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ABSTRACT

Background: Ambient PM_{2.5} was ranked the eighth leading risk for mortality in 2017, with a total of 2.94 million associated deaths globally. Numerous studies have reported associations between long-term exposure to PM_{2.5} and adverse health effects across a broad range of PM_{2.5} concentrations. However, there is little research on the effect of concentrations below the annual PM_{2.5} National Ambient Air Quality Standards (NAAQS) of 12 µg/m³.

Objective: Our objective was to assess the association between the levels of ambient PM_{2.5} below NAAQS and chronic obstructive pulmonary disease (COPD), asthma, myocardial infarction (MI) as captured by hospital admissions; emergency department visits; and mortality.

Methods: We conducted a cross-sectional study on 2014 data from 265 counties of 27 States of the United States (US) retrieved from the Environmental Public Health Tracking Network (EPHTN) of the Centers for Disease Control and Prevention (CDC). We used linear and multiple linear regression models to assess the association using SAS software.

Results: At levels below 12 µg/m³, controlling for heat index, a 1-unit change in annual PM_{2.5} concentrations was linked with an increase of 2.97 (95%CI: 1.32, 6.69)-unit in COPD hospitalizations, a decrease of 0.95 (95%CI: 0.90, 0.99)-unit in COPD EDV, an increase of 2.75 (95%CI: 1.21, 6.23)-unit in asthma hospitalizations, and an increase of 2.83 (95%CI: 1.34, 5.93)-unit in asthma EDV. Additionally, long-term exposure to PM_{2.5} was still associated with some outcomes when concentrations were gradually lowered to level below a 9 µg/m³ threshold.

Conclusion: Our results showed the association between long-term exposure to PM_{2.5} and COPD, asthma, and MI for PM_{2.5} levels below 12.0 µg/m³. Our findings provide evidence of increase health risk below current regulatory standards.

**Adverse Health Effects Associated with Long-term Exposure to Fine Particulate Matter at
Levels below 12 $\mu\text{g}/\text{m}^3$**

by

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Medical Degree, University of Ndjamena, Chad

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A Thesis Submitted to the Graduate Faculty
of Georgia State University in Partial Fulfillment
of the
Requirements for the Degree

MASTER OF PUBLIC HEALTH

ATLANTA, GEORGIA
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Levels below 12 µg/m³**

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Dr. Christina H. Fuller

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KARBET DJEDOUBOUM

Signature of Author

CHAPTER I

INTRODUCTION

1.1 Background

Particulate matter (PM) is a complex mixture of liquid droplets or solids particles suspended in the air (Wilson et al., 2002). PM originate from different sources, the naturally occurring and the anthropogenic. The natural sources are dust clouds from wind storms, salt evaporation, smoke and ash from raging forest fires, and volcanic eruptions. The anthropogenic sources include stationary sources and mobile contributions. The stationary sources are residential heating, chemical plants, electrical plants, factories, manufacturing complexes, oils refineries, and incinerators. Mobile sources are cars, buses, off-road equipment, airplanes, ships, and trains (Friis, 2012). PM sources are also classified based on composition; a silicon factor is classified as soil and crustal material, a lead factor as motor vehicle exhaust, a selenium factor representing coal combustion sources, a vanadium factor for fuel oil combustion, chlorine factor for salt, and other selected metals such as nickel, zinc, or manganese (Laden et al., 2000). Source apportionment methods help to assess the source mostly associated with mortality (USEPA, 2019). PM_{10} are inhalable particles with diameters of $10\ \mu\text{m}$ and smaller. $PM_{2.5}$ pollutants include the fine (aerodynamic diameter of less than $2.5\ \mu\text{m}$) and the ultrafine (aerodynamic diameter of less than $0.1\ \mu\text{m}$) (Friis, 2012).

$PM_{2.5}$ particles can bypass the body's normal defensive system and be inhaled more deeply into the respiratory tract, some reaching the alveoli (Squadrito et al., 2001). $PM_{2.5}$ have oxidative potential and can interact with macrophages and epithelial cells through reduction-

oxidation reactions. When they enter blood circulation, they create inflammation, oxidative stress and alter immunity with susceptibility to infection (Cachon et al., 2014; Riva et al., 2011). PM_{2.5} disturb the oxidative stress and the inflammation system; that mechanism may result in atheroma plaque progression and rupture, endothelial dysfunction with vasoconstriction, impaired fibrinolysis and platelet hyperreactivity leading to thrombotic events, and arrhythmogenesis (Mills et al., 2009).

Ambient PM_{2.5} was ranked as the eighth leading risk for mortality in 2017, with a total of 2.94 million associated deaths globally (Kyu et al., 2018). Correia et al. (2013) have demonstrated, in a 7-year study in the US, that a reduction of 10 µg/m³ in the concentration of PM_{2.5} was associated with an extension by 0.35 years of the life expectancy.

In the United States, the monitoring of PM_{2.5} is part of the mandate of the United States Environmental Protection Agency (USEPA) as defined by the Clean Air Act (CAA) established in 1970. USEPA sets the National Ambient Air Quality Standards (NAAQS) (USEPA, 2017). The CAA went through major revisions in 1977 and 1990. NAAQS are set for six following "criteria" pollutants in the outdoor air: particulate matter, ozone, sulfur dioxide, nitrogen dioxide, carbon monoxide, and lead. The CAA requires USEPA to review the standards of "criteria" pollutants through rigorous risk assessment every five years (USEPA, 2017). The NAAQS for PM_{2.5} is defined to primary and secondary. The primary PM_{2.5} standards are determined to protect the human health effects, including the health of "sensitive" populations such as asthmatics, children, and the elderly; whereas the role of secondary PM_{2.5} standards is for welfare protection, including protection against decreased visibility, damage to animals, crops, vegetation, and buildings. (USEPA, 2016a; USEPA, 2016b).

The 24-hour standard and the annual standard are considered for PM_{2.5} based respectively on their short-term (hours up to one month) or long-term (one month to years) adverse health effects (USEPA, 2016a; USEPA, 2016b). In the United States, the annual geometric mean standard of PM was established to 75 µg/m³ in 1971 (NAPCA, 1969). The annual PM_{2.5} standard was lowered to 12.0 µg/m³ in 2012 (USEPA, 2016a; USEPA, 2016b). The review of the annual PM_{2.5} standard is evidence-based and required by the C.A.A.; it aims to provide increased public health protection (USEPA, 2018a).

Long-term exposure to PM_{2.5} has been reported in many reviews and meta-analyses to be associated with all-cause mortality (Vodanos, Awad, & Schwartz, 2018; Newby et al., 2014; Hart et al., 2015). Annual exposure to PM_{2.5} is associated with incidence and exacerbation of asthma and chronic obstructive pulmonary disease (COPD) (Requia et al., 2018), risk of type 2 diabetes mellitus (Weinmayr et al., 2015; Weinmayr et al., 2016), risk or death for cardiovascular diseases (Ostro et al., 2008; Cesaroni et al., 2014; Shah et al., 2013; Brook et al., 2010), and risk of lung cancer (Hamra et al., 2014). In the United States, the reduction efforts to change the annual PM_{2.5} standard between 2007 and 2020 was estimated to be associated with 1,000 avoided additional premature deaths for adults, \$53 to \$350 million in additional costs, and \$3.7 to \$9 billion of net benefits (Lepeule et al., 2012; USEPA, 2012).

1.2 Gap and Purpose of Study

The annual average concentration of PM_{2.5} was set to 12.0 µg/m³ in 2012 by the USEPA as the level to ensure adequate public health protection. Considerable epidemiological studies about the association between long-term exposure to PM_{2.5} and the health effects have

covered a range of PM_{2.5} levels spanning all concentrations. Little research is done to know whether the levels of PM_{2.5} below USEPA standard are protective of public health (Di et al., 2017). That knowledge would inform future revisions of the NAAQS. We hypothesized that the annual exposure to PM_{2.5} concentrations below the USEPA standard was associated with adverse health outcomes such as COPD, asthma, and myocardial infarction (MI).

The objective of this study is to assess the association between the levels of ambient PM_{2.5} below NAAQS and COPD, asthma, MI as captured by hospital admissions; emergency department visits; and mortality.

