Assessing Associations Between Emergency Room Visits for Respiratory and Cardiovascular Diseases and Criteria Air Pollutants Exposure in New York State

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Assessing Associations Between Emergency Room Visits for Respiratory and Cardiovascular Diseases and Criteria Air Pollutants Exposure in New York State

by

Tamba Solomon Lebbie

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Abstract

Air pollution is a major environmental health hazard for the general population. Approximately 90% of the global population is at risk of both indoor and outdoor air pollution, and it accounts for an estimated 7 million premature deaths every year according to the World Health Organization (WHO). Multiple studies including epidemiological and molecular analyses have confirmed the negative effects of air pollutants on human health even at levels within the WHO guidelines. This study examines the health impacts of releases of criteria air pollution from point sources in New York State (NYS). There is evidence from population studies that have shown that increases in levels of the criteria air pollutants (CAPs) are associated with increases in cardiovascular and respiratory diseases. The criteria pollutants include particulates (PM$_{10}$ and PM$_{2.5}$), sulfur dioxide (SO$_2$), nitrous oxides (NOx), carbon monoxide (CO), ozone (O$_3$), and lead (Pb), as defined by the United States Environmental Protection Agency (USEPA). While emissions from point sources such as fixed industries and power plants are only one relatively minor component of total air pollution, because they are localized can allow one to examine the effects of these releases on the local population. In this ecologic study I have determined the association between emergency room (ER) visits that did not result in hospitalization for respiratory and cardiovascular diseases in NYS among individuals living in zip codes containing point sources of CAPs. Of particular interest is the examination of the release effects of particulates relative to the gaseous pollutants that have been studied less because they are more difficult to measure.

The specific aims of this dissertation project are to assess the associations, if any, between ER visits for asthma, chronic obstruction pulmonary disease (COPD), ischemic heart disease (IHD)
and myocardial infarction (MI) and zip code level exposure to the CAPs, NOx, SO2, CO, and particulates (PM\textsubscript{2.5} and PM\textsubscript{10}) among patients who live in zip codes that have point source emissions of the CAPs in NYS from 2010 to 2018 after control for other sources of air pollution and rates of smoking and level of poverty, and to determine the individual contribution of each criteria pollutant. Unfortunately, the exposure source I will use does not include information on O\textsubscript{3} and there are minimal releases of Pb, so it will not be studied.

This was achieved by using publicly available data sets, the National Emissions Inventory (NEI) by the USEPA for exposure data, the United States Decennial Census (USDC) for population data, the Behavioral Risk Factor Surveillance System (BRFSS) for smoking data, the United States Census Bureau (USCB) for poverty, and the Statewide Planning and Research Cooperative System (SPARCS) for ER visits data. In the first aim, a generalized linear model with Quasi-Poisson regression is used, while the linear mixed effects regression model with a random county level effect is used in the second and third aims to analyze the rates of ER visits for all the diseases in the study and their associations with the CAPs. A \( p \)-value of <0.05 was considered statistically significant. The model fit was assessed with an R-squared likelihood ratio test and performance score as measures of goodness of fit. All analyses were conducted with statistical software package R programming language.

The results of this dissertation show positive associations between all of the CAPs and all of the diseases in the study except MI for which most patients are recorded as hospital admissions (HAs). A major unexpected observation is that the gaseous pollutants (CO, NOx, SO\textsubscript{2}) showed much stronger associations with asthma, COPD and IHD than the particulates (PM\textsubscript{2.5} and PM\textsubscript{10}), although this may in part be because the gaseous air pollutants are greater from point sources. In addition, for COPD there was a greater risk from PM\textsubscript{10} than PM\textsubscript{2.5}, indicating that while larger
particulates do not penetrate deep into the alveoli, they still can increase risk of respiratory
disease. These results demonstrate that CAPs point source pollution results in a small but
significant contribution to the risk of respiratory and cardiovascular diseases in relation to ER
visits that did not result in hospitalization. There are limitations to this study as it uses an
ecologic study design that has the potential for misclassification of the exposure, and has
analyzed only data from ER visits, not hospitalization. There is also a potential for residual
confounding. Future research using more sophisticated study designs could better assess the
research questions of interest.
Acknowledgement

Foremost, I want to offer this endeavor to our God Almighty for the wisdom, strength, peace of mind and good health he bestowed upon me in carrying out this program.

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List of Abbreviations and Acronyms

ACGIH = American Conference of Governmental Industrial Hygienists
ACOS = Asthma-COPD Overlap Syndrome
BRFSS = The Behavioral Risk Factor Surveillance System
CAPS = Criteria Air Pollutants
CDC = Centers for Disease Control and Prevention
CI = Confidence Interval
CO = Carbon monoxide
COPD = Chronic Obstructive Pulmonary Disease
DEC = Department of Environmental Conservation
ED = Emergency Department
EPA = Environmental Protection Agency
ER = Emergency Room
FIPS = Federal Information Processing
GAR = Global Asthma Report
GBD = Global Burden of Disease
GINA = Global Initiative for Asthma
HA = Hospital Admission
ICD-10 = International Classification of Diseases, Tenth Revision
ICD-9 = International Classification of Diseases, Ninth Revision
IHD = Ischemic Heart Disease
IQR = Inter Quartile Range
ISA = Integrated Science Assessment
MI = Myocardial Infarction
NAAQS = National Ambient Air Quality Standards
NEI = National Emissions Inventory
NIH = National Institute of Health
NIOSH = National Institute for Occupational Safety and Health
NO₂ = Nitrogen dioxide
NOₓ = Oxides of nitrogen
NYS = New York State
NYSDOH = New York State Department of Health
O₃ = Ozone
OR = Odds Ratio
OSHA = Occupational Safety and Health Administration
PAHs = Polycyclic Aromatic Hydrocarbons
Pb = Lead
PEL = Permissible Exposure Limit
PM = Particulate Matter
PM₁₀ = Particulate matter with an aerodynamic diameter ≤ 10 µm
PM₂.₅ = Fine particulate matter with an aerodynamic diameter ≤ 2.5 µm
POP = Persistent Organic Pollutant
ROS = Reactive Oxygen Species
RR = Relative risk
SAIPE = Small Area Income and Poverty Estimates
SD = Standard Deviation
SES = Socio Economic Status
SPARCS = Statewide Planning and Research Cooperative System
TLV = Threshold Limit Value
TWA = Time-Weighted-Average
US = United States
USCB = United States Census Bureau
USDC = United States Decennial Census
USEPA = United States Environmental Protection Agency
WHF = World Heart Federation
WHO = World Health Organization
YLD = Years Lived with Disability
Chapter 1

1.0. Introduction: Respiratory and Cardiovascular Diseases Due to Criteria Air Pollutants.

1.1. Air Pollution

Air pollution poses a significant challenge to environmental and public health worldwide and has become a priority in the sustainable development agenda (Yeo & Kim, 2022). Both developed and developing countries are impacted by air pollution but people living in low- and middle-income countries are disproportionately affected (WHO, 2021) compared to high-income countries (Dhimal et al., 2021). While developed countries have instituted controls on release of air pollutants, air pollution remains a serious cause of morbidity and mortality even in the United States (US) (Ou et al., 2020).

Air pollution is a complex mixture of gases, volatile organic compounds (VOCs) and particulate matter (PM) that are released into the air through natural means like volcanic eruptions and wind-blown dusts, or by man-made activities including vehicle emissions, fuel oils and natural gas to heat homes, manufacturing and power generation, particularly coal-fueled power plants, and fumes from chemical production (Almetwally, Bin-Jumah & Allam, 2020; Byrwa-Hill et al., 2020; Jiang et al., 2016). Air pollutants consist of criteria air pollutants (CAPs), including particulates and gases, VOCs including benzene, styrene, and toluene, persistent organic pollutants (POPs) which include dioxins, furans, polychlorinated biphenyls, hazardous air pollutants (HAPs) such as perchloroethylene, methylene chloride, and metals such as cadmium, mercury, and chromium, and polycyclic aromatic hydrocarbons (PAHs) such as acenaphthylene, chrysene, fluoranthene, and naphthalene. However, this study only focuses on the CAPs, smoking and poverty and their association with respiratory and cardiovascular diseases.
Air pollution includes both indoor and outdoor environments and studies have shown indoor air pollutant concentrations are usually higher than outdoor concentrations (Leung, 2015). This is because outdoor pollution concentrations and building airtightness have a great influence on indoor air quality, due to the possibility of transportation of contaminants from outdoors to indoor (Tran et al., 2020). The higher concentration of pollutants from outdoor, coupled with emission strength and less volume for dilution in the indoor environment contribute to high indoor air pollution (Kang et al., 2021). There are many added other sources of indoor air pollution due to heating and cooking as well as releases from building materials, fabrics, and other household items (Al-Kindi et al., 2020; Rosário Filho et al., 2021). However, sources of outdoor pollution including vehicle traffic, industry, as well as burning of fossil fuels, especially coal, have been determined to contribute to indoor air pollution (Chen & Zhao, 2011). Since most people spend a large part of their time indoors, it is important to understand the relationship between indoor and outdoor particles. However, this dissertation project is only looking at the effects of outdoor or ambient air pollution on human health.

Air pollutants have been well documented for their hazardous impacts on human health especially diseases of the respiratory and cardiovascular systems (Dominski et al., 2021; Singh, Rai, & Jadon, 2021; Atkinson et al., 2014; Anenberg et al., 2018). Air pollution also harms the environment (Jiang et al., 2016; Cox, 2017) and increases the risk of death in both children and adults (Dominski et al., 2021).

Since air pollution is widespread and has the potential for extensive public health consequences, the World Health Organization (WHO) underscores the need for air quality improvement, estimating that air pollution accounts for approximately seven million premature deaths annually around the world (WHO, 2021). This was emphasized by the WHO Director General, Dr. Tedros
Adhanom Ghebreyesus during the first WHO Global Conference on Air Pollution and Health in 2018 when he referred to air pollution as a silent public health emergency (Morawska, 2019).

The Southeast Asian and Western Pacific regions bear most of the burden of air pollution (Babatola, 2018) which is due to heavy industrial activities, dense vehicular traffic, the nonpolitical will to stop industries from polluting the environment, and/or the technologies to combat air pollution are either limited or nonexistent. And the criteria pollutants, particulates (PM$_{2.5}$ and PM$_{10}$), carbon monoxide (CO), ozone (O$_3$), nitrogen oxides (NOx), sulfur dioxide (SO$_2$) and lead (Pb) are of major public health concern (WHO, 2021; Tomić-Spirić et al., 2021).

Previous and current epidemiologic studies conducted in various regions of the world have found associations between changes in levels of air pollution and rates of emergency room (ER) visits for different respiratory and cardiovascular conditions (Phosri et al., 2019; Zhou & Zhang, 2023). One way to study effects of air pollution is to compare morbidity and mortality for certain diseases in cities with high levels of air pollution as compared to those with less.

A prospective cohort study was conducted by Dockerty et al. (1993) to estimate the effects of air pollution on mortality in six US cities including Portage in Wisconsin, Topeka in Kansas, Watertown in Massachusetts, St. Louis, Harriman in Tennessee and Steubenville in Ohio. They used a 14 to 16 year mortality follow-up data on 8111 adults and found that cities with greater levels of air pollution showed higher rates of respiratory and cardiovascular morbidity and mortality. The study results found significant associations between air pollutants, particularly PM$_{2.5}$ including sulfates and air pollution related mortality. The results further indicated that air pollution related deaths were mostly for lung cancer, and cardiopulmonary diseases. In comparing the cities, the adjusted mortality rate ratio (RR) for the most polluted of the cities (Steubenville in Ohio) as compared to the least polluted city (Portage in Wisconsin) was 1.2
The results of this study show comparable results with previous population-based cross-sectional studies and daily time-series studies, further solidifying evidence for the conclusion that exposure to air pollution contributes to excess mortality.

Yet another method to study effects of air pollution on human health is to compare rates of morbidity and mortality on days where air pollution is high as compared to days when it is low. This approach allows one to follow the time course of morbidity after high exposure over a period of days following the extreme event. Our colleagues at UAlbany have used this approach extensively in studies in Karachi, Pakistan and in several cities in Saudi Arabia.

Khwaja et al. (2013) conducted a study in Karachi, Pakistan on the effect of air pollution on daily morbidity. They monitored levels of daily PM$_{2.5}$ exposure in two different locations in Karachi, one of the most polluted cities in the world. One of the sampling sites was an industrial and residential neighborhood, while the other site was a commercial and residential area near a major highway. The study results show a significant association between higher levels of PM$_{2.5}$ exposure and considerable elevation in rates of ER visits and hospitalizations for ischemic heart disease (IHD) and myocardial infarction (MI). This is congruent with similar studies (Nayebare et al., 2017;2022) conducted elsewhere in developed and developing countries (Zhang et al., 2018; Wu et al., 2019).

Stieb et al. (2009) conducted a multi city time series analysis on nearly 400,000 emergency department (ED) visits to 14 hospitals in seven Canadian cities during the 1990s and early 2000s to examine associations between CO, NO$_2$, O$_3$, SO$_2$, and particulates(PM$_{2.5}$ and PM$_{10}$), and hospital visits for MI, heart failure (HF), dysrhythmia, asthma, chronic obstructive pulmonary disease (COPD), and other respiratory infections. They found that daily average concentrations of CO and NO$_2$ exhibited the most consistent associations with ER visits for cardiac conditions.
especially at lag day 2. And for every 0.7 ppm increase in CO and 18.4 ppb increased in NO₂ correspondingly increased visits for MI at lag 0 days. O₃ at lag 2 days showed the most consistent associations with visits for respiratory conditions. The particulates were strongly associated with asthma visits during the warm season. These results are consistent with other studies further confirming that air pollution is a major contributing factor to adverse health events.

Another study carried out in Doña Ana county, New Mexico, US investigated the associations of ambient particulates and O₃ with ER visits and HAs for respiratory and cardiovascular visits in adults. Particulates and O₃ from sources within 500km of the study area (Doña Ana) were predominant, which subsequently showed an increase of 3.1% and 2.8% cardiovascular emergencies for a 10μg/m³ increase in PM₁₀ and PM₂.₅ respectively (Rodopoulou et al., 2014).

A third way to study effects of air pollution within a population is to investigate rates of ER visits and/or inpatient admissions to hospitals among people living near to point sources of air pollution as compared to those who do not. These studies make the assumption that there is widespread pollution coming from traffic and other common sources but that the air pollution coming from power plants and factories will add a level of morbidity to local residents that will result in more frequent disease.

This approach was utilized by Lee et al. (2021) in New York State (NYS) to examine associations between rates of ED visits for respiratory diseases from 2011-2015, and residential exposures to PM₂.₅, SO₂, and NO₂ around 15 biorefinery sites and 15 non refinery sites considered as control areas. In addition, the study also assessed whether the observed relationships varied by biomass types, seasons, and respiratory subtypes. The results found respiratory ED visit rates among residents living within 10 km of biorefineries to be significantly
higher with RRs ranged from 1.03 to 3.64 than in those in control areas, especially around corn and soybean biorefineries during spring and winter seasons. NO$_2$ showed the most effects.

Mechanisms whereby air pollutants cause human diseases include oxidative stress and inflammation, mitochondrial dysfunction, and increase autonomic nervous system activation (Shukla et al., 2019; Miller & Newby, 2020). There is strong evidence that while air pollution causes harm to the respiratory system, greater morbidity and mortality are associated with effects on the cardiovascular system (Hamanaka & Mutlu, 2018). This is due to the fact that air pollutants that cross the mucus and cilia of the airway reaching the alveoli of the lung cause oxidative stress by generating reactive oxygen species (ROS) that cause both local and distant cellular damage (Ghelfi, 2011). The endothelial cell of the vascular system is particularly vulnerable to oxidative stress mediated by proinflammatory cytokines and other reactive mediators (Uzoigwe et al., 2013). Permanent production of ROS under exposure of the lung to air toxins causes secretion of cytokines and cellular dysfunction. In consequence, breakdown of the lung is observed and several abnormal conditions, such as COPD, bronchitis, and lung cancer can be initiated (Shahriyari et al., 2022).

### 1.2. Criteria Air Pollutants

In the US, the Clean Air Act established in the 1970s mandates the Environmental Protection Agency (EPA) to establish the National Ambient Air Quality Standards (NAAQS) for six of the most common air pollutants known as criteria pollutants: CO, NOx, O$_3$, PM, SO$_2$, and Pb. These pollutants are ubiquitous across the world and are linked to adverse health outcomes through their diverse concentrations and complex chemical and physical properties (Fiordelisi et al., 2017; Civerolo et al., 2017; Castner et al., 2018).
Particulates have been the most studied. These vary in numbers, sizes, shapes, surface area, chemical compositions, solubility, concentration, and origin (Pope & Dockery, 2006), and are emitted from a wide range of sources. The size of a particulate is a key factor in determining its effects, as is the composition of the particulate. While large particles are trapped in the upper airways and removed through the action of mucus and cilia, small particles can penetrate deep into the alveoli to cause cellular damage (Ali et al., 2019). The smaller the particle size the greater its relative surface area, and this exponentially boosts the increase of biological activity. As a result, the focus of research on air pollution and its health effects has shifted to smaller particles such as PM$_{2.5}$ and ultrafine particles (PM$_{0.1}$) (Chen et al., 2016).

Particulate composition is also important (Zeb et al., 2018). Some particulates are black carbon, consisting only of carbon and hydrogen. Others are simple dirt or sand, with minor contributions of organic material. Others contain various metals bound to the particles. Polyaromatic hydrocarbons may also be bound. In such cases toxicity is not only from the particle size but also added toxicity due to the attached metals or organic molecules.

