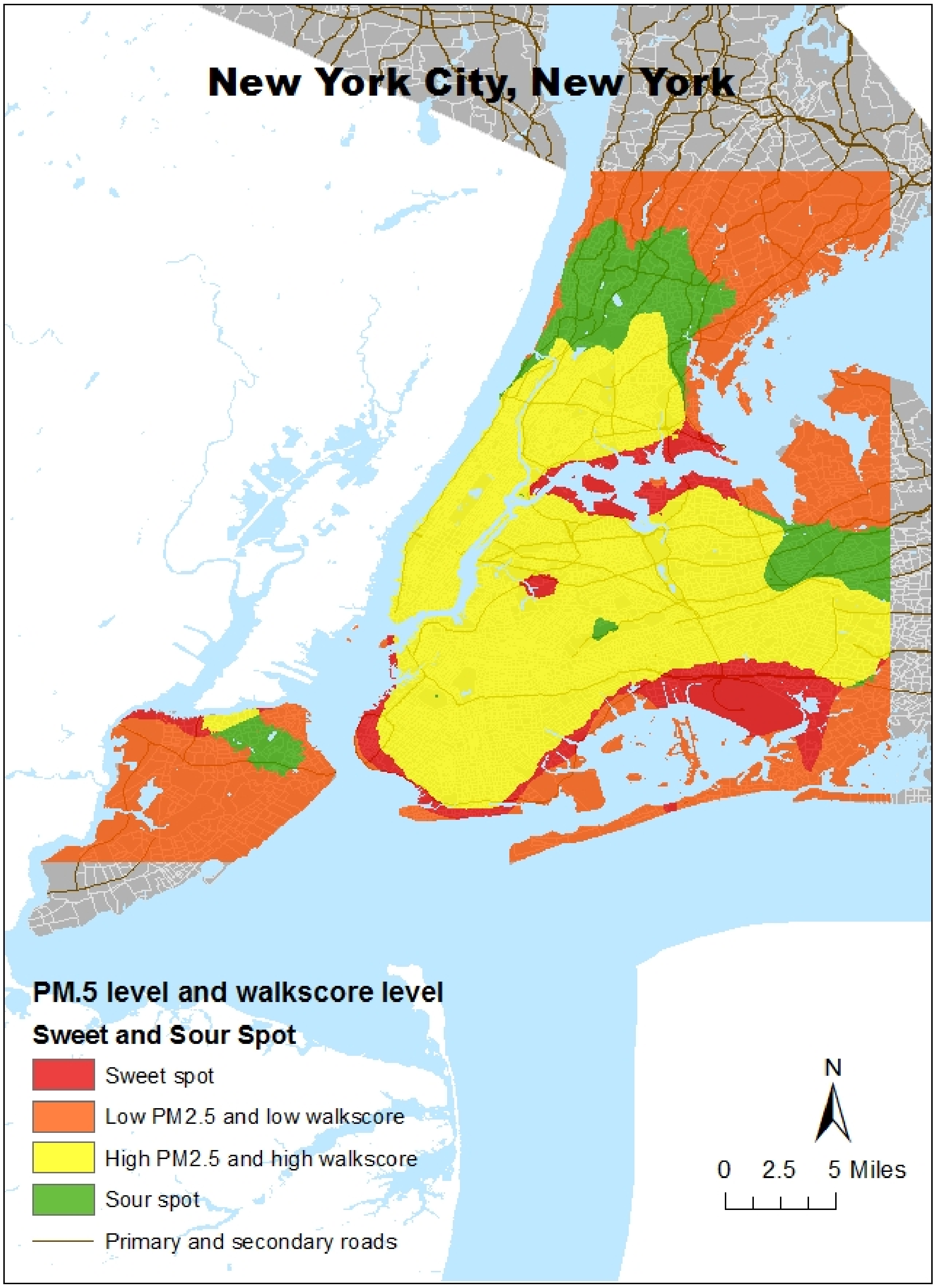
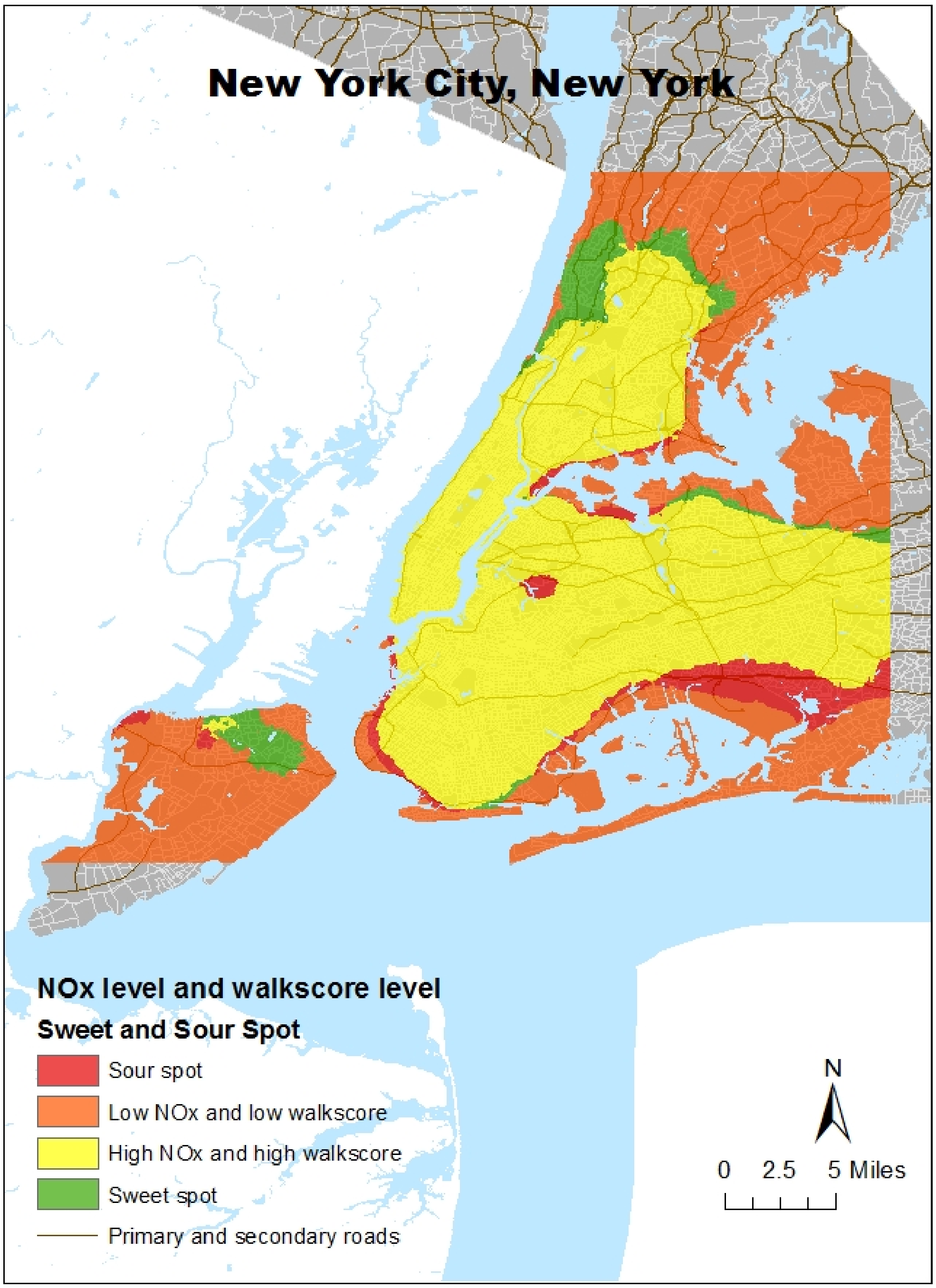