CHAPTER II

REVIEW OF THE LITERATURE

We have searched the literature for previous works that indicated the association between long-term exposure to PM_{2.5} and adverse health outcomes. Furthermore, we looked for published documents that focused on that relationship when the annual concentrations of PM_{2.5} were at levels below the NAAQS. We have used several conclusions from meta-analyses, systematic reviews, and expert panels to support our review.

2.1 Long-term PM_{2.5} exposure and all-cause mortality

The Harvard Six Cities Study, an eight-year cohort study, conducted in six eastern U.S. cities showed that a 10 µg/m³ increase in PM_{2.5} was strongly associated with 1.5% (95%CI: 1.1, 1.9) increment in total daily mortality, with larger increase in COPD death (3.3%) and ischemic heart disease (2.1%) when they controlled for weather (Schwartz et al., 1996). When, weather was not controlled for, they found that a 10 µg/m³ increase in PM_{2.5} was also strongly associated with 1.3% (95%CI: 1.0, 1.7) increment in total daily mortality. An extended follow-up for an additional 11 years of the same study showed that an increase in PM_{2.5} was associated with a rise of 14% (95%CI: 7, 22) in risk of all-cause mortality (Lepeule et al. 2012). Additionally, the American Cancer Society Study conducted on 552,138 adults who resided in 151 metropolitan areas showed that exposure to fine particulate matter was associated with all-cause mortality; the adjusted risk ratio for most polluted areas with the least polluted areas was 1.17 (95%CI: 1.09, 1.26) (Pope et al., 1995). Moreover, a follow-up of the Italian cohort of 1,265,058 subjects provided evidence that long-term exposure to PM_{2.5} is linked with all-cause

mortality (Cesaroni et al., 2014). Also, Morgan et al. (2003) have found in their study, in Sydney metropolitan area, that exposure to low levels of PM_{2.5} was associated with all-cause mortality, including all cardiovascular mortality and all respiratory mortality. Furthermore, Crouse et al. (2012), have found in their analysis of a Canadian cohort of 2.1 million adults that long-term exposure to PM_{2.5} was associated with non-accidental mortality (HR= 1.15, 95%CI: 1.13, 1.16). Additionally, the follow-up of the cohort of all 60,925,443 Medicare beneficiaries in the US from 2000 to 2012 showed 7.3% (95%CI: 7.1, 7.5) increase in all-cause mortality for a 10 µg/m³ increase in long-term exposure to PM_{2.5} (Di et al., 2017); that association is 13.6% (95% CI, 13.1, 14.1) stronger when the analysis was restricted to an exposure below 12µg/m³ (Di et al., 2017). Finally, a cohort from 2000 to 2013 of Medicaid and Medicare beneficiaries above 65 years old in the Northeast and mid-Atlantic region states showed that more Medicaid population would die earlier if exposed to PM_{2.5} at 12 µg/m³ compared to those exposed to an annual average of 7.5 µg/m³ (Schwartz et al., 2018). However, Vodonos, Awad, & Schwartz (2018) found recently in their meta-regression that long-term exposure to PM_{2.5} was associated with premature mortality and that the mortality effect is more important below 10 µg/m³ and above 20 µg/m³. That difference may be explained by the lack of uniformity in the methods used for the different studies included in their review.

2.2 Long-term PM_{2.5} exposure and COPD

The Global Initiative for Chronic Obstructive Lung Disease (GOLD) defines COPD as a preventable and treatable disease with some significant extrapulmonary effects that may contribute to the severity in individual patients (Rabe et al., 2007). The pulmonary component of COPD is characterized by airflow limitation that is not fully reversible. The airflow limitation is

usually progressive and associated with an abnormal inflammatory response of the lung to noxious particles or gases (Rabe et al., 2007).

Recent studies showed the relationship between long-term exposure to PM_{2.5} and COPD. For instance, Yin et al. (2017), in a cohort study of 189,793 men of 40 years old and older in China have indicated that, adjusted for rurality, region and years of education, long-term exposure to PM_{2.5} was associated with COPD mortality (HR=1.12, 95%CI: 1.10, 1.13). Their results contrast with what Atkinson et al. (2015) have found in their cohort of 812 063 patients in the UK. Atkinson et al. (2015) observed inconclusive results for the association between long-term PM_{2.5} exposure and COPD when controlling for covariates such as age, sex, smoking, body mass index and area-level (HR of 1.05, 95% CI: 0.98, 1.13).

2.3 Long term PM_{2.5} exposure and Asthma

Asthma is a chronic disorder of the airways that is complex and characterized by variable and recurring symptoms, airflow obstruction, bronchial hyperresponsiveness, and an underlying inflammation (NHLBI, 1997). The most common symptoms presented by asthma patients are wheezing, cough, chest tightness, and dyspnea; the physical examination can help determine the severity of asthma exacerbation (Patadia, Murrill & Corey, 2014).

Various studies showed the association between annual exposure to PM_{2.5} and asthma. Tétreault et al. (2016) followed in a cohort of 1,183,865 children in Canada and found that, after controlling for year of birth, sex and material and social deprivation, exposure to PM_{2.5} was associated with asthma (HR of 1.33, 95%CI:1.31, 1.34). Nishimura et al. (2013) have determined, in a retrospective case-control of 948 children aged between 8–21 years old in the

US, that first year of life exposure to PM_{2.5} was associated with asthma (OR,1.2, 95%CI: 0.6, 2.3). Similarly, Gehring et al. (2010), in the Netherlands, have observed in their follow-up of 3,863 children, from their date of birth to age 8, that PM_{2.5} levels were linked with an increase in the incidence of asthma (OR,1.28, 95%CI: 1.10, 1.49), prevalence of asthma (OR, 1.26; 95% CI: 1.04, 1.51), and prevalence of asthma symptoms (OR, 1.15; 95% CI: 1.02, 1.28). The US cohort study conducted on 50,884 women indicated that exposure to PM_{2.5} increases the incidence of asthma (Young et al., 2014). In contrast, ESCAPE cohort study, that assessed the liaison between annual exposure to PM_{2.5} and asthma in 23,704 adults in 6 countries and more than 20 different cities across Europe, did not show a significant association (Jacquemin et al., 2015). That observation may be due to the methodology difference between non-homogeneous cohorts.

2.4 Long-term PM_{2.5} exposure and cardiovascular diseases

The association between long-term exposure to PM_{2.5} and the risk and mortality for cardiovascular diseases is extensively reported in the literature. The American Heart Association (AHA) stated, in their updated scientific statement from 2010, that long-term exposure to PM_{2.5} is positively associated with cardiovascular disease mortality (Brook et al., 2010). A similar observation was done by Liu et al. (2018) in their risk-meta-analysis. Newby et al. (2014) have shown the European expert position paper indicating that long-term exposure to PM_{2.5} is associated with various cardiovascular outcomes such as coronary artery disease, heart failure, and cerebrovascular disease. Moreover, Duan et al. (2018) have found, among 1188 women in the Study of Women's Health Across the Nation (SWAN), that long-term exposure to PM_{2.5} may contribute to the increase in atherosclerosis in the post-menopausal

period. Also, To et al. (2015) have indicated, in their 30-year longitudinal cohort study, that the increase in the prevalence of congestive heart failure, ischemic heart disease, and stroke was associated with elevated PM_{2.5} exposure. Furthermore, Gan et al. (2010) have observed, in their cohort study, that the long-term exposure to PM_{2.5} was linked to a rise in coronary heart disease hospitalization and mortality after adjusting for the covariates. Finally, Fu et al. (2018) have obtained an association between PM_{2.5} exposure and risk and mortality for stroke (respectively 1.14, 95% CI 1.08, 1.21 and 1.15, 95% CI 1.07, 1.24).