Several epidemiological and mechanistic studies have documented significant associations between concentrations of the CAPs and the increased risks of ER visits for diseases including asthma, COPD, IHD, and MI (Szyszkowicz et al., 2018; Zheng et al., 2015; DeVries et al., 2017; Tzivian, 2011; Chen et al., 2022; Roy et al., 2014; Lee et al., 2021), and air pollution-related deaths (Maji et al., 2017).

Maji et al. (2017) conducted a time series study to estimate the short-term effects of criteria pollutants on mortality in Delhi, India for the period 2008 to 2010. The study results showed significant associations between short-term exposure to the criteria pollutants and mortality, especially NO$_2$. The study further estimated a 0.14% increase in mortality for every 10μg/m$^3$
increase in PM$_{10}$ concentration. The study found a significant association of all-natural-cause mortality in association with short-term exposure to particulates and gaseous pollutants. The study estimated 0.14% (0.02%-0.26%) percentage increase in all-cause-mortality for every 10μg/m$^3$ increase in PM$_{10}$ concentration. NO$_2$ showed the most significant positive association of 1.00% (0.07%-1.93%) increase with every 10μg/m$^3$ increase in daily NO$_2$ concentration. O$_3$ and CO showed high significance after controlling for the effects of NO$_2$. Age stratified analysis revealed that particulates have maximum effect for people over 65 years [RR=1.002 (1.000-1.004)] and gaseous pollutants exhibited maximum effect estimate [RR=1.016 (1.002-1.030)] for ages 5-44 years.

The United States Environmental Protection Agency (USEPA) in the National Emissions Inventory (NEI) distinguishes CAPs emitted from various sources categorized as point, non-point, on road, non-road, and events. Point source is defined as any single identifiable or confined source of pollution from which pollutants are discharged, such as a pipe, factory smokestack, sewage treatment plants, oil refineries, pulp, and paper mills, chemical, electronics and automobile manufacturers. Nonpoint are small stationary sources of air pollution which by themselves may not emit very much, but when added together, account for a significant portion of the total emissions. Examples include residential heating, commercial combustion, asphalt paving, pesticide use, dry cleaners, gas stations, oil wells or fracking sites. On-road air pollution sources are from vehicles found on roads and highways, including cars, trucks, buses, and motorcycles. While the non-road sources include aircraft, trains, lawnmowers, boats, dirt bikes, construction vehicles, farm equipments, leaf blowers, and more. Event sources are things such as a forest fires which can release a lot of air pollution but is a one-time event.
1.3. Asthma

Asthma is a chronic inflammatory airway disease that affects both children and adults (Sockrider & Fussner, 2020; Liu et al., 2022). It is a serious global health problem that impacted an estimated 262 million people in 2019 and caused 455,000 deaths according to the Global Burden of Disease (GBD) study (WHO, 2023). Currently more than 25 million people in the US have asthma (NIH, 2023; Grant et al., 2022), and up to 339 million people are affected by asthma globally according to the World Health Organization (WHO). Asthma poses an unacceptable burden on health care systems through increased ER visits and HAs, medication dispensations and affects society through loss of productivity in the workplace (Levy et 2023; Battaglia et al., 2016; Curto et al., 2019). Asthma exacerbations result in about 2 million ER visits annually, and 1 in 13 people in US are affected, accounting for over 1000 daily deaths, according to the Centers for Disease Control and Prevention (CDC) (Ho et al., 2021; Zuo et al., 2019).

What causes some people to develop asthma is uncertain, but genetic susceptibility and early life exposures to infections and immune-stimulating agents has been hypothesized as being important (Wang et al., 2023). However, many things can trigger asthma attacks in individuals with asthma. Several factors including genetics, allergies, and environmental exposures contribute to the prevalence and exacerbation of asthma (Murrison et al., 2019). These include environmental risk factors such as allergies due to dust mites and cockroaches, tobacco, and microbes (Global Burden of Disease, 2019; Toskala & Kennedy, 2015). Environmental factors such as cigarette smoke, CAPs and high humidity are all known to trigger asthma in susceptible individuals (WHO, 2023). Even exercise or sudden exposure to cold can cause asthma attacks (D’Amato et al., 2018).
Asthma can either be atopic or non-atopic depending on the prevailing circumstance. Atopic asthma represents the most common form of asthma especially in children (Comberiati et al., 2017; Kuruvilla et al., 2019) and is characterized by eosinophilic airway inflammation associated with specific immunoglobulin E (IgE) antibodies sensitization to various allergens. Atopic asthma accounts for 56.3% of asthma cases in the US (Comberiati et al., 2017). Non-atopic asthma, or non-allergic asthma, is a rarer form of asthma that is not caused by being exposed to allergens, and accounts for 43.7% of all asthma cases (Baos et al., 2018). Non-allergic asthma is generally defined as nonatopic asthma with or without normal serum levels of IgE antibodies (Crespo-Lessmann et al., 2020). It usually doesn’t develop until later in life and affects women more often than men (Kuruvilla et al., 2019; Garcia & Blake, 2020).

Symptoms of asthma include wheezing, persistent cough, shortness of breath or difficulty breathing, and chest tightness, making it difficult to breathe deeply (Orellano et al., 2017; Zuo et al., 2019). Asthma attacks can easily trigger dyspnea and bronchospasms, even leading to death in extreme situations (Barbaro et al., 2011).

There is strong evidence showing air pollution and the various criteria pollutants to be associated with increased risks of asthma attacks and exacerbations. A meta-analysis with 16 studies from the US, Canada, Finland, and Taiwan, using conditional logistic regression, poisson regression and generalized additive models to find the association between PM$_{2.5}$ and asthma ER visits, found PM$_{2.5}$ concentration to be associated with increases in ER visits for asthma [RR=1.5 % per 10μg/m$^3$ (1.2%-1.7 %)], and children were more susceptible [3.6 % per 10 μg/m$^3$ (1.8-5.3 %)] than adults [1.7% per 10 μg/m$^3$ (0.7 %, 2.8 %)] especially during the warm season where it increased by 3.7 % (0.5, 6.9 %) per 10 μg/m$^3$ increase in PM$_{2.5}$, as compared to the cold season 2.6% (0.7-4.6 %) (Fan et al., 2016).
Another systematic review and meta-analysis that was carried out by Zheng et al., (2015) to quantify associations between short-term exposures to O₃, CO, NO₂, SO₂, PM₂.₅, and PM₁₀, and asthma-related ER visits and HAs found significant associations between short-term exposures to air pollutants and increased risks for asthma-related ER visits and HAs. Air pollutants were associated with significantly increased risks of asthma ER visits and HAs with O₃ RR(95%CI), 1.009(1.006-1.011), CO [RR=1.045(1.029-1.061)], NO₂ [RR=1.018(1.014-1.022)], SO₂ [RR=1.011(1.007-1.015)], PM₁₀ [RR=1.010(1.008-1.013)], and PM₂.₅ [RR=1.023(1.015-1.031)]. Stronger associations were found in hospitalized males, children and elderly patients in warm seasons with lag of 2 days or greater. A lag of 2 days means that the ER visits increased two days after the sudden elevation in air pollution.

1.4. **Chronic Obstructive Pulmonary Disease**

COPD is a chronic respiratory disease and a form of progressive lung diseases that includes chronic bronchitis and emphysema, all of which cause difficulty breathing (GOLD, 2017; Soriano & Lamprecht, 2012). It is marked by excessive mucus production, coughing, wheezing, and dyspnea and is characterized by airflow limitation due to chronic inflammation in the airway system (WHO, 2023; de Vries et al., 2023; GOLD, 2017). It can also result from structural damage to the alveoli (Hadzic et al., 2020). COPD affects about 5.7% of all adults in the US and 328 million people worldwide (DeMeo et al., 2022; Sobrino et al., 2017; Qu et al., 2021) and accounted for over 3 million deaths in 2015 globally according to WHO (Qiu et al., 2018). It is predicted to become the third leading cause of death by 2030 (Khatri & Tamil, 2018; Zhu et al., 2023).

The major causes of COPD include smoking and chronic bacterial and viral infection (Taylor, 2010). While there is no specific evidence that air pollution causes COPD, it is a major factor in
triggering the need for ER visits or hospitalization (Ko & Hui, 2012). Studies have shown environmental risk factors to be significantly linked with hospital visits for worsening COPD (Zhu et al., 2023; Tian et al., 2014; Lee et al., 2021).

A time series systematic review was conducted by Li et al., (2016) to evaluate associations between short-term exposure to O$_3$, CO, NO$_2$, SO$_2$, PM$_{10}$, and PM$_{2.5}$ and the risk of COPD exacerbations in various regions of the world. The main aim was to evaluate the associations between short-term exposure to these pollutants and the risk of COPD exacerbations using 59 studies from around the world. The study results found significant associations, particularly for SO$_2$ and NO$_2$ in low-and middle-income countries. There was a significant association between short-term exposure and COPD exacerbation risk for all pollutants in the study especially at lag0 and lag3 days. Health effects of SO$_2$ [RR=1.012 (1.001-1.023)], and NO$_2$ [RR=, 1.019 (1.014-1.024)] showed high significance in low-and middle-income countries. All pollutants showed acute effects on COPD, particularly NO$_2$ [RR=1.04 (1.03-1.06)] and O$_3$ [RR=1.03(1.01-1.04)].

Arbex et al. (2009) conducted an ecological time-series study in São Paulo, Brazil to investigate associations between daily number of COPD ER visits and the daily concentrations of PM$_{10}$, SO$_2$, NO$_2$, CO and O$_3$ using data collected between 2001 and 2003. The study found that CO, PM$_{10}$ and SO$_2$ showed strong associations with COPD ER visits, but NO$_2$ and O$_3$ showed mild effects. The results of the study confirmed previous study results that showed air pollution as a major contributor that affects human health, that eventually lead to ER visits or HAs. The authors concluded that CAPs are relevant risk factors that exacerbate COPD particularly in urban environments. PM$_{10}$ and SO$_2$ showed acute and lagged effects on COPD ER visits with an interquartile range (IQR) =28.3 µg/m$^3$ for PM$_{10}$ and 7.8 µg/m$^3$ for SO$_2$. Both pollutants were associated with a cumulative 6-day increase of 19% and 16% in COPD admissions, respectively.
Increases in CO concentration showed impacts in the female and elderly groups. NO\textsubscript{2} and O\textsubscript{3} had mild effects on the elderly and in women. The authors concluded that they identified associations between air pollution and daily COPD-related ER visits for women and people aged 40 years and older in the city of Sao Paulo, an urban environment in Brazil.

While CAPs can damage the respiratory tract and lungs in everybody, for those individuals that have chronic respiratory diseases such as asthma and COPD, air pollution can make the already bad situation worse, causing acute disease that requires ER visits or hospitalization. The mechanisms of action include obstruction of pulmonary ventilation and gas exchange. Pollutants that are inhaled can induce oxidative stress and inflammation, eventually resulting in airway injury and dysfunction (Li et al., 2016).

1.5. Ischemic Heart Disease

IHD, also known as coronary artery disease, is the most common type of heart disease (NHLBI, 2013). It is described as a condition in which the heart muscle gets damaged or becomes ineffective due to absence of or a reduced blood supply (Szyszko\v{w}icz & Mieczyslaw, 2007; Kasprzyk et al., 2018; Xu et al., 2021) as a result of plaque buildup on the walls of the heart’s arteries leading to inadequate amounts of rich oxygen being delivered to the heart (Severino et al., 2020). The consequences of IHD represent a significant burden on human health, in terms of mortality and morbidity (Severino et al., 2020). It is the main cause of death in adults in the US, and the number one cause of premature death and disability suffering globally. It was estimated to have affected around 126 million people worldwide in 2016 (Khan et al., 2020; Ferreira-González, 2014; Toledo-Chávarri et al., 2020). Around 9 million deaths were attributed to IHD between 2017 and 2019, accounting for 16\% of total deaths globally (Khan et al., 2020; Xu et al., 2021). It is the third leading cause of mortality worldwide and is associated with 17.8 million
deaths annually (Brown et al., 2020). Risk factors include stress, alcohol consumption, smoking, and the metabolic syndrome including elevated glucose, hypertension, visceral obesity, high serum lipids and thrombotic conditions (Kasprzyk et al., 2018). The financial impact of IHD due to ER visits, HAs, treatments, revascularization procedures, and prescribed drug treatments is also significantly high according to the World Heart Federation (WHF) (Khan et al., 2020).

The mechanism by which CAPs affect the cardiovascular system is through oxidative stress and inflammation by generating oxygen free radicals. When CAPs are inhaled, they disrupt cellular homeostasis by inducing the formation of free radicals from the mitochondria and a series of cellular enzymes eventually leading to changes in cell function inducing oxidative stress (Kelly & Fussell, 2017; Miller, 2020). The primary pathological process that leads to IHD is atherosclerosis, an inflammatory disease of the arteries associated with lipid deposition and metabolic alterations due to multiple risk factors. Oxidative stress and the inflammatory response have been suggested as possible pathophysiologic mechanisms for the impact of SO₂ on ischemic heart disease (Montone et al., 2023).

There is a large body of evidence showing that both short- and long-term exposures to criteria pollutants are associated with an increased risk of IHD (Kim et al., 2021). In fact, the harm of CAPs on the cardiovascular system is greater, from a public health point of view, than that on the respiratory system. A cohort study by Kim et al. (2021) in Korea from 2002 to 2013 using 2155 participants with IHD and 8620 control participants analyzed effects of SO₂, NO₂, O₃, CO, and PM₁₀ on IHD. The study was conducted to explore both short and long-term effects of air pollutants on the risk of IHD. The study found short-term exposure to SO₂ and long-term exposures to SO₂, O₃, and PM₁₀ to be associated with increased risk of IHD among older people, males, people of low-income, and urban dwellers. One-month exposure to SO₂ showed an OR
1.36 (1.06-1.75), and a 12-month exposure to SO₂, O₃, and PM₁₀ was associated with an OR=1.58 (1.01-2.47), OR=1.53 (1.27-1.84), and OR=1.14 (1.02-1.26) higher odds for IHD in people aged 60 years and above, males, and low-income people. These results are in line with previous studies that have reported elevated mortality due to short-term exposure to criteria pollutants (Ghozikali et al., 2015; Huang et al., 2018).

Another large population-based study conducted in China found a correlation between increases in CAPs concentrations and corresponding increase in IHD hospitalizations (Xu et al., 2021). The study found that for every 10μg/m³ increase in the PM₂.₅ concentration, the relative risk (RR) of daily ER visits for circulatory system disease was 1.007 (1.001-1.013) at lag 0, RR=1.007(1.000-1.013) in lag1, and RR=1.011(1.002-1.021) for lag3.

Also, a nationwide time-stratified case-crossover study conducted by Liu et al., (2022) in China to evaluate the association of short-term exposure to six criteria pollutants, CO, NO₂, O₃, PM₂.₅, PM₁₀ and SO₂, with the hospitalization of a wide spectrum of cardiovascular diseases. The results revealed significant associations between exposure to these pollutants and increased hospitalization for cardiovascular diseases including IHD, especially at lag 0-1 day. There were large effects for all six air pollutants on lag 0-1 day. Additionally, PM₂.₅, PM₁₀, NO₂, and CO showed significant associations with increased HAs for IHD. NO₂ showed the most effect after adjusting for co-pollutants. This study demonstrated that short-term exposure to multiple air pollutants can significantly increase the risk of cause-specific cardiovascular diseases. These results agree with other studies (Ren et al., 2020; Li et al., 2022; Xu et al., 2022).

1.6. Myocardial Infarction

MI also known as heart attack is caused by decreased or complete cessation of blood flow to a portion of the myocardium, causing death of cardiac tissue (Peters et al., 2004; Thygesen et al.,
MIs can be a result of clots travelling to the heart due to atherosclerosis of peripheral vessels as well as cardiac vessels. It is the most severe manifestation of coronary heart disease (Fathima, 2021), and a leading cause of death globally (Vafaie, 2016). Several health conditions, lifestyle, age, and family history can increase risk for MI (Sagris et al., 2022), and the major symptoms include severe and sustained chest pain, breathlessness, nausea, and sweating, discomfort in the jaw, neck, or back (Tsao et al., 2023; Thygesen et al., 2007), leading to life-threatening clinical situations or sudden death (Mendis et al., 2011). In most cases, those who survive the initial events are likely to be vulnerable to repeat attacks (Mendis et al., 2011; Lu et al., 2015). MI prevalence and deaths are increasing globally (Stevens et al., 2016; Bishu et al., 2020). This is in part due to the fact that death from many other causes has been reduced and everybody has to die of something as they age.

The same risk factors for IHD apply to MI, as they are the ultimate result of IHD (Canto et al., 2011). Recent studies have linked environmental factors such as criteria pollutants as major triggers that lead to increased ER visits and HAs for MI. The results of a study conducted by Bai et al. (2019) showed long-term exposures to PM$_{2.5}$, O$_3$ and NOx to be associated with increased incidence of acute myocardial infarction (AMI). A case-crossover study carried out in Rome to evaluate the relationship between criteria pollutants and HAs for AMI revealed positive associations between total suspended particulate, NO$_2$ and CO and MI (D’Ippoliti et al., 2003). This was more prominent in the warm period of the year, with total suspended particulates showing the most effects.