Figure IV-12. Spatial distributions of sweet- and sour-spot neighborhoods for NO_x/walk score level in New York City, New York.



4.3 Discussion

Different distributions in spatial patterns for sweet spots and sour spots, as indicated by air pollution ($PM_{2.5}$ and NO_x) and walkability (walk scores), were seen in six communities in the U.S. Neighborhoods with a low education level were often more likely to have both higher levels of air pollution and lower walk scores (sour spots) in some study sites. However, the patterns of associations for minority of race were not consistent and in some study sites neighborhoods with greater proportion of poverty were less likely to be sour-spot neighborhoods. Higher walk scores near the MESA participants' residences were associated with higher levels of walking for transport in some communities. Lower $PM_{2.5}$ or NO_x levels were generally not associated with higher levels of walking for transport, but both air pollutants were negatively associated with higher levels of walking for leisure in some communities.

This study is the first to explore the spatial distributions of neighborhood air pollution and walk score in multiple communities across the United States. It furthermore adds to the literature by investigating how neighborhoods with socially disadvantaged populations may differentially experience sweet- or sour-spot neighborhoods. In addition, to our knowledge, this is the first study to elucidate relations between two environmental health attributes, air pollution and walkability, with actual personal walking behaviors. This addresses a key research need of understanding the relationships between physical activities between physical activity and air pollution exposure as identified by the Physical Activity and Air Quality (PAAQ) Workshop sponsored by the U.S. Centers for Disease Control and Prevention (CDC). [26] Additional strengths of this study include the large amount of data on fine-scale predictions of air pollution and walk scores in diverse communities across the United States.