2.5 Long-term PM_{2.5} exposure and diabetes

Various studies concluded on the relationship between long-term exposure to PM_{2.5} and risk for diabetes. A recent cross-sectional and ecological study conducted in Italy by Orioli et al. (2018) found that each 10µg/m³ increment of PM_{2.5} concentration was linked to the odds ratio of 1.04 (95% CI 1.02, 1.07) for diabetes. Similarly, Weinmayr et al. (2015) have demonstrated in a cohort of 3607 individuals in Germany that long-term exposure to PM_{2.5} increases the type 2 diabetes in the general population. Furthermore, Hansen et al. (2016) have found, in the cohort of 28,731 female nurses in Denmark, that PM_{2.5} may be the most associated with diabetes development among women, and non-smokers. However, Janghorbani, Momeni & Mansourian (2014) have demonstrated in their review on air pollution and the risk of diabetes that the association between long-term exposure to PM_{2.5} and diabetes was weak.

2.6 Long-term PM_{2.5} exposure and lung cancer

Several authors have demonstrated the association between chronic exposure to PM_{2.5} and the risk for lung cancer. Chen et al. (2015) have shown, in their meta-analysis, that long-

term exposure to fine particulate matter (1.11, 95% CI: 1.00, 1.22) was significantly associated with risk of lung cancer. The same observation was done by Hamra et al. (2014). They found, in their meta-analysis, that lung cancer was associated (1.09, 95% CI: 1.04, 1.14) with long-term exposure to PM_{2.5}. Similarly, Lepeule et al. (2012) in the extended follow-up of the Harvard Six Cities study, found that a 10 µg/m³ increment in long-term exposure to PM_{2.5} was associated with 37% (95% CI: 7, 75) rise in lung-cancer mortality.

2.7 Long-term PM_{2.5} exposure and neurologic diseases

Studies to date reported the risk of neurologic diseases associated with long-term exposure to PM_{2.5}. Kioumourtzoglou et al. (2015) have followed approximately 9.8 million subjects and observed significant associations between long-term exposure to PM_{2.5} and first admission for dementia, Alzheimer's, or Parkinson's diseases. Moreover, Fu et al. (2018) have indicated, in their review, a significant association between PM_{2.5} exposure and risk for dementia (1.16, 95% CI 1.07, 1.26), for Alzheimer's disease (3.26, 95% 0.84, 12.74), for Autism Spectrum Disorder (ASD) (1.68, 95% CI 1.20, 2.34), and for Parkinson's disease (1.34, 95% CI 1.04, 1.73).

CHAPTER III

MANUSCRIPT

Introduction

The World Health Organization (WHO) estimates that environmental factors account for 23% of global death (Prüss-Üstün et al., 2016). Ambient particulate matter with an aerodynamic diameter below 2.5 μg ($\text{PM}_{2.5}$) was ranked eighth mortality risk factor in 2017 and made a total of 2.94 million deaths globally (Kyu et al., 2018). A study in the US has shown that a reduction of 10 $\mu\text{g}/\text{m}^3$ in the concentration of $\text{PM}_{2.5}$ was associated with the extension of life expectancy by 0.35 year (Correia et al., 2013).

Long-term exposure to $\text{PM}_{2.5}$ was reported in many reviews and meta-analyses to be associated with all-cause mortality (Newby et al., 2014; Hart et al., 2015; Vodonos, Awad, & Schwartz, 2018). It is more associated with all-cause mortality than short-term exposure to $\text{PM}_{2.5}$ (Brook et al., 2010). Additionally, long-term exposure to $\text{PM}_{2.5}$ is associated with risk of asthma and chronic obstructive pulmonary disease (COPD) (Requia et al., 2018), risk of type 2 diabetes mellitus (Weinmayr et al., 2015; Weinmayr et al., 2016), risk or death for cardiovascular diseases (Shah et al., 2013; Cesaroni et al., 2014) and risk of lung cancer (Hamra et al., 2014).

In the United States (US), the monitoring of $\text{PM}_{2.5}$ is part of the mandate of the United States Environmental Protection Agency (USEPA), as defined by the Clean Air Act (CAA). USEPA sets the National Ambient Air Quality Standards (NAAQS) (USEPA, 2016). The NAAQS for the annual $\text{PM}_{2.5}$ standard was set to 12.0 $\mu\text{g}/\text{m}^3$ in 2012, reference level below which there may be

public health protection. (USEPA, 2009; USEPA, 2016a, USEPA, 2016b). The United States (US) has made tremendous advancements in reducing the level of air pollution in general, including the level of annual $PM_{2.5}$ (USEPA, 2018b).

Considerable epidemiological studies about the relationship between long-term exposure to $PM_{2.5}$ and health effects have covered the whole levels of $PM_{2.5}$, whether they were below or above the NAAQS (Vodanos, Awad, & Schwartz, 2018; Newby et al., 2014; Hart et al., 2015; Brook et al., 2010; Correia et al., 2013). Little research is done to know whether keeping the annual $PM_{2.5}$ concentrations below the USEPA standard would not have associated health effects. That knowledge would guide the advocacy about keeping that current standard or inform the need to lower the level to the less harmful. We hypothesized that the annual exposure to $PM_{2.5}$ concentrations below the NAAQS was associated with the health effects such as hospital admissions or emergency department visits (EDV) or mortality for COPD, asthma, and myocardial infarction (MI).

The objective of this study is to assess the association between the levels of ambient $PM_{2.5}$ below NAAQS and COPD, asthma, MI as captured by hospital admissions; emergency department visits; and mortality.

Methods

Study design

Our study covered 265 counties of 27 States of the United States (US). Data were selected for their recent availability on both exposure and outcome variables of interest.

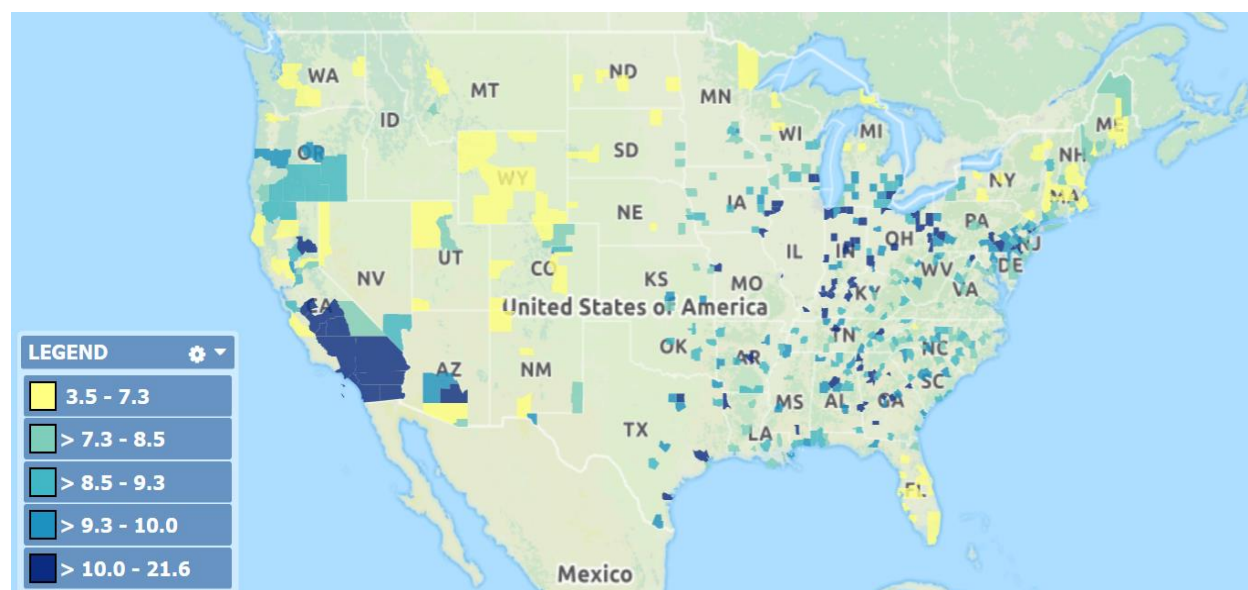


Figure 3.1 Annual PM_{2.5} in US Counties in 2014

(Source: CDC <https://ephracking.cdc.gov/DataExplorer/#/>)

We conducted a cross-sectional analysis using publicly available 2014 data from 265 counties of 27 States of the United States. The observation unit of this study was a county. We used data from the year 2014 on annual particulate matter with diameter below 2.5 μ m (PM_{2.5}) concentration, chronic obstructive pulmonary disease (COPD) hospitalizations, COPD mortality, COPD emergency department visits (EDV), asthma hospitalizations, asthma EDV, MI hospitalizations, and MI mortality from 265 counties of 27 States of the United States. Data were retrieved from the Environmental Public Health Tracking Network (EPHTN) of the Centers for Disease Control and Prevention (CDC) (CDC, 2018). The EPHTN database is fed by various information collected through different methods. State health departments provide data on hospitalizations and EDV, whereas mortality data are given by the National Vital Statistics System from the National Center for Health Statistics (NCHS). The annual PM_{2.5} concentration was measured through the US Environmental Protection Agency (USEPA) approved methods at

various sites in each State. Moreover, we used data on the 2014 county population obtained from the US Census Bureau database (US Census Bureau, 2015) and the 2011 average daily health index from CDC Wonder database (NLDAS, 2012). Finally, the counties in the study were both rural and urban and came from four US regions defined by the US Census Bureau, Midwest, Northeast, South, and West.