Ambient pollutants can induce low-grade inflammation which poses an increased risk for adverse coronary events (Yue et al., 2007). For instance, particulate exposure is associated with elevated levels of C-reactive protein (Peters et al., 2001), a marker of systemic inflammation that
may be an important and independent predictor of cardiovascular disease, that causes inflammatory lung injury, enhanced human alveolar macrophage production of proinflammatory cytokines, elevated blood plasma viscosity, endothelial dysfunction and brachial artery vasoconstriction triggering MI (Pope III et al., 2004).

Liu et al., (2021) conducted a large time-stratified case-crossover study in Hubei province in China to investigate associations of short-term exposure to air pollutants (PM$_{2.5}$, PM$_{10}$, NO$_2$, CO, SO$_2$ and O$_3$) and mortality from MI. The study looked at data for 151,608 individuals that lived and died in the study area between 2013 and 2018 with MI as the underlying cause of death. The study results showed consistent evidence that short term exposure to PM$_{2.5}$, PM$_{10}$, and NO$_2$ was associated with increased risk of MI mortality, with odds of PM$_{2.5}$=4.14%, PM$_{10}$=2.67%, and NO$_2$=1.46% with every 10 µg/m$^3$ increase in exposure. The authors therefore concluded that short-term exposure to PM$_{2.5}$, PM$_{10}$, and NO$_2$ was associated with increased risk of MI mortality.

1.7. **Project Aims and Objectives**

Many studies have reported associations between respiratory and cardiovascular health outcomes and CAPs exposure from multiple sources other than the point source (Zhang & Batterman, 2013; Matz et al., 2019; Li & Managi, 2021). A few studies have found associations or correlations between living around point source emissions such as fuel-fired power (Liu, Lessner, & Carpenter, 2012), and other industrial air emitters (Labelle et al., 2015; Bertoldi et al., 2012) and hospital visits for respiratory and cardiovascular diseases (Wichmann et al., 2009; Labelle et a., 2015; Hendryx et al., 2019; Smargiassi et al., 2009; Labelle et al., 2015). To my knowledge, this is the first study to investigate the impact of point source CAPs on both respiratory and cardiovascular diseases in all zip codes in NYS from 2010 to 2018 using the NEI data or 2011 to 2017.
The hypothesis for this project is that air pollution is a major environmental risk factor for respiratory and cardiovascular ER visits particularly in NYS. The operational objectives that guided this study were to assess associations if any between point source emission of CAPs adjusted for smoking and poverty and outpatient visits for asthma, COPD, IHD, and MI at zip code levels in NYS from 2010 to 2018. And to determine which component of the CAPs that has the most adverse effects. This gives an insight into not only the sources of these air pollutants but also their dose responses, and effects on health. The other emission sources, such as nonpoint, onroad, and nonroad will be adjusted for at the county level total air pollution data since they are not available at the zip code level in the NEI data. Results of other studies have shown point source emissions to be a smaller part of the total air pollution than the other sources (Yu & Stuart, 2017). While air pollutants released from point sources are much less than that from vehicle traffic and other non-point sources (Figure 2.2), use of the point source data allows one to determine diseases in relation to residential proximity, something that cannot easily be done for non-point source emissions (Oluleye & Adabale, 2020; Dunne et al., 2014).

The first specific aim was to assess the association between smoking, poverty, and PM$_{2.5}$ exposure and the rate of ER visits for asthma in NYS from 2010 to 2018. The second specific aim was to assess the associations, if any, between ER visits for asthma and COPD and exposure to CAPs in NYS from 2010 to 2018 at zip code level, and to determine the relative contribution of each of the CAPs to each of the diseases. The third specific aim was to assess the association between ER visits for IHD and MI and exposure to CAPs in NYS from 2010 to 2018, as indicated in the SPARCS ER data, after accounting for other associated factors.
Chapter 2

2.0. Materials and Methods

2.1. Study Area

The study population includes all emergency room (ER) visits due to asthma, chronic obstructive pulmonary disease (COPD), ischemic heart disease (IHD) and myocardial infarction (MI) in New York State (NYS) from 2010 to 2018 covered by the New York State Department of Health (NYSDOH). The study area encompasses all zip codes that the United States Environmental Protection Agency (USEPA) National Emission Inventory (NEI) and NYSDOH Statewide Planning and Research Cooperative System (SPARCS) cover. This study focused on the records collected between 2010 and 2018 for the health data, and 2011 to 2017 for the exposure data. The SPARCS data records contain information on admission date, discharge date, date of birth, 5-digit zip code of residence and demographic information of individuals, while the NEI data has information on the pollutants.

2.2. Health Data

Information on asthma, COPD, IHD and MI ER visits that did not result in hospitalization was retrieved from the NYSDOH SPARCS system database. SPARCS data is NYS widely used and legislatively mandated collection of patient information on principal diagnoses, hospital admissions (HAs) and discharge dates, sources of payment, date of birth, sex, race/ethnicity, length of stay, and street address and charges for each hospital inpatient stay and outpatient visits. SPARCS covers about 95% of all hospitals in NYS but does not include federal institutions such as the Veterans’ affairs hospitals, Indian health services or psychiatric facilities. SPARCS data have been widely used in previous studies examining similar outcomes (Hopke et al., 2020; Alper et al., 2021; He et al., 2021; Madani & Carpenter, 2023).
Asthma and COPD in this study include hospital ER visits from 2010 through 2018. There were 1,245,873 crude ER visits for asthma and 643,066 crude ER visits for COPD, with primary diagnosis using the International Classification of Diseases (ICD), 9th and 10th revisions, Clinical Modification (CM). The study looked at asthma (ICD-9-CM code 493 and ICD-10-CM code J45) and COPD (ICD-9-CM codes 490-496 and ICD-10-CM codes J40-J47). These respiratory diseases were chosen due to well-established associations previously established. The outcome was defined as the number of cases during the period from 2010 to 2018, aggregated by gender, race, and age groups at zip code level. The age stratified category for asthma was (0-5, 6-19, 20-44, 45-64, 65-74, 75+), and COPD age category in years was (35-44, 45-59, 60-74, and 75+). Ages 35-44 years have been used as the median age range at which COPD is usually diagnosed (DeMeo et al., 2022; Divo et al., 2018). This age group was therefore used as reference age for COPD in this study. The age reference used for asthma in this study was 45-64.

Similarly, individual-level data were aggregated into daily counts for both IHD and MI that are identified using both the ICD-9-CM, and ICD-10-CM codes. The analysis included visits for IHD (ICD-9-CM codes 410-414, and ICD-10-CM codes I20-I25), and MI (ICD-9-CM codes 410, and ICD-10- codes I21-I22) as defined by the SPARCS data dictionary. The study only focused on ER visits and narrowed it to primary diagnosis of each disease of interest. For each disease and year, the study looked at variables of concern using the longitudinal patient identifier. Based on SPARCS data for 2010-2018, the study determined the number of ER visits for the diseases. To get the crude numbers of ER visits for each of the diseases by zip code, patients were grouped by their residential zip codes and the rate of ER visits in each zip code was calculated using the total number of ER visits and the population count by zip code. Data was
then stratified by sex (male and female), and age categorized as 0-5, 6-19, 20-44, 45-64, 65-74 and 75+ for both IHD and MI.

Figure 2.1. is a diagrammatic presentation of the numbers of ER visits that did not result in hospitalization for the four diseases studied in this dissertation project. The largest ER visits was registered for asthma, 70% of all ER visits within the study period as shown in navy blue. This was followed in a long distance second by COPD (25%) as shown in orange. IHD shown in green, and MI shown in sky blue registered very small emergency visits, with MI showing the least visits (2%).

Figure 2.1. Distribution for each respiratory and cardiovascular disease for the entire study period in NYS from 2010 to 2018 as indicated in SPARCS

<table>
<thead>
<tr>
<th>Disease</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asthma</td>
<td>70%</td>
</tr>
<tr>
<td>COPD</td>
<td>25%</td>
</tr>
<tr>
<td>IHD</td>
<td>3%</td>
</tr>
<tr>
<td>MI</td>
<td>2%</td>
</tr>
</tbody>
</table>

**Table 2.1.** Crude counts of ER visits for each respiratory and cardiovascular diseases by study year in NYS, based on SPARCS outpatient data for 2010-2018, using ICD-9-CM, ICD-10-CM, and the SPARCS Data Dictionary. The codes of interest are as given in Madani & Carpenter (2023). Patients were grouped to obtain visit counts by zip code, with patient address variable as zip code location.

<table>
<thead>
<tr>
<th>Year</th>
<th>Asthma</th>
<th>COPD</th>
<th>IHD</th>
<th>MI</th>
</tr>
</thead>
<tbody>
<tr>
<td>2010</td>
<td>137756</td>
<td>72832</td>
<td>5889</td>
<td>2900</td>
</tr>
<tr>
<td>2011</td>
<td>141816</td>
<td>74630</td>
<td>6152</td>
<td>3102</td>
</tr>
<tr>
<td>2012</td>
<td>149010</td>
<td>76673</td>
<td>6410</td>
<td>3141</td>
</tr>
<tr>
<td>2013</td>
<td>143225</td>
<td>73149</td>
<td>6464</td>
<td>3219</td>
</tr>
<tr>
<td>2014</td>
<td>146120</td>
<td>74429</td>
<td>6033</td>
<td>3310</td>
</tr>
<tr>
<td>2015</td>
<td>143120</td>
<td>72958</td>
<td>6332</td>
<td>3550</td>
</tr>
<tr>
<td>2016</td>
<td>135123</td>
<td>68123</td>
<td>5485</td>
<td>3828</td>
</tr>
<tr>
<td>2017</td>
<td>126400</td>
<td>66830</td>
<td>5240</td>
<td>3842</td>
</tr>
<tr>
<td>2018</td>
<td>123303</td>
<td>63442</td>
<td>3788</td>
<td>3788</td>
</tr>
</tbody>
</table>

### 2.3. Exposure Data

Exposure data for this study was downloaded from the USEPA’s NEI dataset which is a comprehensive and detailed estimate of emissions of criteria pollutants, their precursors, and the hazardous air pollutants (HAPs). The USEPA NEI distinguishes pollutants including CAPs emitted from various sources categorized as point, non-point, on road, non-road, and events. This study was limited to the point source emissions of the criteria pollutants because NEI provides point source exposure data at the zip code level, but not the other sources. However, data for the other sources such as on-road, non-road and non-point data are provided at the county level. Since the ER data is at the zip code level, this study is limited to exposure to point source pollution. To account for within county variability, county level total VOCs and CAPs were used
as adjusting variables since the CAPs are present with VOC pollutants at county level and the point-source pollution is superimposed on that coming from on-road, non-road, and non-point sources.

Figure 2.2 shows emission distribution of NEI CAPs based on the source categories in NYS for the study period (2011 to 2017). Mobile sources combined (69%) are the largest contributors of CAPs emissions in NYS, with on-road mobile sources accounting for 38%, and non-road sources contributing 31%. Nonpoint sources represent 24%. The remaining 7% is attributable to point sources.

Figure 2.2. All sources of criteria pollutants in NYS 2010-2018 as described by the USEPA NEI
A point source emission is one produced by large and stationary sources like power plants, industries, electrical power plants, solid waste landfills, sewage treatment facilities, breweries and airports, or smaller non-industrial sources.

Table 2.2 shows emissions for CAPs from NEI for different source categories for NYS for the study years. Emissions are in tons per year. Pollutants are emitted from on-road and off-road vehicles, but there are also contributions from the point sources. There is some progress toward reduced CAPs over time.

Table 2.2. Crude counts of CAPs in NYS by study year, based on NEI exposure data for 2011, 2014, 2017, total for 2011, 2014 and 2017 given in tons, and percentage emission for each source.

<table>
<thead>
<tr>
<th>Source</th>
<th>2011</th>
<th>2014</th>
<th>2017</th>
<th>Total</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Point</td>
<td>214,481</td>
<td>166,425</td>
<td>109,652</td>
<td>490,559</td>
<td>7</td>
</tr>
<tr>
<td>Nonpoint</td>
<td>780,106</td>
<td>682,455</td>
<td>248,764</td>
<td>1,711,326</td>
<td>24</td>
</tr>
<tr>
<td>Onroad</td>
<td>1,034,149</td>
<td>1,017,646</td>
<td>651,165</td>
<td>2,702,960</td>
<td>38</td>
</tr>
<tr>
<td>Nonroad</td>
<td>855,782</td>
<td>780,996</td>
<td>607,016</td>
<td>2,243,794</td>
<td>31</td>
</tr>
</tbody>
</table>

Figure 2.3. shows percentage distribution of point source CAPs emissions at both county and zip code levels in NYS from NEI for the study years, and all emissions are in tons. CO exposure registers the highest for county level while NOx registered the highest for zip level emissions,
followed by NOx for county, and CO for zip. SO₂ contributed the third highest for both county and zip levels, PM₁₀ and PM₂.₅ contributed the least for both.

Table 2.3. shows the data for total emission for each of the criteria pollutants for the entire study period as reported by the USEPA NEI. As shown in the table, CO emission showed the highest, followed by NOx and SO₂ (all gaseous pollutants). The particulates showed less emissions compared to the gaseous pollutants, with PM₂.₅ showing the least.
Table 2.3. Total number of emissions for each criteria pollutant at point source zip code level in NYS for the study period, based on NEI exposure data for 2011, 2014, 2017 given in tons.

<table>
<thead>
<tr>
<th>Pollutants</th>
<th>Exposure in tons</th>
</tr>
</thead>
<tbody>
<tr>
<td>CO</td>
<td>186,081</td>
</tr>
<tr>
<td>NOx</td>
<td>145,773</td>
</tr>
<tr>
<td>Pb</td>
<td>5,067</td>
</tr>
<tr>
<td>PM$_{2.5}$</td>
<td>13,074</td>
</tr>
<tr>
<td>PM$_{10}$</td>
<td>18,868</td>
</tr>
<tr>
<td>SO$_2$</td>
<td>126,752</td>
</tr>
</tbody>
</table>

Since NEI data are released every three years, point source pollution information for PM$_{2.5}$, PM$_{10}$, NOx, CO and SO$_2$ were retrieved for the years 2011, 2014, and 2017. However, data for O$_3$, which is also a CAP, is not available in the NEI dataset, and there was so little release of lead that it was not considered for this study. Pollutant site latitude and longitude locations were associated with the zip code in which the facility was located using a scheme that minimized the absolute great circle distance between the zip code centroid and the site location. Data from the USCB was used to determine the land area in square miles in each zip code. For each pollutant, zip code, and year, the pollution per square mile was calculated by summing all point source contributions of the pollutant and dividing by the land area size in square miles of each zip code. The workable data was in pollution per square mile.
2.4. Poverty Data

Poverty data was downloaded from the United States Census Bureau (USCB) website for the years covered in this study. This site provides poverty data from several household surveys and programs, and the official poverty measure defines poverty by comparing pretax money income to a poverty threshold that is adjusted by family composition. Families are considered poor if their total income falls below a certain threshold. All families that fell below the threshold were categorized as below mean, and those above the threshold were categorized as above the mean in this study.
The USCB dataset on poverty was used in this study. Since the 1960s, the USCB has produced poverty estimates to measure the economic well-being of households, families, and individuals in the US. The official poverty measure defines poverty by comparing pretax money income to a poverty threshold that is adjusted by family composition. The Census Bureau provides poverty data from several household surveys and programs and defines poverty by considering families’ income thresholds and these vary based on family composition and size. Data from the small area income and poverty estimates (SAIPE) program at the USCB website was used for this study. These estimates are based on several data sources, such as aggregate tax, supplemental nutrition assistance program (SNAP) benefits, and poverty incidence data. In this data, poverty is defined based on the family’s income. For instance, a family is considered poor when their total income is less than the threshold set by SAIPE.

2.5. Data on Tobacco Smoking

To find an association between asthma rate and tobacco smoking (a risk factor for both asthma and COPD), the Behavioral Risk Factor Surveillance System (BRFSS) database was searched for smoking data. This is a continuous, state-based surveillance system that collects information about modifiable risk factors for chronic diseases and other leading causes of death, and it is the nation’s premier system of health-related telephone surveys that collect state data. The county level data was used to cover a wider range and scope. This data was then averaged over the study period and matched with zip codes which evenly covered the research geographical area. Smoking data were obtained at the county level since the zip code level data was not available.

The behavioral risk factor surveillance system (BRFSS) is a system of health-related telephone surveys that collect state data about US residents regarding their health-related risk behaviors, chronic health conditions, and use of preventive services. The BRFSS database was used to
determine the crude rate of smoking for this study. Smoking data was not available at the zip
code level in the BRFES dataset and county level data was used as a confounder in the models.
Surveys are conducted using landline telephones as well as cellular telephones. For each county,
the crude smoking rates were averaged and used in this study.

2.6. Control Variables

Different adjusted variables that can influence the outcomes of interest were considered, they
included sex (male or female) with female as the reference level, age category with varied
reference levels based on disease type, a poverty category variable with the reference level being
below median poverty, average county level smoking, study years from 2010 to 2018 with
reference level been 2010, county level VOCs, and county level CAPs from all pollutant sources.

2.7. Statistical Analysis

To estimate the association between the CAPs and ER visits of the outcome of interest in this
study, I used the ecological study design, since the unit of observation is the population level at
zip code. Ecological studies use geographical areas to define units of analysis and are generally
used in public health research to make biologic inferences about effects on individual risks or to
make ecological inferences about effects on groups. Such studies focus on comparison of groups,
rather than the individuals and the variables used in ecological analysis are aggregates,
environmental, or global measures. For example, exposure and risk factors are known only at the
group level, such as the average air pollution concentration in different zip codes in New York.
The limitation of ecological study is a type of confounding called an ecological fallacy, which
occurs when relationships identified at group level data are assumed to be true for individuals.