By examining several large communities in the United States, this work has environmental justice contributions. Previous studies on issues of environmental justice with respect to traffic-related air pollution suggested that neighborhoods with higher proportions of minority groups, low education level, and low income level were more likely to have disproportionate exposure to higher level of air pollution[18,19]. In addition, some communities with higher proportion of racial/ethnic minority populations and low socio-economic status (low education level and low income level) have disproportionately limited access to physical activity-friendly environments[20]. Only one other study from Canada, however, has examined the spatial distributions of walkability and air pollution exposure simultaneously. In that work, it was found that “sweet-spot” neighborhoods (low pollution and high walkability) are almost exclusively higher income[71]. In our study, we also find that neighborhoods with higher proportion of individuals with low education are less likely to be sweet-spot neighborhoods, especially for low NO_x level and high walk score level. However, we found inconsistent relations for the minority of race and lower income populations with sweet-spot at the census block group level in some communities. Nevertheless, our findings provide some supportive evidence that socially disadvantaged population may be at risk of health disparity due to disproportionate burden of higher traffic-related air pollution and lower walkability in residential environments.

Previous research has indicated that increases in neighborhood walkability that incorporated land use mix, street connectivity, net residential density, and retail floor area ratios might increase in time spent in physically activity travel[75]. However, other studies did not find statistically significant associations among physical activity levels and physical environmental variables (e.g., presence of sidewalks, street lighting at night, places within walking distance, and places to exercise)[82,83]. In this study, we conceptualized neighborhood walkability slightly differently by utilizing walk score. This method is a valid measure of estimating neighborhood walkability in multiple geographic locations and at multiple spatial scales[84]. Our findings provide supportive evidence on the hypothesis that better neighborhood walkability, was positively related to more personal walking time for both walking for transport. While air pollution levels were not consistent associated with walking for transport, we did observe that higher ambient air pollution level related to less personal walking time spent on for leisure. Possible explanations for these findings are that accessibility various destinations in the neighborhood and more friendly pedestrian street designs could facilitate people’s walking to get places such as to the bus, work, or stores, while people’s time spent on walking for leisure was more about how pleasant the environment was including the air pollution levels.

One limitation of our study is that the MESA participants’ personally reported time spent on walking for transport and for leisure in the questionnaire was not specific to their neighborhoods. Thus, the walkability and air pollution in the census block group near the home may not be the relevant measures if they did their reported walking at a site distant from the census block group of the home residence.

Another potential weakness of this analysis was our use of aggregated air pollution, walk score and social disadvantage covariates at the census block group scale for analysis. While we hypothesized that this spatial scale was appropriate due to the likelihood that most walking would occur close to home and a larger unit might mask heterogeneity in these variables, this approach may not capture all of the relevant information and we may be prone to bias due to the well-known modifiable areal unit problem[85,86].

4.4 Conclusions

In summary, the findings of this study indicated that geographical distributions of neighborhoods characterized as sweet or sour spots are spatially different across different study sites in the U.S. Secondly, neighborhoods with greater proportion of lower education level tended to also be "sour-spot" living environments in some communities. Finally, our findings support the idea that neighborhood walk score and air pollution concentrations may have independent positive and negative effects on personal walking activity.

CHAPTER V

Conclusions

Results from this research do not provide strong support for the hypothesis that long-term exposure to ambient $PM_{2.5}$, NO_x, or $PM_{10-2.5}$ contribute to the onset of hypertension. One of the composition chemicals of $PM_{10-2.5}$, phosphorus, was positively associated with the prevalence of hypertension whereas other composition chemicals were not associated with hypertension outcomes. This finding suggests that PM from different sources may have differential effects on the development of hypertension so future epidemiological and toxicological studies may be warranted to explore source-specific relationships with blood pressure in more detail. Geographical maps showed that spatial distributions of sweet- and sour-spot neighborhoods were different within six communities in the U.S. In addition, socially deprived neighborhoods marked by greater proportion of minority of race and of lower education level tended to be "sour-spots". This finding implies that disproportionate burden of both high air pollution and low walkability could contribute to health disparities for socially disadvantaged subgroups. Finally, our findings provided evidence that neighborhood environments with higher levels of ambient air pollution and higher walk scores may have negative and positive influences on personal walking activity for transport and leisure, respectively. This provides supportive evidence that when developing revisions to national physical activity guidelines, experts should take the health cost of air pollution into consideration, especially for susceptible populations (e.g., the elderly).

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