Institutional Review Board Approval

Our research was approved by the Institutional Review Board (IRB) of Georgia State University on October 25, 2018, under reference number 351592 and designated as “not human subjects research.”

Exposure

The independent or exposure variable was PM_{2.5}. It represented the annual average ambient concentrations of PM_{2.5} in micrograms per cubic meter ($\mu\text{g}/\text{m}^3$). The EPA extracted the raw air quality data from the Air Quality System (AQS) for the monitors designated as Federal Reference Methods or equivalent. Then, for each monitoring site, EPA retained the maximum concentration at the site for each monitored day. The annual average of PM_{2.5} is calculated using the site-level daily monitoring data for the monitors with completed quarterly and annual data. EPA calculated the quarterly average for each calendar quarter and then compute the annual average for each monitor with four valid quarters by averaging the quarterly averages.

Outcomes

There were seven dependent or outcome variables: COPD hospitalizations, COPD mortality, COPD EDV, asthma hospitalizations, asthma EDV, MI hospitalizations, and MI mortality.

The variable COPD EDV was the age-adjusted rate of emergency department visits among persons 25 and over for COPD per 10,000 population. That variable derived from the following measures: the numerator was the emergency department visits during a calendar year with COPD as the primary diagnosis and defined from the ninth revision of the International Classification of Diseases (ICD-9), the denominator was the midyear resident population estimates for state and by county, and the age-adjustment was done by the direct method to the year 2000 U.S. Standard Population.

The variable COPD hospitalizations was the age-adjusted rate of hospitalization for COPD among persons 25 and over per 10,000 population. That variable was calculated from the following elements: the numerator was the resident hospitalizations during a calendar year with COPD as the primary diagnosis and defined from the ninth revision of the International Classification of Diseases (ICD-9), the denominator was the midyear resident population estimates, and the age-adjustment was done by the direct method to the year 2000 U.S. Standard Population.

The variable COPD mortality was the annual age-adjusted death rates among persons 25 and over per 100,000 population. That variable was calculated as the following: the numerator was the total number of deaths with COPD in the geographic region of interest, during a calendar year from the death certificate data, defined from the ninth revision of the International Classification of Diseases (ICD-9), the denominator was the midyear resident population estimates for state and by county from U.S. Census Populations With Bridged Race Categories, and the age-adjustment was done by the direct method to the year 2000 U.S. Standard Population.

The variable asthma hospitalizations was the age-adjusted rate of hospitalization for asthma per 10,000 population. It was calculated from the following elements: the numerator was the resident hospitalizations for asthma as the primary diagnosis and defined from the ninth revision of the International Classification of Diseases (ICD-9), the denominator was the midyear resident population, and the age-adjustment was done by the direct method to the year 2000 US standard population.

The variable asthma EDV was the annual age-adjusted rate of emergency department visits for asthma per 10,000 population. That variable was calculated as follow: the numerator was the emergency department visits during a calendar year with asthma as the primary diagnosis and defined from the ninth revision of the International Classification of Diseases (ICD-9), the denominator was the midyear resident population, and the age-adjustment by the direct method to the Year 2000 US Standard population.

The variable MI hospitalizations was the age-adjusted rate of hospitalization for MI among persons 35 and over per 10,000 population. It was calculated as following: the numerator was the resident hospitalizations for acute myocardial infarction as the primary diagnosis and defined from the ninth revision of the International Classification of Diseases (ICD-9), the denominator was the midyear resident population, and the age-adjustment was done by the direct method to the Year 2000 US Standard population.

The variable MI mortality was the annual age-adjusted death rate among persons 35 and over per 100,000 population. That variable was calculated as the following: the numerator was the total number of deaths with acute MI, in the geographic region of interest, during a calendar year from the death certificate data, the denominator is the total number of residents

at the midyear in the geographic region of interest, during a calendar year from the US Census, and the age-adjustment was done by the direct method to the Year 2000 US Standard population.

Covariate

The main covariate was the heat index. The heat index was the reported measures of the average daily maximum heat index of the year 2011. Heat Index data are available for days with temperatures at or above 80 degrees Fahrenheit or 26.7 degrees Celsius. It was calculated from the ambient dry bulb temperature (in degrees Fahrenheit) and the relative humidity (integer percentage). With seasonal variability, there is evidence showing associations between meteorological factors such as ambient temperature and relative humidity and risk for respiratory diseases, and cardiovascular diseases (Qiu et al., 2013; Phung et al., 2016; Bunker et al., 2016; ...). As the temperature is a component of the heat index, we found it important to include heat index as the covariate for that association.

The other variables of the study were the rurality and the US region of the counties as defined by the US Census Bureau. They were included in the analysis for the reason both the exposure and the outcomes may not be uniformly distributed into differently US regions.

Statistical Analysis

We have used the Statistical Analysis System SAS (SAS Institute Inc., Cary, NC, USA) software program version 9.4 for all data analyses. The excel data set was developed from the information taken from the databases and then imported into SAS. The missing values of the continuous variables were coded by a period (".") and are not taken into consideration for the analysis.

We used the Shapiro-Wilk test to assess for normality of the outcome variables. We considered the natural logarithm transformation of outcome variables when the normality assumptions were not met. Then, exponentiation is done for both the slopes and the 95% confidence interval (CI).

We conducted univariate analyses using linear regression models to check the association between the exposure variable and each outcome variable. Moreover, multiple linear regression models were used for multivariate analyses to check for the association between PM_{2.5} and COPD hospitalizations, COPD mortality, COPD EDV, asthma hospitalizations, asthma EDV, MI hospitalizations, and MI mortality, controlling for the heat index.

Additionally, we tested for significance to include the interaction term between PM_{2.5} and heat index and used r-square and cp criteria to ensure the selection of the best-fitted model. The significance level, alpha, for the decision, was set at 0.05.

Moreover, we checked for an association between heat index and PM_{2.5} to help determine the role played by that covariate in the relationship between PM_{2.5} and the outcomes.

Finally, we performed a sensitivity analysis on multivariate analyses considering levels of annual PM_{2.5} concentrations below 11, below 10 and below 9 µg/m³ to determine the strength of association between each outcome and the annual PM_{2.5}, controlling for heat index, at each level.

Results

Basic characteristics of variables

A total of 265 counties from the four US regions were included in the study; 86% of them were rural and 14% urban. The average annual PM_{2.5} was 8.53 (SD: 2.22). The average maximum heat index was 90.41 (SD: 3.81). The median age-adjusted rate of hospitalization for COPD among persons 25 and over per 10,000 population was 21.40 (IQR: 14.60). The median age-adjusted rate of emergency department visits for COPD among persons 25 and over per 10,000 population was 63.20 (IQR: 41.85). The median age-adjusted death rates for COPD among persons 25 and over per 100,000 population was 61.70 (IQR: 23.50). The median age-adjusted rate of hospitalization for asthma per 10,000 population was 8.60 (IQR: 5.80). The median age-adjusted rate of EDV for asthma per 10,000 population was 56.10 (IQR: 23.10). The median age-adjusted rate of hospitalization for MI among persons 35 and over per 10,000 population was 27.80 (IQR: 8.70). The median age-adjusted rate of mortality for MI among persons 35 and over per 10,000 population was 51.80 (IQR: 21.70).