The Quasi-Poisson regression and the Log linear mixed effects models were implemented to
quantify the exposure-response associations between criteria pollutants and ER visits for asthma,
COPD, IHD and MI per 100,000 person-years. Quasi-Poisson regression is a regression method used for modeling overdispersed count outcomes, and accounting for overdispersion helps avoid biased estimation. The log linear mixed-effects modeling allows one to examine the condition of interest while also taking into account variability within and across other factors simultaneously. For example, the log linear mixed effect was used in this study for the zip code level data and to account for the within county variability since county level data were used as adjusting variables.

2.7.1. Missing Exposure Data

Exposure data for this study covers 2011, 2014, and 2017, and for these years, there were some disparities in reporting emissions across zip codes because some emitting units did not report in some of the given years. This is likely due to the fact that while reporting is mandatory in NYS for emissions from large point sources, both at site and unit levels, they are often not enforced. Also, reporting standards were dropped for certain polluters based on the title V requirements. It is reasonable to assume that these stationary sources are operating over the period used in this study, and that they are still producing emissions even though they were not reported. Since point sources do not move, it is reasonable to assume that units still produced emissions but were not reported. Missing data for emissions for those years were imputed using emitting sites and unit IDs for each zip code. Sites and missing unit IDs were inserted, and their emissions were replaced by the mean value of emissions reported assuming emissions were the same and for the samples provided by that unit for the year(s) it did report. Units that did not report any emissions during the period (2011 to 2017) do not appear in zip code level emission totals. The largest source of missing data is cryptic and is not reflected in this study data because it consists of emitting units within a site and a zip code that failed to report in any of these years. This is a limitation of this dataset.
This means that the total number of zip codes reporting may not change much after imputation, but the pollutant totals do. Changes in zip codes during the study period were resolved by using a reference set of codes from 2011. The total number of zip codes in the state of NY is estimated at 1792, and a little less than that reported some point source pollution for at least one of the target pollutants in 2011, 2014, and 2017, which also had cases of the diseases in this study. Those zip codes with disease cases but without point source data over the study period were given a point source emission rate of zero. Zip codes with zero population were assumed to be post office boxes and were not considered in the analysis. Similar analysis was described in Madani et al., 2023.

2.7.2. Single Pollutant Models

Datasets were created by merging data across years for each pollutant and all years were analyzed together. Pollutant data for 2011 was associated with zip code disease rates for 2010, 2011, and 2012. Pollutant data from 2014 was joined to disease data from 2013, 2014, and 2015, and pollutant data from 2017 were used with disease data from 2016, 2017, and 2018. Data from all years were then stacked to complete the file.

Log-linear mixed effects regression models with random intercepts at the county level were used in this study to analyze the rates of ER visits that did not result in hospitalization for asthma and COPD and their associations with the CAPs, and a p-value < 0.05 was considered statistically significant. The R-squared likelihood ratio test was used as a measure of goodness of fit.

Adjusted associations between the rates of ER visits, scaled to per $10^5$ population, and pollutants at zip code level were estimated using log-linear mixed effects models with a random effect to account for within-county variability. Models were adjusted for sex (reference level female), age category (reference level at 45-64 for asthma, 35-44 for COPD), a poverty category variable
(reference below median poverty), average county level smoking, study year (reference level 2010), and county level VOCs and CAPs from all sources. All numeric covariates are standardized and the outcome case rate by zip code was log-transformed to achieve normality.

All data preparation and analysis were performed with the R programming language and R studio software version 2022.07.1 (Build 554).

To create datasets for each of the pollutants in this study, data were merged across years for each pollutant and all years were analyzed together. Pollutant data for 2011 was associated with 2010, 2011, and 2012 zip code disease rates. For 2014, pollutant data were joined to disease data from 2013, 2014, and 2015, while 2017 pollutant data were also matched with disease data from 2016, 2017, and 2018. These were then assembled to get a complete workable dataset needed for the study. To accurately estimate pollutants at the zip level, and account for within county variability, the log-linear mixed effects model with a random effect was used. Adjusted associations between the rates of ER visits were scaled to 100,000 population. This study models were adjusted for sex using female as the reference level, age level category was determined by disease type based on previous studies. For the poverty level category, below median poverty was used as the reference, while 2010 was used as the reference for the study years. Average county level smoking, county level VOCs, and CAPs from point, non-point, on-road, and non-road sources. Covariates that are numeric were standardized and disease rates at the zip codes were log-transformed for normality. Standardized effect sizes were created to compare across outcomes and exposures.
Chapter 3


3.1. Abstract:

Asthma is a serious health issue all over the world, and its prevalence is increasing among all age groups. Asthma affects millions of children and adults in the United States (US) and affects a wide range of people across the globe, according to the Centers for Disease Control and Prevention (CDC). Approximately 15% to 20% or more of the general population in many countries suffer from asthma and which does not recognize boundaries according to the Global Asthma Report (GAR). Asthma has been increasingly recognized as a heterogeneous disease comprised of both allergic and non-allergic phenotypes. While the cause of asthma is poorly understood but involves genetics and early life immune system development. Once a person becomes asthmatic, there are many known triggers for asthma attacks, which are an acute threat to respiration that in extreme cases can be fatal.

Most studies of risk factors for asthma attacks have focused on indoor environmental exposures such as mold, dampness, indoor allergens such as dust mites and pet allergens, oxides of nitrogen associated with gas cooking and heating, volatile organic compounds (VOCs), and environmental tobacco smoke. Outdoor air pollutants, including diesel particles, other petrochemicals, particulates and low socioeconomic status or poverty as some of the major risk factors that increase asthma exacerbation, emergency room (ER) visits and hospitalization. Multiple studies have linked both outdoor and indoor particulates and gaseous pollutants with increased asthma ER visits and hospital admissions (HAs) globally.
In recent years, epidemiological studies have strongly suggested that an increased risk of asthma exacerbation is associated with elevated exposure to air pollution including the criteria air pollutants (CAPs), especially fine particulates (PM$_{2.5}$).

In addition to the CAPs, tobacco smoke has also been found to contribute to asthma attacks and eventual ER visits. Tobacco smoke is a major risk factor for morbidity and mortality worldwide, and it has been well-documented that smoking or exposure to secondhand smoke (SHS) among asthmatics increases asthma-related morbidity and disease severity and subsequent ER visits or HAs and can contribute to a decline in lung function. The World Health Organization (WHO) described tobacco smoking as a significant public health problem that affects human health, and causes social, economic, and environmental damages. Tobacco use accounts for numerous deaths annually, including deaths from nonsmokers involuntarily exposed to SHS according to WHO. Studies of patients that visit the ER with asthma exacerbations have demonstrated that 1 in 3 patients would be current smokers. Prospective observational studies conducted in various regions of the world have indicated impacts of tobacco smoke on adult asthma outcomes with asthmatic patients.

Another major risk factor for development of asthma that has been extensively studied is socio economic status (SES), in this case low SES or poverty. The United States Census Bureau (USCB) has produced poverty estimates to measure the economic well-being of households, families, and individuals in the US. The official poverty measure defines poverty by comparing pretax money income to a poverty threshold that is adjusted by family composition. Studies have suggested that low SES or poverty, and exposures connected to poverty are associated with asthma exacerbations and ER visits, and mortality. Residence in poor neighborhoods is often associated with asthma-related ER visits and hospitalizations. Even in lower income populations,
those living in inner-city areas are at higher risks of asthma-related ER visits and hospitalizations than those living in other kinds of neighborhoods.

This study focuses on the impact of PM$_{2.5}$, smoking, and poverty on asthma ER visits that did not result in hospitalization at zip code level in New York State (NYS) from 2010 to 2018 by focusing on asthma attacks that are reported as ER visits in Statewide Planning and Research Cooperative System (SPARCS) data. The quasi-poison family regression models were used to assess associations between ER visits for asthma and exposure to PM$_{2.5}$, smoking, and poverty, for crude and adjusted analysis. The models show positive associations between PM$_{2.5}$, smoking, poverty, and ER visits for asthma. These results suggest that zip code level exposure to PM$_{2.5}$, smoking and poverty have an adverse impact on asthma ER visits. This confirms that air pollution is positively associated with the risk of asthma attacks, and people of low SES and/or smokers are more susceptible.

### 3.2. Introduction

Asthma attacks are characterized by varying degrees of allergic responses, airflow obstruction and inflammation leading to symptoms including cough, wheezing, chest tightness, and shortness of breath (Spiro et al., 2020; Baïz & Annesi-Maesano, 2012). The increase in prevalence of asthma in most countries around the world poses a substantial global health burden to people in all geographic locations consisting of low- and high-income countries (Hammad & Lambrecht, 2021). Asthma affects around 25 million people in the United States (US), which is approximately 7.7% of adults and 7.5% of children and adolescents (Most et al., 2021), and well over 300 million people worldwide (Enilari & Sinha, 2019), and this is expected to increase in the future (Dharmage et al., 2019). Given the high prevalence worldwide, asthma is still responsible for 250,000 potentially preventable deaths annually (Khan et al., 2022; Ober & Yao,
It imposes a growing burden on society in terms of morbidity, quality of life, and healthcare costs (Toskala & Kennedy, 2015). Asthma also accounts for the loss of over 15 million disability adjusted life years (DALY) annually and ranks among the highest causes of DALY for children (Asher & Pearce, 2014). In the US, an estimated $1,500 is spent per emergency room (ER) visit and over $3,000 is spent per year per patient on medical expenses on asthma (Wang et al. 2014). More than 11 million people each year suffer an asthma attack (Law, Oraka & Mannino, 2011), resulting in 1.8 million asthma-related outpatient visits to the ER annually (Wang et al., 2014). Asthma costs the US between $56 and $82 billion annually (Barnett & Nurmagambetov, 2011; Kilpatrick et al., 2024). Reports have estimated a total of 4,145 asthma-related deaths in 2020, accounting for less than 1% of all US deaths that year (CDC, 2022; Kilpatrick et al., 2024).

Evidence is strong for an increased risk of asthma associated with allergenic exposure, respiratory infections, air pollutants, tobacco smoke, SHS, dust mites, pets, pests, mold, and allergic rhinitis (Baïz & Annesi-Maesano, 2012). Epidemiologic studies have highlighted many associations between various criteria air pollutants (CAPs) and subsequent risk for asthma exacerbation especially in the urban environment (Chatkin, Correa & Santos, 2022), and with closer residential exposure to air pollution from fossil fuel combustion in traffic, power plants, and industrial facilities (Castner, Guo & Yin.,2018; Rovira et al., 2014). Recent daily time-series studies have reported associations between daily mortality rates and changes in air pollution, specifically particulate pollution in different parts of the world (Naybare et al., 2017;2022; Wang et al., 2016; Sarnat et al., 2013). Evidence has linked seasonal changes in particulate matter (PM) levels and composition with exacerbating existing asthma, particularly by contributing to oxidative stress and allergic inflammation (Weinmayr et al., 2010). Most air pollution studies on
asthma have mostly focused on either total PM (Tecer et al., 2008), ambient urban and traffic-related air pollutants (Patton et al., 2014; Fallah-Shorshani et al., 2017) or on specific point sources (Liu et al., 2012). These studies showed lots of evidence that pollutants concentration increases the risk of ER visits for asthma, but much less information on the impact of all point sources within a geographical location on top of the general background. Additionally, several studies of the effects of fine particulate matter (PM$_{2.5}$) on ER visits have looked at specific pollution types or sources.

This study is unique in that it is an ecological study of all point sources of PM$_{2.5}$ at zip code level in the state of New York (NY) and their impacts on ER visits for asthma. The primary objective of this study is to assess the association if any, between PM$_{2.5}$, poverty, and smoking and ER visits for asthma in New York State (NYS) from 2010 to 2018. The purpose of this study therefore is to be able to test whether even a small additional background PM$_{2.5}$ coming from point sources, zip code level poverty and smoking are sufficient to cause an elevation in ER visits for asthma. While there are many sources of air pollution that are not from point sources, point source pollution will provide information about localized pollutants and their health outcomes.

3.3. Fine Particulate Matter

PM is a mixture of solid particles and liquid droplets that affect human health depending on their size, chemical composition, and type (EPA, 2020). The most recent calculations estimated that about 3.2 million deaths per year are attributable to PM, which places it among the leading 10 risk factors for global mortality (Brook et al., 2010; 2018; Rückerl et al., 2011). Coarse particles (PM$_{10}$) have a diameter of less than 10μm, while PM$_{2.5}$ has diameter less than 2.5μm. Compared with coarse particles, due to their small size, PM$_{2.5}$ can remain suspended for a
relatively longer time in the air and can be easily inhaled and deposited into the alveoli in the respiratory tract, thereby causing or exacerbating lung diseases (Fiordelisi et al., 2017; EPA, 2020; Lu, Li & Yan, 2021). PM$_{2.5}$ can either be directly emitted into the air as primary particles or be formed in the atmosphere as secondary particles from gaseous precursors such as sulfur dioxide (SO$_2$), oxides of nitrogen, ammonia, and non-methane volatile organic compounds (VOCs), and can also travel long distances (Chen, Chang & Tsai, 2017; Hodan & Barnard, 2004).

Ambient PM$_{2.5}$ exposure, considered the leading environmental risk factor globally, is estimated to be associated with millions of premature deaths (Anenberg et al., 2018). Associations between short and long-term exposures to PM$_{2.5}$ and asthma morbidity and mortality have been observed in population, time-series, and natural intervention studies (Amnuaylojaroen & Parasin, 2024; Pope, Ezzati & Dockery., 2009) including asthma exacerbation in children and adults (Nassikas et al., 2022; Ma et al., 2019; Vu et al., 2021; Shukla et al., 2022). Long-term exposures to PM$_{2.5}$ are associated with diseases such as aggravated asthma, chronic bronchitis, acute respiratory symptoms, and COPD (Amoatey et al., 2020), while short-term exposures lead to eye irritation, can aggravate nasal suffering, and the lungs may be affected (Kloog, 2013; Yitshak-Sade et al., 2018; Wang et al., 2022). Increased rates of hospitalization and ER visits for asthma and atherosclerotic vascular plaque rupture due to PM$_{2.5}$ have also been reported (Hopke et al., 2019; Tian et al., 2021; Schweizer et al, 2023). PM$_{2.5}$ often contains toxic substances like acid sulfates and trace metals, and sometimes evades defense mechanisms of the respiratory system making it very virulent.

The most important pathogenic mechanism of PM$_{2.5}$ to the respiratory system is oxidative stress (Ren et al., 2016). The mechanisms through which PM$_{2.5}$ causes asthma exacerbations is related
to overexpression of several transcription factor genes and inflammation-related cytokine genes that cause inflammatory injury leading to numerous respiratory diseases including asthma (Lu, Li & Yan, 2021). Also, metals and the organic components of PM$_{2.5}$ can induce free radical production to oxidize lung cells, which may be the primary cause of body injury (Xing et al., 2016). When PM$_{2.5}$ is inhaled into the lungs, it can enter the blood circulation through blood-air barrier and reach other tissues and organs, and eventually damages the respiratory, circulatory, reproductive, and central nervous systems (Wang et al., 2021).

Multiple studies have found associations between changes in air pollution patterns and asthma disease response over time. For instance, Hopke et al. (2019) conducted a case-crossover design study to ascertain changes in the acute response of respiratory diseases due to PM$_{2.5}$ in NYS from 2005 to 2016. They split the study into three periods; ‘before’ (2005 to 2007), ‘during’ (2008–2013), and ‘after’ (2014–2016), indicating PM$_{2.5}$ emission changes. Results showed that for each 6.8 μg/m$^3$ increase in PM$_{2.5}$ on the same day was associated with ‘before’ 0.4% (0.0%–0.8%), ‘during’ 0.3% (-0.2%–0.7%), and ‘after’ 2.7% (1.9%–3.5) increases in the rate of asthma ER visits. This result suggests that the same mass concentration of PM$_{2.5}$ was more toxic in the ‘after’ period, than the ‘before’ and ‘during’ periods. The authors concluded that increased rates of asthma hospitalizations and ER visits in NYS are associated with short term increases in ambient PM$_{2.5}$ concentrations.

Studies have also shown correlations between long- and short-term exposures to PM$_{2.5}$ and the worsening of asthma in asthmatics in cities around the world. A study by Zuo et al. (2019) is a classic example of this. This was a time-series study conducted to assess associations between short-term exposure to PM$_{2.5}$ and acute exacerbation of asthma in Yancheng, China. The aim was to explore the relationship between PM$_{2.5}$ and acute asthma exacerbation in a coastal city of
China. A total of 3,520 cases of acute asthma exacerbation records, with a daily average of 3, from 2015 to 2018 were retrieved from outpatient visits data. Positive and significant associations of PM$_{2.5}$ on lag 1, 2, lag 02, and lag 03 day were observed. And each 10-µg/m$^3$ increase in PM$_{2.5}$ (lag 02), increases asthma by 3.15% (0.99%-5.31%). The study results showed PM$_{2.5}$ was associated with increased risk of acute asthma exacerbation, particularly among males and younger asthma patients. Another observed result was that asthma patients were more susceptible during the cold season. The study results show evidence of the association of PM$_{2.5}$ with acute asthma exacerbation.

Chankaew et al., (2022) also conducted a pilot prospective observational study to assess the association between PM$_{2.5}$ exposure and asthma exacerbation in children living in Bangkok Metropolitan Region and Chiang Mai Province in Thailand from June 2020 to February 2021. Seventy children with asthma, aged 5-18, with median age 9.7 were recruited. Estimated average daily PM$_{2.5}$ exposure levels were calculated at exacerbation day, three days before exacerbation (lag day 3), and 7 days before exacerbation (lag day 7). The study found the daily PM$_{2.5}$ level at lag day 3 to be correlated with an acute asthmatic attack ($r = 0.62$, $p< 0.01$). Also, for every 10µg/m$^3$ daily increase in PM$_{2.5}$, asthmatic exacerbation would also increase by 0.2 events. The results of the findings suggest that asthmatic children are sensitive to daily PM$_{2.5}$ levels, and exposure to high daily PM$_{2.5}$ levels can lead to asthma exacerbation within three days.

Other studies that found associations between PM$_{2.5}$ exposure and asthma exacerbations and ER visits include the one conducted by Anenberg et al. (2018), who estimated that in 2015 alone, 5 to 10 million annual asthma ER visits globally were attributable to exposure to PM$_{2.5}$. Thus, the associations of exacerbations of asthma with elevations in short-term exposures to PM$_{2.5}$ are well established (Hopke et al., 2019). Furthermore, the number of deaths attributable to exposure to
PM$_{2.5}$ increased from 3.5 to 4.2 million cases from 1990 to 2015 (Cohen et al., 2017). Toxicological evidence suggests that exposure to PM$_{2.5}$ can cause lung inflammation and affect pulmonary immune function (Xu et al., 2016).

To investigate the association between asthma exacerbation in children and exposure to air pollutants in France, Bouazza et al. (2019) used a database of 1,264,585 pediatric ER visits from 2010-2015 for 20 emergency departments (EDs) in Paris. A total of 47,107 visits were classified by pediatricians as asthma exacerbations and were used for the analysis in their study. The study results showed significant association between outdoor air pollution by PM$_{2.5}$ and the number of ER visits for pediatric asthma exacerbations in the largest urban French area, with ($p<10^{-4}$) at PM$_{2.5}$ concentration of 13.5 µg/m$^3$. The authors concluded that there was an association between daily asthma exacerbation in pediatric visits to the ER and PM$_{2.5}$ air pollutants.

Wang et al. (2017) conducted a population-based study to evaluate the short-term association between PM$_{2.5}$ concentrations and its constituents on hospital ER visits for asthma in southern Taiwan during the period 2008-2010. The quasi-poisson generalized additive model was used to explore the associations between PM$_{2.5}$ and hospital ER visits for asthma. Average daily ER visits for asthma was 20.0, mean 24-h average PM$_{2.5}$ was 39.4µg/m$^3$. Results indicated that children were more susceptible to the effects of PM$_{2.5}$ exposure on asthma ER visits, RR=1.016 (1.002-1.030) at a lag 0 day, and RR=1.018 (1.002-1.034) lag 0-1 day for every 10µgm$^{-3}$ increase in PM$_{2.5}$. In conclusion, both PM$_{2.5}$ concentration and its chemical constituents were associated with ER visits for asthma in southern Taiwan and children less than 18 years of age are more susceptible.
3.4. Tobacco Smoking and Asthma

The Global Burden of Disease (GBD) study estimates that tobacco smoking caused 7.7 million deaths globally in 2019 and is considered the leading risk factor for DALYs years among men (GBD, 2019; Theilmann et al., 2022). Tobacco smoke and exposure is one of the biggest public health epidemics that lead to many preventable diseases, chief among them is cancer, and other cardiovascular and respiratory diseases (Al-Kuwari et al., 2022; WHO, 2022). Tobacco smoking refers to smoking of any tobacco product including cigarette, waterpipe tobacco, cigars, cigarillos, heated tobacco, roll-your-own tobacco, pipe tobacco, bidis and kreteks, and smokeless tobacco products (Perez-Warnisher et al., 2018; WHO 2022). Cigarette smoking is the most common form of tobacco use worldwide (Prijić & Igić, 2021), but electronic cigarettes (E-cigarettes) have been the most widely used tobacco product among young individuals since 2014 (Roh et al., 2023; Gentzke et al., 2019). Tobacco in any form kills and sickens millions of people every year and there is no safe level of exposure to tobacco smoke (WHO, 2019; Makadia et al., 2017). As of 2020, almost one billion people worldwide were estimated to smoke tobacco (Theilmann et al., 2022), and approximately one third of the global population starts smoking at the age of 15 (Prijić & Igić, 2021). The 2020 National Health Interview Survey (NHIS) indicated that 12.6% of US adults in 2020 were current cigarette smokers and 4.7% were current e-cigarette users (Adjaye-Gbewonyo and Boersma, 2022; Gentzke et al., 2019), and 30% of adult population in the European Union are smokers (Kamga et al., 2022). The number of cigarettes smoked was around 5.5 trillion in 2016 (Drope et al., 2018) and this number is expected to reach 9 trillion by 2025 (Soleimani et al., 2022).

Tobacco-related health consequences including deaths are considered the largest health problem of our time with growing challenges to the health care systems (WHO 2022; Theilmann et al.,
The Centers for Disease Control and Prevention (CDC) attributes 480,317 annual deaths to cigarette consumption alone in the US (Jain et al., 2023), and more than 41,000 deaths from SHS exposure (Sands, 2014; Makadia et al., 2017). WHO holds tobacco responsible for 8 million annual deaths globally (Jain et al., 2023). Tobacco use is also a burden on global economic development. In the US alone, the estimated economic cost related to tobacco consumption is $289 billion per year (Islami et al., 2015).

The American Lung Association (ALA) indicated that approximately 600 chemicals are present in unburnt cigarette (Mitra, 2016), and smoke from a lighted cigarette contains more than 7,000 chemicals including hydrogen cyanide, formaldehyde, arsenic, ammonia, polonium-210, benzene, etc. (Mitra, 2016; Soleimani et al., 2022). In addition, tobacco smoke also contains several heavy metals such as cadmium, chromium, lead, and nickel that can accumulate in tissues and fluids after smoking (Caruso et al., 2014), and can damage different tissues in the body (Prijić & Igić, 2021; Pietinalho, Pelkonen & Rytilä, 2009). Exposure to the harmful tobacco particles contained in some of these chemicals is one of the most important preventable causes of increased morbidity and mortality related to asthma (Pietinalho, Pelkonen & Rytilä, 2009).

Tobacco use during childhood and adolescence and smoke exposures that occur during the prenatal period, infancy, childhood, and adolescence all contribute to a myriad of detrimental and adverse health effects in the pediatric population (Makadia et al., 2017).

Research has shown that tobacco smoke is responsible for millions of deaths each year, including an estimated 1.3 million non-smokers who are exposed to SHS, and around 80% of the world's 1.3 billion tobacco users live in low- and middle-income countries (WHO 2023; Hromiš et al., 2018). Research has also suggested that exposure to harmful tobacco particles is an important preventable cause of increased morbidity and mortality related to asthma and smoking seems to
be more prevalent among individuals with asthma than those without (Stapleton et al., 2011).

Tobacco smoke can contribute both to the onset of asthma in those who are healthy and to the worsening of symptoms in people with asthma (Molarius & Hasselgren, 2023), and poses a greater risk for unscheduled ER visits and HAs for asthma (Tommola et al. 2016).

Tobacco smoke causes toxic cell damage directly, and the chemical compounds therein begin several reactions in cells. Smoke from tobacco and its oxygen radicals activate inflammatory cells, which contribute to the activation of growth factors and matrix metalloproteinases and can cause protease-antiprotease imbalance and advancing tissue destruction (Hromiš et al., 2018).

Tobacco smoke exposure (passive or active) can stimulate the immune response that can co-occur with asthma, and lead to the development of bronchial hyperactivity and chronic inflammation of the respiratory tract, thus favoring the onset of asthma during childhood, as well as adulthood (Hromiš et al., 2018). Also, exposure to tobacco smoke can directly modulate the functions of airway epithelial, smooth muscle, or neural cells to evoke airway hyper-responsiveness, and induce neutrophilic inflammation and airflow obstruction, alter the airway inflammatory phenotype of asthma, and exacerbate airway (Panettieri, 2016; Guo et al., 2019).

Kim et al. (2017) conducted a cross-sectional study of Korea Youth Risk Behavior, to investigate the associations of active, passive, and E-cigarette smoking with asthma in Korean adolescents (2011, 2012 and 2013). Active smoking was significantly associated with asthma adjusted odd ratios (AOR) of smoking ≥20 days/month = 1.57 (1.38-1.77), p < 0.001. Passive smoking was also related with asthma AOR of smoking ≥5 days/week = 1.40 (1.28-1.53), p < 0.001. E-cigarettes showed a positive relation with asthma AOR = 1.12 (1.01-1.26), p = 0.027.

Another study by Cerveri et al. (2012) focuses on the impact of cigarette smoking on asthma. This was a population-based international cohort study that investigated changes in smoking
habits and their effects on forced expiratory volume in 1s (FEV1) 1,045 asthma patients compared with 9,092 non-asthmatics. Asthmatics who were already ex-smokers at the beginning of the follow-up had the highest mean asthma score (range 0-5), probably as a result of the healthy smoker effect (2.80 vs. 2.44 in never smokers, 2.19 in quitters and 2.24 in smokers; p < 0.001). The influence of smoking on FEV1 decline did not depend on asthma status. Smokers had the highest proportion of subjects with chronic cough/phlegm (p< 0.01). The results suggest that 1 in 4 subjects with asthma continue smoking and report significant chronic cough and phlegm than nonsmokers and ex-smokers. This study suggests that cigarette smoking is a major risk factor for asthma exacerbation, even in those with less severe asthma.

A study by Annesi-Maesano and colleagues (2004) examined rates of asthma among adolescent smokers in France via self-report measures. Overall, smokers were more likely to report a lifetime asthma diagnosis than non-smokers (14.2% versus 11.9%). And active smokers also were more likely to report severe asthma (OR = 4.02). After controlling for demographic factors and passive smoking, active smoking was associated with a greater risk of both current (OR = 1.85) and lifetime (OR = 1.4) asthma. Hublet and colleagues (2007) examined prevalence rates of smoking among 15-year-olds with and without asthma in six countries (Belgium, Canada, Denmark, Finland, France, Netherlands) through self-report measures. The authors indicated that daily smoking was higher among adolescents with asthma (20.5%) than those without (17.9%; OR = 1.26). These studies suggest that smoking can become a cause of asthma, not just a trigger for an asthma attack.

Bircan et al. (2021) evaluated the association between e-cigarette use and self-reported diagnosis of asthma, COPD, and asthma-COPD overlap syndrome (ACOS) using a large nationally representative sample of adults aged ≥18 years in the US. E-cigarette users had increased odds of
self-reported ACOS OR=2.27 (2.23-2.31), asthma OR=1.26 (1.25-1.27) and COPD OR=1.44 (1.42-1.46). The authors suggested that e-cigarette use is associated with an increased odd of self-reported asthma, COPD, and ACOS.

3.5. Poverty and Asthma

Poverty is one of the most significant yet understudied social conditions of the 21st century (Beech et al., 2021), and can be defined as the lack of resources necessary to meet basic human needs (Ngoma et al., 2017). The level of relative poverty in the US is measured by the federal poverty level (FPL), and for a single-person household, the 2020 relative poverty level was $12,760 a year, or just under $35 a day (Beech et al., 2021). Studies have demonstrated that low socioeconomic status (SES) and exposures connected to poverty are strongly associated with both developing asthma and subsequent poor asthma outcomes including pulmonary function symptom burden, and exacerbations (Sullivan & Thakur, 2020). A large literature has documented that children from low SES families are more likely to live in poor environments that have greater exposure to toxic substances and is less conducive for children's development (Evans & Kantrowitz, 2002). A study by Eum and colleagues (2019) examined the relationship between community-level SES indicators and asthma-related emergency department (ED) utilization for school-aged children in 2011 and 2015. The results indicated that both median household income and health insurance coverage were key socioeconomic predictors of a child's asthma-related ED utilization. The Asthma Surveillance United States (ASUS) 2006-2018 report indicated that asthma prevalence is differed by poverty level. The report furthered that asthma exacerbation is more prevalent among persons with family incomes below the FPL.

Children from poor families often live in neighborhoods with toxic wastes, and such neighborhoods, often located in the inner city, are also more dangerous and lack social support
and critical social infrastructure (Sampson et al., 2002). Low income is generally referred to as poverty and has been repeatedly linked to increased asthma prevalence, exacerbations, hospitalizations, and intensive care unit (ICU) admission (Grant, Croce & Matsui, 2022).

A systematic review and meta-analysis by Redmond et al (2022) to investigate the impact of SES on asthma health care utilization, exacerbations, and mortality utilized 61 studies, comprised of 1,145,704 asthma patients. The study found that lower SES was consistently associated with increased secondary health care utilization including ER visit OR=1.61 (1.40-1.84), hospitalization OR=1.63 (1.34-1.99), readmission OR=1.31(1.19-1.44), borderline significance for increased exacerbations OR=1.18 (0.98-1.42) and mortality OR=1.12 (0.92-1.37) in deprived groups. The authors concluded that asthma patients with lower SES increasingly use secondary health care.

Perez and Coutinho (2021) in their study on the overview of health disparities in asthma in the US, reported 2.4 times higher ER visits for asthma for people of low SES neighborhoods, (median 63.5 (interquartile range (IQR) 34.3)) than those in high SES neighborhoods (median 26.5 (IQR 18.4)), even after adjusting for other forms of pollution. The risk ratio (RR) for residents of low SES neighborhoods with asthma related ER visit was almost 40% higher than those in high SES neighborhoods RR=1.39 (1.21-1.57). An added factor here is that many poor people do not have a primary care physician and receive most health care from emergency rooms.

Poverty and the associated disadvantages of lack of personal and social resources often lead to unsafe habitation (Samuels et al., 2022), unhealthy diets, poor water quality, increased exposure to infectious diseases, environmental pollution and toxins (Beech et al., 2021; Ngoma et al. 2017). And the primary care service that is a cornerstone for building a strong healthcare system...
that ensures positive health outcomes and health equity for people living in poverty (Board on Population Health, 2012; Shi, 2012) is often not accessible to the poor because they are more likely to be uninsured or are enrolled in Medicare (Pennel et al., 2016; Al-Arifi & Al-Rashdi, 2018). Also, their lack of reliable transportation to get to the healthcare facilities (Syed, Gerber & Sharp, 2013) coupled with increased number of rural hospital closures in recent years (Wishner et al., 2017) in low socioeconomic neighborhoods often force the poor to go to the nearest ER for medical emergencies and even their regular routine checks (Madani & Carpenter, 2023).

Respiratory diseases including asthma infections are linked to infectious agents (Gern, 2008), and other factors such as poverty, and smoking (Cortes-Ramirez et al., 2021). This study was undertaken in order to assess and have a clear knowledge of the relationship between smoking, poverty and PM$_{2.5}$ exposure and ER visit for asthma. A major goal of this study therefore was to determine the relative importance of outdoor exposure to PM$_{2.5}$ air pollution in relation to the impact of smoking and poverty on ER visits for asthma attacks.

3.6. Materials and Methods

3.6.1. Health Data

From New York State Department of Health (NYSDOH), Statewide Planning and Research Cooperative System (SPARCS) database, asthma ER visits that did not result in hospitalization from 2010 to 2018 were retained. Included were subjects with a primary diagnosis at time of ER visit for asthma. For each year, the study calculated the number of ER visits for asthma using the International Classification of Diseases, Ninth Revisions, Clinical Modification (ICD-9-CM) code 493 and the International Classification of Diseases, Tenth Revisions, Clinical Modification (ICD-10-CM) code J45. SPARCS covers about 95% of hospitals in NYS but does not include
federal institutions such as the veterans’ affairs hospitals, or psychiatric facilities. SPARCS data includes a primary diagnosis and up to twenty-four other comorbidity diagnoses assigned at the time of hospital admission or ER visits as well as patient demographic and billing information.

Hospitals located in and regulated by NYS are required to report all diagnoses, up to fifteen per inpatient or ER visits to the NYSDOH upon discharge. This diagnostic reporting system, established in 1979, is known as SPARCS. The total number of ER visits, the primary diagnoses of asthma for each year, and the age structure were calculated as shown in tables 3S1-3S6.

3.6.2. Exposure Data

This study focused primarily on PM$_{2.5}$, and data was accessed from the United States Environmental Protection Agency (USEPA), National Emissions Inventory (NEI) database. This data is a comprehensive and detailed estimate of air emissions of air pollutants including the criteria pollutants, their precursors, and hazardous air pollutants (HAPs) from air emissions sources. This is released based primarily upon data provided by state, local, and tribal air agencies for sources in their areas and supplemented by data developed by USEPA. NEI has data on point, non-point, on-road, non-road, and event source. However, this study focuses only on the point sources to assess the impact of living in zip codes with point sources of criteria air pollutants (CAPs) on ER visits for asthma.

The NEI reports are released every third year. This study used information released in 2011, 2014, and 2017. It is important to note that only those point sources that are designed as Title V facilities are included in NEI for NYS. A Title V permit is an operating permit that is required by facilities that are major sources of air pollutants. These operating permits must be legally enforceable, and they are issued by permitting agencies to facilities that are sources of air pollution and are required by the Department of Environmental Conservation (DEC) for any
point source facility deemed to be considered under department regulations. Those facilities holding Title V permits are required to have pollution control measures in place and to report amounts of emissions to the Department of Conservation (DEC) on a regular basis. The total PM$_{2.5}$ exposure for this study was divided by the total land area per square mile in each geographical location. The final workable data was in pollution per square mile.