Univariate and multivariate analyses for the US

At levels below 12 $\mu\text{g}/\text{m}^3$, a 1-unit increment in the annual PM_{2.5} concentrations was linked with an increase of 1.06 (95%CI: 1.02, 1.09)-unit in COPD hospitalizations, an increase of 1.06 (95%CI: 1.03, 1.09)-unit in asthma hospitalizations, an increase of 1.04 (95%CI: 1.01, 1.08)-unit in asthma EDV, an increase of 1.03 (95%CI: 1.01, 1.05)-unit in MI hospitalizations, and an increase of 1.04 (95%CI: 1.01, 1.07)-unit in MI mortality. Inversely, an increase in the annual PM_{2.5} concentrations was not associated with an increase in age-adjusted rate of COPD EDV and in age-adjusted rate of COPD mortality (respectively p=0.1317 and p=0.4941).

At levels below $12 \mu\text{g}/\text{m}^3$, controlling for heat index, a 1-unit increment in the annual $\text{PM}_{2.5}$ concentrations was linked with an increase by 2.97 (95%CI: 1.32, 6.69)-unit in COPD hospitalizations a decrease of 0.95 (95%CI: 0.90, 0.99)-unit in COPD EDV, an increase of 2.75 (95%CI: 1.21, 6.23)-unit in asthma hospitalizations, and an increase of 2.83 (95%CI: 1.34, 5.93)-unit in asthma EDV.

Heat index was associated with both $\text{PM}_{2.5}$ (0.18, 95%CI: 0.13, 0.23) and each outcome [COPD hospitalizations (0.07, 95%CI: 0.06, 0.08), COPD EDV (0.07, 95%CI: 0.05, 0.09), COPD mortality (0.01, 95%CI: 0.01, 0.02), asthma hospitalizations (0.04, 95%CI: 0.02, 0.05), asthma EDV (0.03, 95%CI: 0.01, 0.04), MI hospitalizations (0.02, 95%CI: 0.01, 0.03), MI mortality (0.03, 95%CI: 0.02, 0.04)].

Multivariate analyses by county rurality

In urban counties, at the levels below $12 \mu\text{g}/\text{m}^3$, controlling for heat index, a 1-unit increase in the annual $\text{PM}_{2.5}$ concentration was associated with an increase of 2.74 (95%CI: 1.34, 5.64)-unit in COPD hospitalizations, a decrease by 0.29 (95%CI: 0.12, 0.73)-unit in COPD EDV, a decrease of 0.46 (95%CI: 0.28, 0.77)-unit in COPD mortality, an increase of 3.10 (95%CI: 1.35, 7.10)-unit in asthma hospitalizations, an increase of 2.92 (95%CI: 1.28, 6.69)-unit in asthma EDV, and an increase of 1.03 (95%CI: 1.01, 1.06)-unit in MI mortality.

In rural counties, at the levels below $12 \mu\text{g}/\text{m}^3$, controlling for heat index, a 1-unit increase in the annual $\text{PM}_{2.5}$ concentrations was associated with any change in the outcomes COPD hospitalizations (7.10, 95%CI: 0.03, 1864.10), COPD EDV (0.27, 95%CI: 0.00, 126.20), COPD mortality (1.27, 95%CI: 0.12, 14.07), asthma hospitalizations (1.77, 95%CI: 0.04, 75.19),

asthma EDV (1.82, 95%CI: 0.16, 20.29), MI. hospitalizations (0.94, 95%CI: 0.06, 15.03), and MI. mortality (0.99, 95%CI: 0.90, 1.09).

Multivariate analyses by the US regions

In the Midwest region, at the levels below $12 \mu\text{g}/\text{m}^3$, controlling for heat index, a 1-unit increase in the annual $\text{PM}_{2.5}$ concentrations was associated with a decrease of 0.90 (95%CI: 0.19, 0.99)-unit in heart attack mortality.

In the Northeast region, at the levels below $12 \mu\text{g}/\text{m}^3$, controlling for heat index, a 1-unit increase in the annual $\text{PM}_{2.5}$ concentrations was associated with a decrease of 0.08 (95%CI: 0.01, 0.78)-unit in COPD hospitalizations, a decrease of 0.08 (95%CI: 0.01, 0.93)-unit in COPD mortality, a decrease of 0.11 (95%CI: 0.02, 0.73)-unit in MI. hospitalizations, and an increase of 1.04 (95%CI: 1.00, 1.09)-unit in MI. mortality.

In the South region, at the levels below $12 \mu\text{g}/\text{m}^3$, a 1-unit increase in the annual $\text{PM}_{2.5}$ concentrations was associated with an increase of 1.12 (95%CI: 1.05, 1.20)-unit in MI. mortality, controlling for heat index.

In the West region, at the levels below $12 \mu\text{g}/\text{m}^3$, a 1-unit increase in the annual $\text{PM}_{2.5}$ concentrations was associated with an increase of 8.41 (95%CI: 1.65, 42.52) in COPD hospitalizations, controlling for heat index.

Sensitivity analysis

Sensitivity analysis revealed that for levels below $11 \mu\text{g}/\text{m}^3$ to below $9 \mu\text{g}/\text{m}^3$, controlling for heat index, a 1-unit increase in the concentration of the annual $\text{PM}_{2.5}$ was strongly associated with an increase in COPD hospitalizations, an increase in asthma hospitalizations, and an increase in asthma EDV. A decrease in COPD EDV was seen for a 1-unit

increase in the concentration of the annual $PM_{2.5}$ for levels below $9 \mu\text{g}/\text{m}^3$. A decrease in COPD mortality was observed for a 1-unit increase in the concentration of the annual $PM_{2.5}$ for levels below $11 \mu\text{g}/\text{m}^3$ and below $9 \mu\text{g}/\text{m}^3$. No change was observed for MI hospitalizations and MI mortality when there was a 1-unit increase in the concentration of the annual $PM_{2.5}$ for levels below $11 \mu\text{g}/\text{m}^3$ and below $9 \mu\text{g}/\text{m}^3$.

Discussion

This study assessed the association between the annual exposure to $PM_{2.5}$ at levels below NAAQS standard of $12 \mu\text{g}/\text{m}^3$ and hospital admissions or EDV or mortality for COPD, asthma, and MI, controlling for heat index. Overall, we found that long-term exposure to $PM_{2.5}$ at levels below $12 \mu\text{g}/\text{m}^3$ was positively associated with COPD hospitalizations, asthma hospitalizations, asthma EDV, MI hospitalizations, and MI mortality. Furthermore, controlling for heat index, long-term exposure to $PM_{2.5}$ at levels below $12 \mu\text{g}/\text{m}^3$ was positively associated with COPD hospitalizations, asthma hospitalizations, and asthma EDV. However, controlling for heat index, long-term exposure to $PM_{2.5}$ at levels below $12 \mu\text{g}/\text{m}^3$ was negatively associated with COPD EDV. Various associations were observed for urban counties, whereas none was seen for rural counties. The results for rural counties may be explained by the lower mean concentration of $PM_{2.5}$ observed in rural counties compared to urban one or the low number of rural counties covered in our study. Similarly, controlling for heat index, the types and strengths of associations between long-term exposure to $PM_{2.5}$ at levels below $12 \mu\text{g}/\text{m}^3$ and the different outcomes were slightly different for each US region. Those differences may be partially explained by the differences in mean concentrations of $PM_{2.5}$ and heat index in the regions; but also by the difference in the levels of other air pollutants and covariates not

covered in our study. Finally, some of the associations between long-term exposure to $PM_{2.5}$ at levels below $12 \mu\text{g}/\text{m}^3$ and the different outcomes were observed even when the concentrations of the annual $PM_{2.5}$ were lowered until the level below $9 \mu\text{g}/\text{m}^3$. The covariate heat index is a confounder for each of the associations between $PM_{2.5}$ and the outcomes.