3.6.3. **Data on Poverty**

The US Census Bureau (USCB) collects data and publishes estimates on income and poverty in order to evaluate national economic trends and to understand their impact on the well-being of households, families, and individuals. The USCB has produced poverty estimates to measure the economic well-being of households, families, and individuals in the US since the 1960s. The official poverty measure defines poverty by comparing pretax money income to a poverty threshold that is adjusted by family composition. The USCB provides data on poverty from several household surveys and programs, and defines poverty by considering family income, variations, family composition and size. A family is poor when their total income falls below a set threshold. Poverty data by zip code was downloaded from the small area income and poverty estimates (SAIPE) program at the USCB website and were used in this study. The SAIPE program provides annual estimates of income and poverty statistics for all states, counties, and school districts of the US.

3.6.4. **Data on Tobacco Smoking**

Data on tobacco smoking data were accessed at the Behavioral Risk Factor Surveillance System (BRFSS) database. The BRFSS is the nation’s premier system of health-related telephone surveys that collect state data about US residents regarding their health-related risk behaviors, chronic health conditions, and use of preventive services. Established in 1984 with 15 states,
BRFSS now collects data in all 50 states as well as the District of Columbia and three US territories. BRFSS completes more than 400,000 adult interviews each year, making it the largest continuously conducted health survey system in the world. Since smoking data at the zip code level was not available in the BRFSS dataset, the county level data was. For each county, the crude smoking rates in the year under review were averaged and merged with the other data at zip code level.

3.7. Statistical Analysis

To determine how the rate of ER visits for asthma is affected by exposure to PM$_{2.5}$, smoking, and poverty, I employed a Quasi-Poisson family regression model. The decision to use Quasi-Poisson model was borne out of the fact that this is an ecological study using an overdispersed count data that exhibited more variation than given by the mean. A common way to deal with overdispersion for counts is to use the Quasi Poisson family model which is a generalization of the poisson regression family appropriate for modeling overdispersed count variables. This study is based on zip code level aggregated data, in which the pollutants (zip code and county level) and health data (primarily zip code level) were merged with rates of ER visits for asthma and pollutant per square mile at the zip code. The regression models were conducted with $P < 0.05$ as the threshold for statistically significant association. This was done to assess the association between PM$_{2.5}$ and asthma ER visits, smoking and asthma ER visits and poverty and asthma ER visits. Response variable was the rate of ER visits for asthma, and the predictor variable in the first group of models was PM$_{2.5}$, in the second group of models was poverty, and in the third group of models was smoking, all unadjusted.

Among adjusted models, the first group of regression model assesses the association between exposure to PM$_{2.5}$ and the rate of asthma ER visits adjusted for poverty. The second group of
regression model examines the association between PM$_{2.5}$ and the rate of asthma ER visits adjusted for smoking, and the third group of multiple regression analyses was run to find the relationship between PM$_{2.5}$ and asthma adjusted for both poverty and smoking. The R programming language and R software version 2022.07.1 (Build 554) was used in this study.

3.8. Results

3.8.1. Regression models

In selecting the best model for this analysis, different statistical regression metrics were employed such as the Root Mean Squared Error (RMSE) which is one of the two main performance indicators for a regression model, and Sigma, a key-component of regression models were calculated to measure the performance of a regression model. Table 2.1 shows the results of RMSE, Sigma and the performance score of the different regression family models. The Quasi-Poisson model emerged as the best model to analyze the association between exposure to PM$_{2.5}$, smoking and poverty, and ER visits for asthma.

Table 3.1. Comparing models with different regression model

<table>
<thead>
<tr>
<th>Disease</th>
<th>Name</th>
<th>Model</th>
<th>RMSE</th>
<th>Sigma</th>
<th>Performance Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asthma</td>
<td>Quasi-Poisson</td>
<td>glm</td>
<td>1.125</td>
<td>1.125</td>
<td>99.88 %</td>
</tr>
<tr>
<td></td>
<td>Negative binomial</td>
<td>glm</td>
<td>132.242</td>
<td>1.071</td>
<td>50.00%</td>
</tr>
<tr>
<td></td>
<td>Gaussian</td>
<td>lm</td>
<td>132.228</td>
<td>9.415</td>
<td>46.82%</td>
</tr>
<tr>
<td></td>
<td>Linear</td>
<td>glm</td>
<td>132.225</td>
<td>132.227</td>
<td>6.40e-03%</td>
</tr>
</tbody>
</table>
3.8.2. Results for the Unadjusted and Adjusted Associations Between PM$_{2.5}$, Poverty, and Smoking on Asthma

A summary of the associations between PM$_{2.5}$ and asthma, poverty and asthma, and smoking and asthma is shown in Table 3.2. The table shows significant associations between asthma related ER visits with all of the independent variables (PM$_{2.5}$, smoking, and poverty), with poverty showing the strongest effect.

3.8.2.1. Model A: Unadjusted Associations Between Asthma and PM$_{2.5}$, Asthma and Poverty, Asthma and Tobacco Smoking

The results of the crude model (model A) in Table 3.2 indicate that PM$_{2.5}$, poverty and smoking are all positively associated with ER visits for asthma. The results show a positive and statistically significant association between outdoor PM$_{2.5}$ and ER visits for asthma ($p=0.003$), which clearly suggests that the risk of asthma ER visits increases much more as PM$_{2.5}$. Smoking and smoke exposure was also found to be positively associated with ER visits for asthma in this study ($p=< 0.0001$). Comparable results were found in other studies (Stapleton et al., 2011; Eisner & Iribarren, 2007). The study results also showed positive and statistically significant association ($p = < 0.0001$) between poverty and ER visit for asthma in NYS between 2010 and 2018. This adds to numerous studies that linked poverty to increased asthma prevalence, ER visits and hospitalizations.

3.8.2.2. Model B: Association Between Asthma and PM$_{2.5}$, Adjusted for Smoking and Association Between Asthma and PM$_{2.5}$ Adjusted for Poverty

Model B in Table 3.2 summarizes the results of the association between PM$_{2.5}$ and asthma adjusted for smoking and then adjusted for poverty. When adjusted for smoking, both PM$_{2.5}$ and smoking showed positive associations with asthma, with smoking showing a higher effect. When adjusted for poverty, PM$_{2.5}$ did not show a strong significant association with asthma, although
its p-value (0.0729) showed that it was almost significant. However, poverty showed a positive association with asthma when used as an adjusting variable.

3.8.2.3. Model C: Association Between PM$_{2.5}$ and Asthma Adjusted for Both Smoking and Poverty

Model C in Table 3.2 shows the results of ER visit for asthma with PM$_{2.5}$ exposure and adjusted for both poverty and smoking. Here the results show a significant association between asthma ER visits and exposure to PM$_{2.5}$ when adjusted for both smoking and poverty. Also, both smoking and poverty showed strong positive and significant associations with asthma ER visits when used as adjusting variables. The table showed poverty to have the strongest effect, followed by smoking, and then PM$_{2.5}$. This can be summarized to mean that in the fully adjusted model, all the variables showed statistically significant association with asthma ER visits. These results appear to show that poverty is a major risk factor for ER visits than smoking and PM$_{2.5}$ in this study.

Table 3.2 Comparing the three models used to assess statistical significance in the first aim.

<table>
<thead>
<tr>
<th>Model</th>
<th>Term</th>
<th>β Estimate</th>
<th>Lower CI</th>
<th>Upper CI</th>
<th>p-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>A. Crude</td>
<td>Intercept</td>
<td>4.267</td>
<td>4.253</td>
<td>4.28</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td></td>
<td>PM$_{2.5}$</td>
<td>0.05</td>
<td>0.016</td>
<td>0.081</td>
<td>0.0026</td>
</tr>
<tr>
<td></td>
<td>Intercept</td>
<td>4.099</td>
<td>4.057</td>
<td>4.143</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td></td>
<td>Smoking</td>
<td>1.148</td>
<td>0.871</td>
<td>1.426</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td></td>
<td>Intercept</td>
<td>3.641</td>
<td>3.615</td>
<td>3.667</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td></td>
<td>Poverty</td>
<td>0.039</td>
<td>0.038</td>
<td>0.041</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>B. Multivariate</td>
<td>Intercept</td>
<td>4.267</td>
<td>4.253</td>
<td>4.281</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td></td>
<td>PM$_{2.5}$</td>
<td>0.058</td>
<td>0.024</td>
<td>0.089</td>
<td>0.0004</td>
</tr>
<tr>
<td></td>
<td>Smoking</td>
<td>0.058</td>
<td>0.044</td>
<td>0.071</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>------------------</td>
<td>---------</td>
<td>-------</td>
<td>-------</td>
<td>-------</td>
<td>----------</td>
</tr>
<tr>
<td>intercept</td>
<td>3.641</td>
<td>3.615</td>
<td>3.667</td>
<td>&lt; 0.0001</td>
<td></td>
</tr>
<tr>
<td>PM₂⁵</td>
<td>0.037</td>
<td>-0.006</td>
<td>0.074</td>
<td>0.0729</td>
<td></td>
</tr>
<tr>
<td>Poverty</td>
<td>0.039</td>
<td>0.038</td>
<td>0.039</td>
<td>&lt; 0.0001</td>
<td></td>
</tr>
</tbody>
</table>

C. Multivariate

<table>
<thead>
<tr>
<th></th>
<th>Intercept</th>
<th>3.641</th>
<th>3.615</th>
<th>3.667</th>
<th>&lt; 0.0001</th>
</tr>
</thead>
<tbody>
<tr>
<td>PM₂⁵</td>
<td>0.043</td>
<td>0.0004</td>
<td>0.08</td>
<td>0.036</td>
<td></td>
</tr>
<tr>
<td>Smoking</td>
<td>0.037</td>
<td>0.021</td>
<td>0.052</td>
<td>&lt; 0.0001</td>
<td></td>
</tr>
<tr>
<td>Poverty</td>
<td>0.039</td>
<td>0.038</td>
<td>0.04</td>
<td>&lt; 0.0001</td>
<td></td>
</tr>
</tbody>
</table>

*p*-values give the significance of adjusted associations between zip code level pollutant exposure and the outcome.

### 3.9. Discussion on the Association Between PM₂⁵, Poverty, and Smoking on Asthma

#### 3.9.1. Association Between Asthma and PM₂⁵

As referenced in the literature cited several studies and reviews have highlighted the association between PM₂⁵ and asthma, especially for exacerbating existing asthma, but also with an increase of new-onset asthma. The first model in the crude model in Table 3.2 looked at the association between PM₂⁵ and ER visits for asthma. The results showed a positive and statistically significant association between the two with a *p*-value of 0.003, which clearly suggests that the risk of asthma ER visits increases much more as PM₂⁵. This study shows that exposure to PM₂⁵ increases the risk of ER visits for asthma, and it is consistent with numerous studies (Liu, Hua, & Song., 2022; Fan et al. 2016; Vu et al., 2021), even at levels below the WHO air quality guideline limit of 15 µg/m³ (Sun et al., 2024).
3.9.2. Association Between Asthma and Smoking

In all three models, smoking was found to have a positive and highly significant association with ER visits for asthma. This is congruent with many studies that have found environmental factors to be important triggers of asthma, including cigarette smoking and secondhand smoke (Stapleton et al., 2011; Eisner & Iribarren, 2007). A groundbreaking study by Dockerty et al. (1993) called the Harvard six cities study found mortality rates to be strongly associated with cigarette smoking. This was also confirmed by Tiotiu et al. (2020) indicating that active tobacco smoking is associated with poorer asthma control and frequent exacerbations and hospital visits. In conclusion, the association between asthma and tobacco smoking showed the importance of smoking as a major and an avoidable risk factor for asthma (Silverman et al., 2003; Khokhawalla et al., 2015; Patel et al., 2009).

3.9.3. Association Between Asthma and Poverty

Model C looked at poverty as a risk factor for asthma ER visits. The study found a positive and statistically significant association ($p = < 0.0001$) between poverty and ER visit for asthma in NYS between 2010 and 2018. This confirms previous studies in which poverty has been extensively linked with increased asthma prevalence, ER visits and hospitalizations for asthma exacerbations (Espaillat, Hernandezb, & Burbank, 2023; Keet et al., 2017). The strong association between poverty and asthma is not surprising because poor people are generally believed to live in areas that are more contaminated, coupled with their lack of health insurance, which often leads them to the nearest ER (Keet et al., 2017; Alcala et al., 2023). Poverty causes diseases, which in turn results in poverty (Ngoma et al., 2017).
3.10. Conclusion

The current study showed three findings. First, there were associations between PM$_{2.5}$ and asthma, smoking and asthma, and poverty and asthma. Secondly, when adjusted for tobacco smoking, both PM$_{2.5}$ and smoking showed positive and statistically significant associations with asthma. However, PM$_{2.5}$ did not show a strong significant association with asthma when adjusted for poverty, it only showed marginal significance ($p=0.073$), but poverty did show a strong significant association with asthma when used as an adjusting variable. Thirdly, when adjusted for both smoking and poverty, PM$_{2.5}$ did show an association with asthma ($p$-value of 0.036), so did smoking and poverty with $p$-values of $<0.0001$ and $<0.0001$ respectively. They all showed significant associations with asthma ER visits, with poverty showing the most effect.

The main aim for this study was to assess an association between PM$_{2.5}$ exposure and ER visits for asthma, and also the association between poverty and smoking and ER visits for asthma. This study has established that there were indeed such associations. It is therefore advised that embarking on PM$_{2.5}$ reduction strategies, including smoking and poverty reduction or elimination strategies will help improve quality of life. For example, Kheirbek et al. (2013) in one of the scenarios in their study, suggested that improvements in PM$_{2.5}$ are estimated to result in 210 avoided premature deaths, 140 avoided hospitalizations for cardiovascular and respiratory diseases, and 400 fewer ED visits for asthma, annually across NYC.

In overall models, the study observed positive and statistically significant associations between PM$_{2.5}$ and ER visit for asthma among poor people and smokers. The strong association that was observed in this study between poverty and asthma is consistent with a study by Lenick et al. (2017) in which they observed stronger associations between air pollution and pediatric asthma in extremely low SES neighborhoods compared with areas of higher SES. Air pollution is
positively associated with the risk of asthma, and low SES environments and smoking confer vulnerability to a variety of health conditions.

There are limitations to this study, and these limitations are important for consideration and adjustment in the studies that follow. We have no measurements of indoor air pollution, and most people spend more time indoors than outdoors. While outdoor air pollution does get inside a home, the many indoor sources of particulates dominate, these are not captured in this study. In addition, there is no information on access to primary health care, which is often lacking for people of low socio-economic status. Thus, poor people mostly use the ER for illnesses for which people with health insurance and having a primary care physician would not need to access. In addition, our measures of poverty and smoking are at the county level, not zip code and certainly not at the individual level.
Chapter 4


4.1. Abstract

People of all ages suffer from respiratory diseases such as asthma and respiratory allergies, chronic obstructive pulmonary disease (COPD), occupational lung diseases and pulmonary hypertension. Respiratory diseases affect the lives of more than one billion people worldwide and more than 500 million of them live in developing countries or in deprived populations according to the global burden of disease (GBD, 2017). Chronic respiratory diseases are increasing in prevalence and are responsible for a significant burden of disease from direct healthcare costs, significant disability, premature mortality, lost productivity, and social consequences, and account for over four million deaths annually. Close to 545 million people in the world had a chronic respiratory disease and accounted for 3·9 million deaths in 2017, an increase of 39·8% since 1990 (Soriano et al., 2020). Respiratory diseases are among the most common non-communicable diseases worldwide, largely due to environmental, occupational, and behavioral exposure risk factors such as tobacco smoke, indoor and outdoor air pollution. Growing evidence indicates that ambient air pollutants including the criteria pollutants particulate matter (PM), nitrogen oxides (NOx), sulfur dioxide (SO2), carbon monoxide (CO), lead (Pb) and ozone (O3) have been among the world’s most serious environmental problems and play a pivotal role in the exacerbation of chronic diseases such as asthma and COPD. Studies have found strong associations between criteria pollutants exposure whether short term or long-term and respiratory disease exacerbation and eventual emergency room (ER) visits. It is important to note that depending on the prevailing circumstances, different pollutants may have widely different exposure-response characteristics. Urban ambient air pollution is the result of
emissions from multiple sources, that are stationary, industrial, from domestic fossil fuel combustion, and resulting from petrol and diesel vehicle emissions, and the resuspension of dust particles. Multiple epidemiology studies have established the relationship between ER visits and hospitalizations for respiratory diseases and air pollution exposures.

The goal of this project was to assess the association, if any between ER visits for asthma and COPD, two of the most common respiratory diseases, and exposure to criteria air pollutants (CAPs) at zip code levels in New York State (NYS) from 2010 to 2018. Exposure data on the point source CAPs was retrieved from the United States Environmental Protection Agency (USEPA) National Emission Inventory (NEI) database, the ER visits data for asthma and COPD were acquired from the New York State Department of Health (NYSDOH) Statewide Planning and Research Cooperative System (SPARCS) datasets. The statistical method used was the log-linear mixed effects models, and adjusted for year, sex, age category, county level poverty, county level smoking, county level PM$_{2.5}$, county level volatile organic compounds (VOCs) and CAPs from all pollution sources within the study period. This was also used to adjust for associations between the rates of ER visits, scaled to per 10$^5$ population, and criteria pollutants at the zip code level, especially to account for within-county variability. Results clearly show associations between ER visits for asthma and COPD, and most of the pollutants in the study, even after adjusting for the effects of poverty and smoking. The findings suggest that localized point source pollution due to CAPs, while being only a small portion of overall air pollution from all sources, poses a small but significant contribution to the risk of respiratory disease-related ER visits.
4.2. Introduction

Asthma and chronic obstructive pulmonary disease (COPD) are respiratory diseases known for affecting the quality of life of people of all ages throughout the world (Khatri & Tamil, 2018; Li et al., 2020). They pose serious public health concerns and are estimated to have caused millions of deaths worldwide (Li et al., 2020). Asthma is a chronic disease, but asthma attacks are a reversible respiratory event that is characterized by a response to hypersensitivity of airways, while COPD, for which asthma is one of the risk factors, is characterized by non-reversible airways obstruction (Khatri & Tamil, 2018; Cukic et al., 2012; Silva et al., 2004). In other words, asthma attacks are manifested as intermittent and reversible airway obstruction, while COPD is progressive and irreversible (Zeki et al., 2011). Both diseases are disorders that are associated with increased inflammation (Green & Turner, 2017). Also, some patients with airway disease have features of both asthma and COPD (Morissette et al., 2022), indicating that both diseases can cause airway obstruction and are associated with chronic inflammation of the airways (Barnes, 2017). Exacerbations of both asthma and COPD are responsible for approximately 1.5 million and 2 million yearly visits to the ER respectively in the US (Khatri & Tamil, 2018; Simkovich et al., 2019). Respiratory diseases are among the leading causes of morbidity and mortality worldwide, and were responsible for approximately 3, 914, 196 deaths in 2017 (Soriano et al., 2020). Ambient air pollution accounts for an estimated 8% of the portion of disease burden for respiratory infections (Szyszkowicz et al., 2018). Asthma development and exacerbation is linked to air pollution from fossil fuel combustion in traffic, power plants, and industrial facilities (Castner et al., 2018). The relationship between air pollution and asthma attacks has been well-established particularly in countries with rapid urbanization and industrialization (Nsemo, 2019).
The undermentioned are some of the underlining mechanisms of action that have been published by epidemiological and mechanistic studies. When inhaled, ambient air pollutants induce airway inflammation and oxidative stress in bronchial epithelial cells, which often lead to the development of asthma or COPD (Shin et al., 2021). This is supported by epidemiological and clinical investigations suggesting that exposure to outdoor air pollutants including CAPs induces airway inflammation, hyper-responsiveness and oxidative stress leading to the exacerbations of asthma and COPD (Madaniyazi and Xerxes, 2021; Samoli et al. 2011; Mahler et al., 2023). Several studies conducted in different parts of the world have found that day-to-day increases in pollution levels are associated with the exacerbation of asthma. Zheng et al.,(2015) undertook a meta-analysis to quantify associations between short-term exposures to ozone (O₃), carbon monoxide (CO), nitrogen dioxide (NO₂), sulfur dioxide (SO₂), and particulates (PM₁₀ and PM₂.₅) and asthma-related emergency room (ER) visits and hospital admissions (HAs). The study found associations between these pollutants and significant increased relative risks (RRs) in asthma ER visits and HAs with O₃: RR=1.009(1.006, 1.011), CO: RR=1.045(1.029, 1.061), NO₂: RR=1.018(1.014, 1.022), SO₂: RR=1.011(1.007, 1.015), PM₁₀: RR=1.010(1.008, 1.013), and PM₂.₅: RR=1.023(1.015, 1.031). The study concluded that short-term exposures to the criteria pollutants account for increased risks of asthma-related ER visits and HAs that constitute a considerable healthcare utilization and socioeconomic burden.

Additional studies of air pollution have documented relationships between ambient air pollution and respiratory disease related ER visits for children that are considered to be the most susceptible group. Strickland et al.(2010) conducted a study to investigate short-term associations between ambient air pollutant concentrations and ER visits for pediatric asthma. A total of 91,386 children aged 5 to 17 years that visited the ER were collected from 41
metropolitan Atlanta hospitals between 1993 and 2004. The study results showed association
between the ambient pollutants and pediatric asthma ER visits even at relatively low ambient
concentrations, O₃: RR=1.062 (1.031-1.093), NO₂: RR=1.036 (1.018-1.055), CO: RR=1.023
(1.006-1.041), PM₂.₅: R=1.020 (1.002-1.039), and PM₁₀ [RR=1.020 (1.003-1.038)]. The study
concluded that ambient pollutants contribute to the burden of ER visits for pediatric asthma.

Byers et al. (2016) also undertook a time-series study to estimate short-term associations
between daily changes in SO₂, PM₂.₅ and O₃ and daily asthma-related ER visits in Indianapolis,
US. The study population comprised of 165, 056 asthma-related ER visits from 2007 to 2011.
The study results show interquartile range (IQR) increases in 3-day moving averages for SO₂
significantly associated with an increased risk of 3.3% (0.2%, 6.5%), especially during the warm
season for age group 5-44.

A multi-city assessment study by Alhanti et al. (2016) investigated short-term relationships
between ER visits for asthma and exposure to ambient O₃, CO, NO₂, SO₂, and fine particulate
matter (PM₂.₅) in Atlanta (1993-2009), Dallas (2006-2009), and St. Louis (2001–2007). The study
was age stratified by using city-specific daily time-series analyses. The study results
suggest that age and race are susceptibility factors for asthma exacerbations in response to air
pollution. Effects were stronger for the 5-18-year-olds, and there were stronger associations with
O₃ and NO₂ particularly among non-whites [RRs of 1.15 (1.11, 1.19)] per 28 ppb O₃ and
RRs=1.09 (1.06, 1.11) per 12 ppb of NO₂ than among whites [RRs =1.01 (0.96, 1.06)] per 28
ppb of O₃ and RR=1.02 (1.00, 1.05) per 12 ppb of NO₂. The results also showed stronger
association among males than females for CO and NO₂ with associations among males (RRs
=1.05 (1.03, 1.06) per 0.5 ppm of CO and RRs=1.07 (1.05, 1.09) per 12 ppb of NO₂ than among
females [RRs=1.01 (0.99, 1.03)] per 0.5 ppm of CO and RRs=1.03 (1.01, 1.06) per 12 ppb of NO₂.

Similarly, a time stratified case-crossover study investigating associations between short-term fluctuations in ambient air pollution concentrations and asthma ER visits in Windsor, Canada was conducted by Lavigne et al. (2012). The study observed significant associations between 1-day lagged exposure to SO₂, NO₂, CO, O₃ and ER visits for asthma. Additionally, significant association was also observed for 1-day lagged exposure to CO and asthma visits among children throughout the year with OR=1.15 (1.02-1.31). In conclusion, positive associations between ambient levels of SO₂, NO₂, CO, O₃ and ER visits for asthma were found, particularly among children.

Another common respiratory disease that is considered in this study is COPD which is characterized by progressive irreversible airflow limitation and chronic inflammation of the lungs. COPD costs the US around $29.5 billion in direct costs, and $20.4 billion indirect costs (DeVries, Kriebel & Sama, 2017). While air pollution is not the major cause of COPD, it can be an important trigger for exacerbations of symptoms resulting in the necessity of going to the ER (GOLD, 2015). Epidemiological studies have investigated the short-term effects of outdoor air pollution on COPD-related ER visits, HAs, and mortality, and most of these studies report significant positive associations for exposures to criteria pollutants. One such study (Li et al., 2016) was a systematic review that includes 59 studies in which the authors evaluated associations between short-term exposure to criteria pollutants (O₃, CO, NO₂, SO₂, PM₁₀, and PM₂.₅) and the risk of COPD exacerbations. The result showed an association between short-term exposure to the criteria pollutants and increased risk for COPD exacerbations. SO₂ and NO₂
exposure showed more significance especially in low-/middle-income countries, \( \text{SO}_2 \) [RR=1.012 (1.001, 1.023)] and \( \text{NO}_2 \) [RR=1.019 (1.014, 1.024)].

DeVries et al. (2016) also conducted a case crossover analysis to assess associations between short term exposures to \( \text{SO}_2 \), \( \text{NO}_2 \), and \( \text{PM}_{2.5} \), and COPD exacerbations among 168 patients in central Massachusetts between 2012 and 2013. The study found significant associations between short-term \( \text{SO}_2 \) exposure and increased COPD exacerbation risk [OR = 2.45 (1.75-3.45)] per 1 ppb increase, and short-term exposure to \( \text{NO}_2 \) showed an association, but not as strong as the one for \( \text{SO}_2 \) [OR = 1.17 (1.05-1.30)] per 1 ppb increase. \( \text{PM}_{2.5} \) however did not show a positive association.

Faustini et al., (2012) conducted a large 4-year study in Rome by following COPD patients (n=145,681) aged 35+, and a comparison group of people without COPD (n=1,710,557). COPD patients showed higher mortality rates due to \( \text{PM}_{2.5} \), \( \text{PM}_{10} \), and \( \text{NO}_2 \) exposures but the comparison group did not, and \( \text{PM}_{10} \) showed a five times larger effect estimate for total mortality. The observed effect of \( \text{PM}_{10} \) was 3-7 times higher in the COPD patients 3.5% (-0.1% to 7.2%) than in non-COPD patients 0.7% (-0.8% to 2.2%). Respiratory mortality among COPD subjects was \( \text{PM}_{2.5} \) (interquartile range (IQR)=11 \( \mu \text{g/m}^3 \)) 11.6% (2.0% to 22.2%) and \( \text{NO}_2 \) (IQR=24 \( \mu \text{g/m}^3 \)) 19.6% (3.5% to 38.2%). The authors concluded that COPD patients are more susceptible to air pollutants such as \( \text{PM}_{10} \) and \( \text{NO}_2 \).

Most air pollution studies on respiratory diseases do so at air pollution sources other than point sources. Also, the point source pollution is just a minor part of the entire air pollution exposures. However, this study was meant to determine whether emissions from the point source that are considered small can still contribute to respiratory disease exacerbation. The goal of this study therefore was to assess the associations between rates of ER visits for asthma and COPD and
CAPs exposure as reported in the EPA NEI dataset in the state of NY from 2010 to 2018 in relation to living in zip codes with point sources of CAPs. Previous studies have reported elevated rates of hospitalization and ER visits for these diseases from non-point exposures (Delfino et al., 2014; Sinclair et al., 2014; ) and a few studies focused on individual point sources (Hendryx et al., 2019; Labelle et al., 2015; Smargiassi et al., 2009). This project will look at exposures to the CAPs for all point sources at zip code levels in the state of NY and their associations with ER visits for asthma and COPD from 2010 to 2018.

4.3. Criteria Air Pollutants and Respiratory Diseases

The USEPA listed the six common CAPs under the Clean Air Act in the 1970s. The primary CAPs include CO, SO\textsubscript{2}, NO\textsubscript{2}, O\textsubscript{3}, PM and Pb. Short or long-term exposures to these pollutants are known to cause adverse health effects that often lead to hospitalizations or ER visits (Saxena & Sonwani, 2019). Especially for respiratory diseases including asthma and COPD, and in some cases even lead to premature deaths (Shen et al, 2020; Viegi et al., 2020).

4.3.1. Carbon Monoxide and Respiratory Diseases

CO is a colorless, odorless, and tasteless gaseous pollutant primarily from traffic or industry (Wang et al., 2019), produced by incomplete combustion of fossil fuels such as in motor vehicles (Liu et al., 2018), and cigarette smoke (Hoyt, 2013). It is a ubiquitous air pollutant (Rochette et al., 2013), and its toxicity is the most common type of fatal air poisoning in most countries including the US. CO is responsible for hundreds of deaths and thousands of ER visits every year (Hess, 2017). The pathophysiological mechanism on the effect of CO is tissue hypoxia, due to its ability to bind with hemoglobin to form carboxyhemoglobin (Lee et al., 2020) and prevent the delivery of oxygen to tissues. Therefore, it is not surprising that exposure to an air pollutant that
reduces delivery of oxygen would exacerbate diseases that already have reduced the delivery of oxygen to tissue.

In the US, exposure limit in the workplace has been set by the Occupational Safety and Health Administration (OSHA) at 50 ppm time-weighted-average (TWA) over 8 hours, 25 ppm short-term exposure limit, and 200 ppm ceiling, while the National Institute for Occupational Safety and Health (NIOSH) sets a recommended exposure limit of 35 ppm 8 h TWA (Hess, 2017).

Epidemiological studies have found that ambient CO has significant adverse effects on public health worldwide (Wang et al., 2019) and has been linked to increases in ER visits for asthma, COPD and other respiratory diseases (Castner et al., 2018). It is also responsible for approximately 15,000 ER visits for respiratory diseases and 500 related deaths annually (Roderique et al., 2015). To examine the effects of particulates and CO concentrations on asthma exacerbation among urban children, Evans et al. (2014) conducted a pilot study to explore the relationship between asthma exacerbation and ambient concentrations of particles and CO. The results showed that ultrafine particles (PM$_{0.1}$) and CO increase exacerbation risk in urban children. IQR for PM$_{0.1}$=2088 p/cm$^3$ [OR=1.27 (0.90-1.79)] and CO IQR= 0.17 ppm, [OR=1.63 (1.03-2.59)]. Their findings regarding CO and pediatric asthma events were consistent with previous studies showing increases in the risk of ER visits and hospitalizations for asthma in children.

Song et al., (2023) with a total of 72,430 hospitalized cases in Ganzhou, Southeast China conducted a time series study to evaluate the association and the exposure–response relationship between ambient CO exposure and the risk of hospitalization for total and specific respiratory diseases including asthma, COPD, upper respiratory tract infection (URTI), lower respiratory tract infection (LRTI), and influenza-pneumonia. Results showed CO exposure was significantly
associated with hospitalization risk for all the respiratory diseases, and further indicated that for each 1 mg/m$^3$ increased in CO at lag 0-2, hospitalizations for total respiratory diseases. Asthma increased by OR =17.74 (1.34%, 36.8%), COPD increased by OR =12.45 (2.91%, 22.87%). Women were more susceptible to ambient CO exposure-associated hospitalizations for asthma. The authors concluded that they found significant positive exposure–response relationships between ambient CO exposure and exposure-associated respiratory hospitalizations.

Similarly, an ecological time series study, including 4,534 COPD hospitalizations in Ahvaz, Iran, carried out by Raji et al. (2020) found positive association between ambient CO exposure and COPD hospitalizations [RR=1.643 (1.233–2.191)].

Another time-series study conducted by Zhao et al (2019) examined short-term association between ambient CO and ER visits for respiratory diseases in Dongguan, China from 2013 to 2017 with a total of 89,484 outpatient visits for respiratory diseases including asthma, COPD, pneumonia and bronchiectasis cases. Results showed every IQR increase in CO at lag 0-3 corresponded to 5.62% (3.24%, 8.05%) for all respiratory diseases, 8.86% (4.89%, 12.98%) for asthma, 6.67% (0.87%, 12.81%) for bronchiectasis and 7.20% (2.35%, 12.29%) for pneumonia. The study concluded that short-term exposure to ambient CO was associated with increased risk of outpatient visits for respiratory diseases.

4.3.2. **Lead Exposure and Respiratory Diseases**

Pb is an environmental toxin that is associated with numerous adverse health effects in children and adults (Delgado et al., 2018; Boskabady et al., 2018). It is a persistent metal in all parts of the environment, in air, water and soil, and is primarily derived from a variety of manufactured products like leaded gasoline, paints, ceramics, solders, water pipes, hair dye, cosmetics,
airplanes, farm equipment, shielding for x-ray machines (Boskabady et al., 2018). And it is very toxic to certain body cells such as neurons (Delgado et al., 2018; Moyebi et al., 2024).

Exposure occurs through ingestion of Pb-contaminated substances and inhalation of Pb particles that come from the burning of Pb-containing materials, such as leaded gasoline and residential paint are the primary routes of exposure to Pb (Boskabady et al., 2018; Al Osman, Yang & Massey, 2019). And exposure to Pb plays a major role in exacerbating respiratory diseases (Boskabady et al., 2018), including COPD, pulmonary dysfunction, antioxidant activity (Gogoi et al., 2019), asthma (Farkhondeh et al., 2015), and neurodevelopmental impacts (Al Osman, Yang & Massey, 2019; Moyebi et al., 2024). Correspondingly, soil and water Pb distribution have been shown to be associated with patterns of respiratory disease burden in Iran (Skalny et al., 2020). Pb-induced asthma includes effects on immune balance, oxidative stress, and inflammatory responses (Samarghandian et al., 2015), resulting to seizures, headache, coma and even death (Pfadenhauer et al. 2014). While air levels of lead have been dramatically reduced in the US, it is still a problem at some specific sites. However, there is little release of lead from point sources in NYS. Since lead exposure was very low and variable, I decided not to include it in the study analysis.

4.3.3. Particulate Matter and Respiratory Diseases

PM is of great public health concern because it is capable of penetrating deep into the lungs and reaching the pulmonary alveolar region, this is particularly the case for PM$_{2.5}$ and the ultra-fine PM$_{0.1}$ (Harrison and Yin, 2000; Kim et al., 2015; Bergmann et al., 2023).

Studies have shown correlations between PM$_{0.1}$ and different respiratory diseases in different parts of the world. For example, Bergmann et al. (2023) examined association between short-term exposure to PM$_{0.1}$ and mortality and hospitalizations in Copenhagen, Denmark. The results
showed significant associations between exposure to PM$_{0.1}$ and hospitalizations for asthma and mortality for COPD. One IQR increase in PM$_{0.1}$ was associated with an OR=1.04 (.01, 1.07), lag 0-4, and 1.02 [1.00, 1.04], lag 0-1, was associated with COPD mortality [OR=1.13 (1.01, 1.26)] and asthma hospitalization [OR=1.08 (1.00, 1.16)] at lag 0-1. The study findings showed that short-term exposure to PM$_{0.1}$ can trigger respiratory disease mortality and morbidity in Copenhagen, Denmark.