Several studies have shown that long-term exposure to $PM_{2.5}$ is associated with risk or mortality for COPD, asthma or MI. Morgan et al. (2003) have observed in their study, in Sydney metropolitan area, that exposure to low levels of $PM_{2.5}$ was associated with all-cause mortality, including all cardiovascular mortality and all respiratory mortality. Moreover, in the Harvard Six Cities Study, Schwartz et al. (1996) have observed, when controlling for weather, that a $10 \mu\text{g}/\text{m}^3$ change in $PM_{2.5}$ was strongly associated with 1.5% (95%CI: 1.1, 1.9) increase in total daily mortality but when they controlled for weather, they found the association at 1.3% (95%CI: 1.0, 1.7). Their results are similar to ours for MI. in the non-adjusted analysis [3% (95%CI: 1.0, 5.0)] whereas they contrast with what we have observed in the adjusted models where there was no association. The differences observed may be explained by the use of limited number of covariates in our study. In a cohort of 189,793 men of 40 years old and older in China, Yin et al. (2017) have observed that long-term exposure to $PM_{2.5}$ was linked to COPD mortality (HR=1.12, 95%CI: 1.10, 1.13). Their results contrast with what we have obtained for COPD mortality. That difference may be explained by the mean $PM_{2.5}$ concentration in their study that was higher compared to ours. Conversely, Atkinson et al. (2015) have found in their cohort of 812 063 patients in the UK a piece of inconclusive evidence for the associations between long-term $PM_{2.5}$ and COPD (OR of 1.14, 95% CI: 0.96, 1.36). That result may indicate a lack of statistical power as they used COPD admissions that may unlikely reflect the burden of

the disease in the population. Only COPD patients with severe or poorly controlled symptoms would be admitted in hospitals. For asthma, Gehring et al. (2010) have conducted a study in children and found that PM_{2.5} levels were associated with a significant rise in the incidence of asthma (OR,1.28, 95%CI: 1.10, 1.49), prevalence of asthma (OR, 1.26; 95% CI: 1.04, 1.51), and prevalence of asthma symptoms (OR, 1.15; 95% CI: 1.02, 1.28). Moreover, Nishimura et al. (2013) have determined, in their retrospective case-control in children in the US, that first year of life exposure to PM_{2.5} was associated with asthma (OR,1.2, 95%CI: 0.6, 2.3). Finally, the US cohort study conducted on 50,884 women showed that exposure to PM_{2.5} is associated with a higher incidence of asthma (Young et al., 2014). The association between long-term exposure to PM_{2.5} has also been described in the literature. For instance, the European expert position paper (Newby et al., 2014) and the AHA (Brook et al., 2010) have concluded on the evidence that long-term exposure to PM_{2.5} is associated with various cardiovascular outcomes, including myocardial infraction.

Our results seem to support the existing knowledge on the association between long-term exposure to PM_{2.5} and COPD, asthma, and MI. Moreover, that association was still observed when we controlled for heat index. We distinguished our findings from previous research by limiting the exposure to the annual PM_{2.5} concentration at levels 12.0 µg/m³. Our results went beyond the existing literature by indicating that, at the population level, controlling for heat index or not, long-term exposure to PM_{2.5} at levels below 12.0 µg/m³ may still be harmful to public health. When we controlled for heat index, the strength of the association was higher at lower PM_{2.5} concentrations for COPD hospitalizations, asthma hospitalizations, and asthma EDV.

This study was not exempt from limitations. Our analysis performed in only one-year data could not assess the magnitude of how the change in the concentrations of PM_{2.5} over time may affect the outcomes. Also, PM_{2.5} concentrations and heat index may have seasonal variations that were not captured in our study. Longitudinal studies covering many years and including seasonal information would better capture precise association. Also, the average daily maximum heat index used as covariate did not consider days with low heat index that may influence differently the association. Moreover, there may be a possibility for misclassification of fine PM with other PM or confounding with other pollutants and covariates not included in our study. Furthermore, there might be reasons that influenced some counties to monitor the pollutant. Additionally, COPD is a disease that affects in different way children and adults; the data we used for COPD cover only adult populations above 25 years old. Therefore, the effect size we observed for that outcome may not reflect the picture in the general population. Finally our research, may suffer fallacies as all ecological studies if we try to link the observed associations at the population level with any individual subject.

Our findings suggest that long-term exposure to PM_{2.5} at levels below the current NAAQS of 12.0 µg/m³ was associated with adverse health effects, controlling or not for heat index. Based on our existing NAAQS, there was 197% excess risk for COPD hospitalizations, 175% excess risk for asthma hospitalizations, 183% excess risk for asthma EDV, and 5% lower risk for COPD EDV. Additional studies are indicated to better understand those relationships and to support health risk reduction efforts.

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TABLES AND FIGURES – RESULTS

Table 3.1 Basic characteristics of variables

Variable	N	Mean	Std Dev	Median	IQR
Heath index	265	90.41	3.81	91.00	5.00
PM _{2.5}	265	8.53	2.22	8.60	2.40
COPD H. ^a	257	24.56	17.53	21.40	14.60
Asthma H. ^c	262	9.83	4.83	8.60	5.80
MI H. ^d	265	29.79	8.34	27.80	8.70
COPD M. ^b	265	63.89	19.12	61.70	23.50
MI M. ^e	265	58.83	25.11	51.80	21.70
COPD E.D.V. ^a	188	75.09	54.66	63.20	41.85
Asthma E.D.V. ^c	195	57.05	21.90	56.10	23.10

^a Age-adjusted rate of hospitalizations (COPD H) and emergency department visits (COPD EDV) for COPD for persons 25 and over per 10,000 population

^b Age-adjusted death rate from COPD among persons 25 and over per 100,000 population (COPD Mortality)

^c Age-adjusted rate of hospitalizations (Asthma H) and emergency department visits (Asthma EDV) for asthma per 10,000 population

^d Age-adjusted rate of hospitalizations for myocardial infarction (MI. H.) among persons 35 and over per 10,000 population

^e Age-adjusted rate of death from myocardial infarction among persons 35 and older per 100,000 population (MI. Mortality)

Table 3.2 Basic characteristics of variables per rurality

Variable	N		Mean		Std Dev		Median	
	Urban	Rural	Urban	Rural	Urban	Rural	Urban	Rural
Heath index	228	37	90.53	89.65	3.77	4.04	91.00	90.00
PM _{2.5}	228	37	8.66	7.70	2.22	2.07	8.70	8.00
COPD H. ^a	221	36	22.73	35.75	10.09	38.16	20.90	25.10
Asthma H. ^c	225	37	10.20	7.61	4.93	3.50	9.10	6.50
MI H. ^d	228	37	29.04	34.46	7.62	10.88	27.40	30.00
COPD M. ^b	228	37	61.35	79.55	16.57	25.62	60.35	71.00
MI M. ^e	228	37	55.83	77.00	19.99	41.36	50.75	60.20
COPD E.D.V. ^a	159	29	66.24	123.61	36.94	96.79	57.60	84.80
Asthma E.D.V. ^c	165	30	57.84	52.76	23.19	12.03	56.90	51.40

^a Age-adjusted rate of hospitalizations (COPD H) and emergency department visits (COPD EDV) for COPD for persons 25 and over per 10,000 population

^b Age-adjusted death rate from COPD among persons 25 and over per 100,000 population (COPD Mortality)

^c Age-adjusted rate of hospitalizations (Asthma H) and emergency department visits (Asthma EDV) for asthma per 10,000 population

^d Age-adjusted rate of hospitalizations for myocardial infarction (MI. H.) among persons 35 and over per 10,000 population

^e Age-adjusted rate of death from myocardial infarction among persons 35 and older per 100,000 population (MI. Mortality)

Table 3.3 Basic characteristics of variables per region

Variable	N				Mean				Std Dev				Median			
	MW [†]	NE ^{††}	S ^{†††}	W ^{††††}	MW	NE	S	W	MW	NE	S	W	MW	NE	S	W
Heath index	60	71	68	66	93.0	89.2	93.6	86.1	2.3	1.3	1.9	3.5	92.0	89.0	94.0	85.5
PM_{2.5}	60	71	68	66	8.8	8.1	8.7	8.6	1.3	1.9	1.5	3.5	8.8	8.2	9.0	7.7
COPD H.^a	53	70	68	66	22.7	24.0	37.5	13.4	8.7	5.2	27.7	5.1	21.2	23.3	33.4	12.7
Asthma H.^c	60	69	67	66	8.48	12.6	11.2	6.8	4.3	6.3	3.4	1.9	7.0	11.5	11.5	6.6
MI H.^d	60	71	68	66	30.1	29.8	35.5	23.7	7.5	5.9	10.1	4.0	27.5	28.8	32.7	23.6
COPD M.^b	60	71	68	66	59.3	54.4	74.4	47.1	24.5	12.9	35.5	11.0	54.9	50.7	63.2	45.0
MI M.^e	37	53	45	53	64.6	61.8	127.8	50.9	32.0	28.8	2.2	21.4	57.6	56.9	95.4	48.6
COPD E.D.V.^a	43	54	45	53	46.7	68.3	68.7	44.2	16.0	25.1	17.6	13.2	46.6	63.0	65.4	43.4
Asthma E.D.V.^c																

^a Age-adjusted rate of hospitalizations (COPD H) and emergency department visits (COPD EDV) for COPD for persons 25 and over per 10,000 population

^b Age-adjusted death rate from COPD among persons 25 and over per 100,000 population (COPD Mortality)

^c Age-adjusted rate of hospitalizations (Asthma H) and emergency department visits (Asthma EDV) for asthma per 10,000 population

^d Age-adjusted rate of hospitalizations for myocardial infarction (MI. H.) among persons 35 and over per 10,000 population

^e Age-adjusted rate of death from myocardial infarction among persons 35 and older per 100,000 population (MI. Mortality)

MW[†]: US Midwest region

NE^{††}: US Northeast region

S^{†††}: US South region

W^{††††}: US West region

Table 3.4 Univariate analyses for the association between PM_{2.5} and outcomes variables (PM_{2.5}<12 µg/m³)

Outcome variables	N	Effect size ^a	95%CI	P-value
COPD Hospitalizations	245	1.06	(1.02, 1.09)	0.0040
COPD EDV ^b	177	1.04	(0.99, 1.09)	0.1317
COPD Mortality	253	1.01	(0.99, 1.03)	0.4941
Asthma Hospitalizations	250	1.06	(1.03, 1.09)	0.0007
Asthma EDV ^b	184	1.04	(1.01, 1.08)	0.0065
MI ^c Hospitalizations	253	1.03	(1.01, 1.05)	0.0005
MI ^c Mortality	253	1.04	(1.01, 1.07)	0.0051

^a Unit change in outcome for 1-unit increase in annual PM_{2.5} concentration

^b EVD: emergency department visits

^c MI: myocardial infarction

Table 3.5 Multivariate analyses for the association between PM_{2.5} and outcomes variables (PM_{2.5}<12 µg/m³)

Outcome variables	N	Effect size ^a	95%CI	P-value
COPD Hospitalizations	245	2.97	(1.32, 6.69)	0.0085
COPD EDV ^{**}	177	0.95	(0.90, 0.99)	0.0455
COPD EDV ^b	253	0.99	(0.97, 1.01)	0.4168
COPD Mortality	250	2.75	(1.21, 6.23)	0.0155
Asthma Hospitalizations	184	2.83	(1.34, 5.93)	0.0070
Asthma EDV ^b	253	1.01	(0.99, 1.03)	0.2092
MI ^c Hospitalizations	253	1.01	(0.98, 1.04)	0.3978
MI ^c Mortality				

^a Unit change in outcome for 1-unit increase in annual PM_{2.5} concentration

^b EVD: emergency department visits

^c MI: myocardial infarction

Table 3.6 Multivariate analyses for the association between PM_{2.5} and outcomes variables for urban counties (PM_{2.5}<12 µg/m³)

Outcome variables	N	Effect size ^a	95%CI	P-value
COPD Hospitalizations	210	2.74	(1.34, 5.64)	0.0062
COPD EDV ^b	149	0.29	(0.12, 0.73)	0.0090
COPD Mortality	217	0.46	(0.28, 0.77)	0.0034
Asthma Hospitalizations	214	3.10	(1.35, 7.10)	0.0081
Asthma EDV ^b	155	2.92	(1.28, 6.69)	0.0109
MI ^c Hospitalizations	217	1.42	(0.93, 2.18)	0.1030
MI ^c Mortality	217	1.03	(1.01, 1.06)	0.0360

^a Unit change in outcome for 1-unit increase in annual PM_{2.5} concentration

^b EVD: emergency department visits

^c MI: myocardial infarction

Table 3.7 Multivariate analyses for the association between PM_{2.5} and outcomes variables for rural counties (PM_{2.5}<12 µg/m³)

Outcome variables	N	Effect size ^a	95%CI	P-value
COPD Hospitalizations	35	7.10	(0.03, 1864.1)	0.4788
COPD EDV ^b	28	0.27	(0.00, 126.2)	0.6617
COPD Mortality	36	1.27	(0.12, 14.07)	0.8322
Asthma Hospitalizations	36	1.77	(0.04, 75.19)	0.7580
Asthma EDV ^b	29	1.82	(0.16, 20.29)	0.6166
MI ^c Hospitalizations	36	0.94	(0.06, 15.03)	0.9651
MI ^c Mortality	36	0.99	(0.90, 1.09)	0.8654

^a Unit change in outcome for 1-unit increase in annual PM_{2.5} concentration

^b EVD: emergency department visits

^c MI: myocardial infarction

Table 3.8 Multivariate analyses for the association between PM_{2.5} and outcomes variables for the US Midwest region (PM_{2.5}<12 µg/m³)

Outcome variables	N	Effect size ^a	95%CI	P-value
COPD Hospitalizations	53	0.25	(0.02, 3.90)	0.3135
COPD EDV ^b	37	0.09	(0.00, 1.84)	0.1143
COPD Mortality	60	0.66	(0.26, 1.72)	0.3926
Asthma Hospitalizations	60	0.33	(0.02, 6.69)	0.4693
Asthma EDV ^b	43	0.15	(0.01, 1.70)	0.1208
MI ^c Hospitalizations	60	0.29	(0.06, 1.46)	0.1305
MI ^c Mortality	60	0.90	(0.19, 0.99)	0.0272

^a Unit change in outcome for 1-unit increase in annual PM_{2.5} concentration

^b EVD: emergency department visits

^c MI: myocardial infarction

Table 3.9 Multivariate analyses for the association between PM_{2.5} and outcomes variables for the US Northeast region (PM_{2.5}<12 µg/m³)

Outcome variables	N	Effect size ^a	95%CI	P-value
COPD Hospitalizations	69	0.08	(0.01, 0.78)	0.0300
COPD EDV ^b	53	1.60	(-2.62, 94.63)	0.8191
COPD Mortality	70	0.08	(0.01, 0.93)	0.0445
Asthma Hospitalizations	68	6.05	(0.07, 513.86)	0.4204
Asthma EDV ^b	54	0.93	(0.02, 54.05)	0.9725
MI ^c Hospitalizations	70	0.11	(0.02, 0.73)	0.0229
MI ^c Mortality	70	1.04	(1.00, 1.09)	0.0465

^a Unit change in outcome for 1-unit increase in annual PM_{2.5} concentration

^b EVD: emergency department visits

^c MI: myocardial infarction

Table 3.10 Multivariate analyses for the association between PM_{2.5} and outcomes variables for the US South region (PM_{2.5}<12 µg/m³)

Outcome variables	N	Effect size ^a	95%CI	P-value
COPD Hospitalizations	67	0.17	(0.00, 39.65)	0.5154
COPD EDV ^b	44	0.02	(0.00, 584.06)	0.4608
COPD Mortality	67	2.64	(0.06, 127.74)	0.6178
Asthma Hospitalizations	66	0.25	(0.01, 9.30)	0.4491
Asthma EDV ^b	44	31.19	(0.23, 4315.6)	0.1659
MI ^c Hospitalizations	67	1.80	(0.08, 40.04)	0.7039
MI ^c Mortality	67	1.12	(1.05, 1.20)	0.0010

^a Unit change in outcome for 1-unit increase in annual PM_{2.5} concentration

^b EDV: emergency department visits

^c MI: myocardial infarction

Table 3.11 Multivariate analyses for the association between PM_{2.5} and outcomes variables for the US West region (PM_{2.5}<12 µg/m³)

Outcome variables	N	Effect size ^a	95%CI	P-value
COPD Hospitalizations	56	8.41	(1.65, 42.52)	0.0114
COPD EDV ^b	43	2.64	(0.17, 40.85)	0.4781
COPD Mortality	56	2.29	(0.11, 6.69)	0.1294
Asthma Hospitalizations	56	2.25	(0.77, 6.49)	0.1334
Asthma EDV ^b	44	2.56	(0.54, 12.18)	0.2305
MI ^c Hospitalizations	56	1.88	(0.88, 3.97)	0.1020
MI ^c Mortality	56	1.00	(0.97, 1.04)	0.9052

^a Unit change in outcome for 1-unit increase in annual PM_{2.5} concentration

^b EDV: emergency department visits

^c MI: myocardial infarction

Table 3.12 Sensitivity analysis table

Outcome variables	Levels of PM _{2.5}	N	Effect size ^a	95%CI		P-value
COPD Hospitalizations ^b	<11	236	2.86	1.19	6.90	0.0194
	<10	210	4.86	1.58	14.96	0.006
	<9	151	9.15	1.96	42.84	0.0052
COPD EDV ^b	<11	173	0.95	0.90	1.00	0.0621
	<10	156	0.96	0.90	1.02	0.1793
	<9	123	0.90	0.84	0.97	0.0066
COPD Mortality ^c	<11	244	0.48	0.27	0.84	0.0113
	<10	217	1.00	0.98	1.03	0.8107
	<9	155	0.36	0.14	0.95	0.0382
Asthma Hospitalizations ^d	<11	241	2.93	1.20	7.12	0.018
	<10	215	4.35	1.54	12.28	0.0057
	<9	154	13.73	3.39	55.52	0.0003
Asthma EDV ^d	<11	180	3.71	1.64	8.41	0.0018
	<10	163	6.39	2.38	17.13	0.0003
	<9	127	8.48	2.25	31.99	0.0018
MI. Hospitalizations ^e	<11	244	1.01	0.99	1.04	0.2857
	<10	217	1.02	0.99	1.04	0.2305
	<9	155	1.01	0.98	1.04	0.6402
MI. Mortality ^f	<11	244	1.01	0.98	1.04	0.4666
	<10	217	1.01	0.98	1.05	0.5385
	<9	155	1.01	0.96	1.06	0.7337

^a Unit change in outcome for 1-unit increase in annual PM_{2.5} concentration, controlling for heat index

^b Age-adjusted rate of hospitalizations (COPD H) and emergency department visits (COPD EDV) for COPD for persons 25 and over per 10,000 population

^c Age-adjusted death rate from COPD among persons 25 and over per 100,000 population (COPD Mortality)

^d Age-adjusted rate of hospitalizations (Asthma H) and emergency department visits (Asthma EDV) for asthma per 10,000 population

^e Age-adjusted rate of hospitalizations for myocardial infarction (MI. H.) among persons 35 and over per 10,000 population

^f Age-adjusted rate of death from myocardial infarction among persons 35 and older per 100,000 population (MI. Mortality)

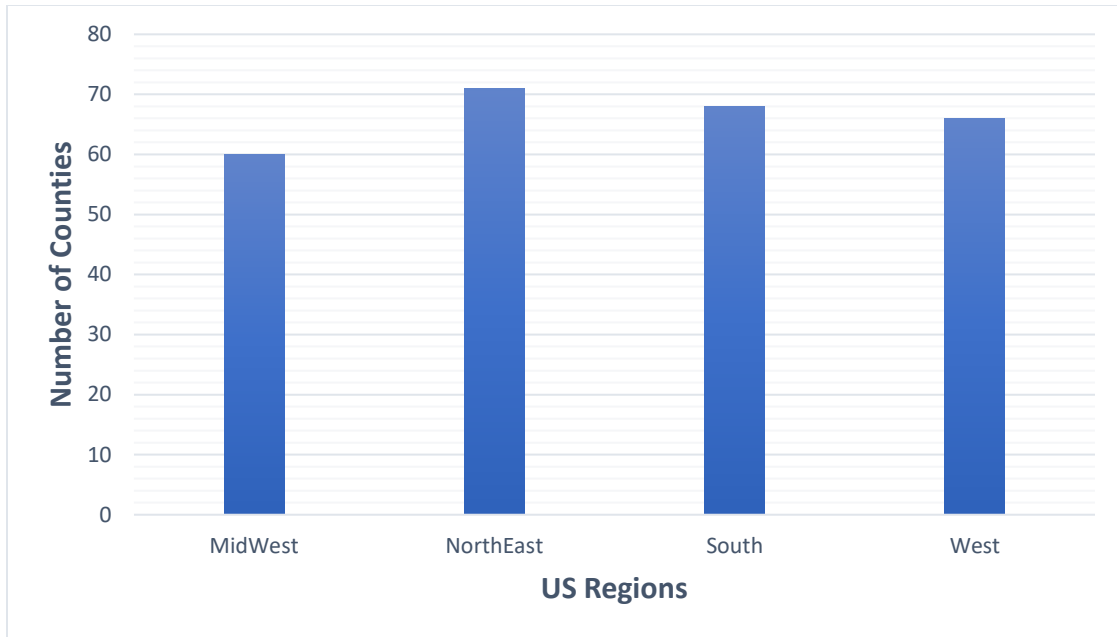


Figure 3.2. US counties covered in the study by US Regions

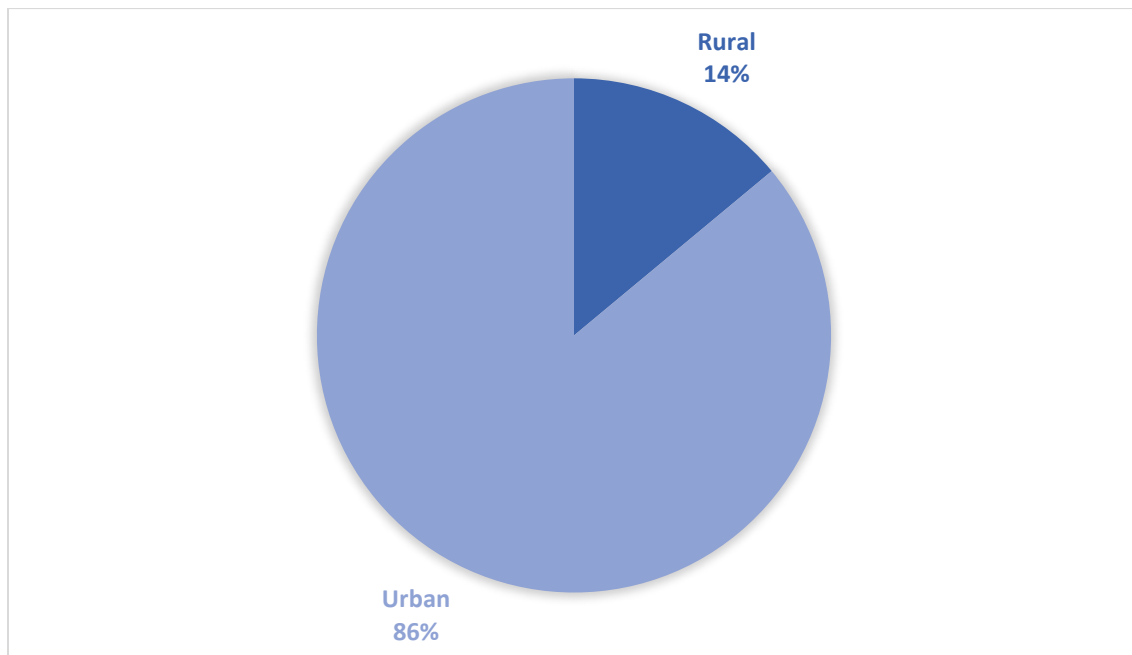


Figure 3.3 US counties covered in the study by rurality

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