PM$_{2.5}$ has also been associated in multiple epidemiological studies with ER visits for respiratory diseases (Shukla et al., 2022; Kyung & Jeong, 2020), and has also been found to cause lung function reduction and airway inflammation (Gauderman et al., 2004; Wang et al., 2013), COPD, and asthma exacerbations (Pope et al., 2009; Nachman and Parker 2012; Tsai et al., 2013). A multicity time-series study involving 112 cities in the US conducted by Zanobetti & Schwartz (2009) showed that a 10-μg/m$^3$ increase in 2-day averaged PM$_{2.5}$ resulted in a 1.68% increase (1.04-2.33) in respiratory deaths.

It has been suggested by multiple studies that PM may exacerbate asthma symptoms and increase incidence risks of asthma (Deng et al., 2015; Matthews et al., 2016). The global burden of outdoor air pollution on asthma ER visits in 2015 alone was estimated to be between 5 and 10 million globally. This was attributable to PM, where 12% of these estimates were observed in China (Madaniyazi & Xerxes, 2021). Duan, Hao, & Yang (2020) indicated that for every 10μg/m$^3$ increase in PM$_{2.5}$ concentration, the risk of hospitalization increases by 1.61% in COPD patients in the US, and 0.82% in Beijing, China.

Although most studies focus on the smaller particulates, thinking the larger particles are usually removed from the respiratory and do not enter the alveoli, some studies have found associations between larger particulates and respiratory diseases. Kang et al. (2023) in their nationwide
retrospective cohort study of 121,423 adults in South Korea found associations between PM$_{10}$ exposure and mortality for severe exacerbation of respiratory diseases. But if one only measures PM$_{10}$, that measure will include smaller particulates that may in fact be the responsible factor.

Another study on PM$_{10}$ was conducted in London, United Kingdom (UK) by Canova et al. (2012). This was a case-crossover study to investigate PM$_{10}$ induced HAs for asthma and COPD with 234 admissions, between May 2008 and July 2010. The study found that every 10 μg/m$^3$ increase in PM$_{10}$ was related to an increase in asthma or COPD admission rate, especially in lag 0-3 days [OR=1.35 (1.04-1.76)]. In summary, PM$_{10}$ outdoor concentrations were associated with increased HAs for exacerbation of asthma or COPD among adults in London.

### 4.3.4. Sulfur Dioxide and Respiratory Diseases

SO$_2$ is one of the six criteria pollutants in the air quality index that can be emitted by natural and anthropogenic sources (Khalaf et al., 2022). SO$_2$ is generated from the burning of sulfur-containing fuel like coal and is one of the prevalent air pollutants released from natural sources such as volcanoes or anthropogenically from burning of fossil fuel and biomass at large industrial plants such as oil refineries and power stations (Bǎlǎ et al., 2021; Khalaf et al., 2022). Recent studies have shown SO$_2$ is also a biological gas in various mammalian tissues (Huang et al., 2022), and people with asthma are especially susceptible to its effects (Li et al., 2010). Short term exposures of asthmatic individuals to elevated levels of SO$_2$ while exercising at a moderate level may result in breathing difficulties, wheezing, chest tightness, and shortness of breath (Sims et al., 2020). Orellano et al., (2021) conducted a systematic review and meta-analysis to evaluate the effect of short-term exposure to ambient SO$_2$ on all-cause and respiratory mortality. The study found that every 10 μg/m$^3$ in acute SO$_2$ exposure was significantly associated with all-cause mortality [RR=1.0059 (1.0046-1.0071)], and respiratory mortality [RR=1.0067 (1.0025-
The authors concluded that there were positive associations between short-term exposure to ambient SO₂ and all-cause and respiratory mortality.

A cohort study comprised of 351 asthmatics and 327 non-asthmatic children in Puerto Rico from 2009 to 2010 was conducted by Rosser et al. (2020). The study evaluated the effects of annual average 1-hour daily maximum SO₂ on asthma, atopy, total IgE, and lung function. Results showed annual SO₂ exposure (per 1 ppb) was significantly associated with asthma [OR=1.42 (1.05-1.91)] and atopy [OR=1.35 (1.02-1.78)]. The study conclusion was that SO₂ exposure is linked to asthma and atopy, and long-term SO₂ exposure also showed association with reduced FEV1/FVC, particularly in the asthmatics.

SO₂ exposure has been correlated with increased overall ER visits for asthma, COPD, upper respiratory infection, pneumonia, dysrhythmia, hypertension, abdominal pain, depression, and headache (Castner et al., 2015). Health effects and symptoms related to this pollutant include burning to the nose and throat, sore throat, difficulty inhaling deeply, altered sense of smell, and increased susceptibility to respiratory infections. SO₂ combines with water in the respiratory tract to form sulfuric acid (Khalaf et al., 2022) which is likely responsible for some of the symptoms (Soltan-Abad et al., 2021). SO₂ has been linked to an accelerated decline in lung function, which is a special concern for developing children and people who have underlying COPD, asthma, or other chronic respiratory diseases (Castner et al., 2015). SO₂ is also a bronchoconstrictor that promotes systemic inflammation and oxidative stress, especially in people with asthma (Zhu et al., 2014). Madaniyazi & Xerxes (2021) indicated that the association between SO₂ exposure and exacerbation of asthma has been investigated extensively, and it has been confirmed to be a key risk factor for asthma even at low levels.
A meta-analysis on the short-term exposure to SO₂ and the mortality of asthma in East Asian
countries reported that hospital utilization for asthma among children increased by 5.7% for
every 10μg/m³ increase in the daily mean concentration of SO₂. Like NO₂ and O₃, SO₂ has also
been strongly associated with asthma and exacerbations (Madaniyazi & Xerxes, 2021), and
elevated SO₂ levels can cause coughing, mucus secretion, and aggravation of asthma (Smargiassi
et al., 2008; Kim et al., 2013; Brand et al., 2016; Byers et al., 2016).

4.3.5. **Nitrogen Oxides and Respiratory Diseases**

NOₓ are produced from natural sources such as volcanic activity, biomass burning and bacterial
activity (Ghaly & Ramakrishnan, 2015) or from anthropogenic sources such as burning of fossil
fuels in stationary sources like industrial plants, or in motor vehicles (César, Carvalho &
Nascimento, 2015). NOₓ causes respiratory irritation and can trigger cell damage and
inflammatory processes throughout the respiratory system, from the nose to the pulmonary
alveoli (Ghosh et al., 2012). Nitric oxide (NO), nitrous oxide (N₂O) and nitrogen dioxide (NO₂)
generate nitrogen oxides (NOₓ), which are considered primary air pollutants (César et al., 2015).
NO is a free radical that produces oxidants with low water solubility and can trigger cell damage
and inflammatory processes throughout the respiratory system, from the nose to the pulmonary
alveoli (Theodorakidou & Lambrou, 2017; Gorguner & Akgun, 2010). NOₓ causes respiratory
problems such as coughing, dyspnea, wheezing, bronchospasm, and pulmonary edema at high
concentrations (Ihedike & Ling, 2022). NOₓ is a free radical-producing oxidant with low water
solubility, and a deep lung irritant, (Bălă et al., 2021). It is a precursor to ground level ozone and
participates in the secondary formation of PM₂.₅. Nitric oxide has diverse roles on the immune
system from innate resistance to suppression of Th1 functions to induction of oxidative injury
(Ghosh et al., 2012; Solomon et al., 2000; Akaike and Maeda, 2000). A longitudinal study was
conducted by Ghosh et al., (2012) in the Czech Republic to assess ambient NO$_x$ exposure and early childhood respiratory illnesses. Children were followed from birth to 4.5 years of age. For the first 2 years of life, an IQR increase in the 30-day average of NO$_x$ resulted in an OR=1.31 (1.07, 1.61) for bronchitis and OR = 1.23 (1.01-1.49) for two- to 4.5-year-olds. The results from this longitudinal study demonstrate an association between NOx and respiratory illnesses especially for bronchitis.

Many studies have reported the effects of short-term exposure to NO$_x$ on human morbidity and mortality (Sun et al. 2017). Meng et al. (2021) in their multilocation analysis in 398 cities found that a 10 $\mu$g/m$^3$ increase in NO$_2$ concentration on lag 1 day was associated with 0.47% (0.21% to 0.72%) increases in respiratory mortality. The authors therefore concluded that NO$_2$ is associated with considerable health risks even at levels below health-based standards and guidelines, including the current WHO air quality guidelines.

NO$_x$ exposures can exacerbate existing respiratory disease by impairing the functions of epithelial cells and alveolar macrophages, contributing to airway inflammation (DeVries et al., 2017). Increased levels of NO$_x$ have been correlated with increased use of ER visits, specifically for asthma, COPD, respiratory infections, otitis media, cardiovascular diseases, hypertension, dysrhythmia, abdominal pain, depression, and headache (Castner et al., 2015). A recent study was conducted by Kowalska et al. (2020) to assess the risk related to NOx and NO$_2$ concentration increase, and daily hospital visit due to bronchitis and asthma exacerbation in Poland. Results showed a significant association between outpatient visits and hospitalizations for bronchitis and asthma exacerbation and daily NOx concentrations. The strongest relationship was observed in the case of NO$_2$, and outpatient visits due to bronchitis, RR = 1.434 (1.308-1.571). In addition to traffic related air pollution, evidence from previous studies has shown that people who live near
contaminated sites known as point sources showed abnormalities of serum immunoglobulins and suffer from more frequent hospitalization for respiratory infections, chronic bronchitis, and COPD (Carpenter, Ma & Lessner., 2008). Power plants account for approximately 16% of NOx emissions in the US (Sims, Leggett, and Myla., 2020). This research focuses on addressing the critical gap of assessing associations between CAPs from all point sources at zip code levels in NYS and ER visits for asthma and COPD from 2010-2018. And to determine which of the CAPs has the most effect on the outcomes of interest.

4.4. Materials and Methods

4.4.1. Study Population and Study Area

The study population includes all ER visits due to asthma and COPD in NYS from 2010 to 2018 covered by NYSDOH. This study covered the entire population of NYS at a zip code level, covered by the NEI dataset and SPARCS.

4.4.2. Health Related Data

Information on asthma and COPD ER visits that did not result in hospitalization was retrieved from the NYSDOH SPARCS system database. This data is NYS widely used and legislatively mandated collection of health data information on HAs and discharges including ER visits and covers about 95% of all hospitals in NYS but does not include federal institutions such as the veterans’ affairs hospitals, Indian health services or psychiatric facilities. SPARCS data include information on principal diagnoses, HAs and discharge dates, sources of payment, date of birth, sex, race/ethnicity, length of stay, and street address. SPARCS data have been widely used in previous studies examining similar respiratory outcomes (Hopke et al., 2020; Alper et al., 2021). Asthma and COPD in this study include hospital ER visits from 2010 through 2018. There were 643,066 ER visits for asthma and 254,549 for COPD, with primary diagnosis using the
International Classification of Diseases (ICD), 9th and 10th revisions, Clinical Modification (CM). The study looked at asthma (ICD-9-CM code 493 and ICD-10-CM code J45) and COPD (ICD-9-CM codes 490-496 and ICD-10-CM codes J40-J47). These respiratory diseases were chosen due to well-established associations previously established. The outcome was defined as the number of cases during the period from 2010 to 2018, aggregated by gender, race, and age groups. The age stratified category for asthma was (0-5, 6-19, 20-44, 45-64, 65-74, 75+), and COPD age category in years was (35-44, 45-59, 60-74, and 75+). Ages 35-44 years have been used as the median age range at which COPD is usually diagnosed (DeMeo et al., 2022; Divo et al., 2018). This age group was therefore used as reference age for COPD in this study. The age reference used for asthma in this study was 45-64.

4.4.3. Data on CAPs Exposure

Air pollution sources are categorized as point, non-point, on-road, non-road, and event, according to EPA NEI. This study was limited to the point source emissions of the criteria pollutants because NEI provides point source exposure data at the zip code level, but not the other sources. However, data for the other sources such as on-road, non-road and non-point data are provided at the county level. Since the ER data is at the zip code level, this study is limited to exposure to point source pollution. To account for within county variability, county level total VOCs and CAPs were used as adjusting variables since the CAPs are present with VOC pollution at county level and the point-source pollution is superimposed on that coming from on-road, non-road, and non-point sources.

A point source emission is one produced by large and stationary sources like power plants, industries, airports, or smaller non-industrial sources. Point source pollution information for PM$_{2.5}$, CO, Pb, NOx, and SO$_2$ for the years 2011, 2014, and 2017 was retrieved at the USEPA.
NEI website. However, data for O₃, which is also a CAP, is not available in the NEI dataset, and there was so little release of lead that it was not considered. Pollutant site latitude and longitude locations were then associated with the zip code in which the facility was located using a scheme that minimized the absolute great circle distance between the zip code centroid and the site location. Data from the USCB was used to determine the land area in square miles in each zip code. For each pollutant, zip code, and year, the pollution per square mile was calculated by summing all point source contributions of the pollutant and dividing by the land area size of the zip code region. The workable data was in pollution per square mile.

4.4.4. Data on Poverty

Poverty data was downloaded from the United States Census Bureau (USCB) website for the years covered in this study. This site provides poverty data from several household surveys and programs, and the official poverty measure defines poverty by comparing pretax money income to a poverty threshold that is adjusted by family composition. County level poverty data was used in this study since the USCB did not have poverty data at the zip code level. Families are considered poor if their total income falls below a certain threshold. All families that fell below the threshold were categorized as below mean, and those above the threshold were categorized as above the mean in this study.

4.4.5. Smoking Data

To find an association between asthma rate and smoking (a risk factor for both asthma and COPD), the Behavioral Risk Factor Surveillance System (BRFSS) database was searched for smoking data. This is a continuous, state-based surveillance system that collects information about modifiable risk factors for chronic diseases and other leading causes of death, and it is the nation’s premier system of health-related telephone surveys that collect state data. The county
level data was used to cover a wider range and scope. This data was then averaged over the study period and matched with zip codes which evenly covered the research geographical area. Smoking data were obtained at the county level since the zip code level data was not available.

4.4.6. Statistical Analysis

4.4.6.1. Missing CAPs Exposure Data

The study years were 2011, 2014, and 2017, because these are the years for which EPA report data. Reporting for these years had some inconsistencies across zip codes. For instance, in some zip codes emitting units did not report in all given years. This can be attributed to the fact that although reporting is mandatory for pollution emitters to report point source emissions, both at site and unit levels, in the state of NY they are often not enforced. Since point sources do not move, it is reasonable to assume that units still produced emissions even though they were not reported. Therefore, missing data for those years were inputted using emitting sites and unit IDs per zip code. For each zip code and site ID, missing unit IDs were inserted, and their emissions were replaced by the mean value of emissions reported assuming emissions were the same and for the samples provided by that unit when it did report. If the unit did not report at any time during the period sampled (2011 to 2017), it will not appear in zip code level emission totals. The largest source of missing data is cryptic and is not reflected in this study data because it consists of emitting units within a site and a zip code that failed to report in any of these years. This is a limitation of this dataset.

This means that the total number of zip codes reporting may not change much after imputation, but the pollutant totals do. Changes in zip codes during the study period were resolved by using a reference set of codes from 2011. The total number of zip codes in the state of NY is estimated at 1792, and a little less than that reported some point source pollution for at least one of the target
pollutants in 2011, 2014, and 2017, which also had cases of the diseases in this study. Those zip codes with disease cases but without point source data over the study period were given a point source emission rate of zero. Zip codes with zero population were assumed to be post office boxes and were not considered in the analysis.

4.4.6.2. Single Pollutant Models

Datasets were created by merging data across years for each pollutant and all years were analyzed together. Pollutant data for 2011 was associated with zip code disease rates for 2010, 2011, and 2012. Pollutant data from 2014 was joined to disease data from 2013, 2014, and 2015, and pollutant data from 2017 were used with disease data from 2016, 2017, and 2018. Data from all years were then stacked to complete the file.

Log-linear mixed effects regression models with random intercepts at the county level were used in this study to analyze the rates of ER visits for asthma and COPD and their associations with the CAPs. This model was chosen because it allows for both fixed and random effects, and the data in the study has hierarchical structures that include both zip code and county level data. A \( p \)-value of \(<0.05\) was considered statistically significant, and the R-squared likelihood ratio test was used as a measure of goodness of fit.

Adjusted associations between the rates of ER visits, scaled to per \(10^5\) population, and pollutants at zip code level were estimated using log-linear mixed effects models with a random effect to account for within-county variability. Models were adjusted for sex (reference level female), age category (reference level at 45-64 for asthma, 35-44 for COPD), a poverty category variable (reference below median poverty), average county level smoking, study year (reference level 2010), and county level VOCs and CAPs from all sources. All numeric covariates are standardized and the outcome case rate by zip code was log-transformed to achieve normality.
All data preparation and analysis were performed with the R programming language and R studio software version 2022.07.1 (Build 554).

4.5. Results

4.5.1. Association Between Asthma and the Criteria Air Pollutants in the Study

Table 3.1 shows the estimates, 95% CIs and the corresponding \( p \)-values for the CAPs in the study and their associations with asthma ER visits. All the measured pollutants are positive and significantly associated with asthma except for PM\textsubscript{2.5} which is also positive but not statistically significant. SO\textsubscript{2} showed the most effect closely followed by NO\textsubscript{x} and then CO. PM\textsubscript{10} showed significance, but the effect size is not as strong as the gaseous pollutants. This is clearly shown in figure 4.1.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Pollutant</th>
<th>( \beta ) Estimate</th>
<th>Lower CI</th>
<th>Upper CI</th>
<th>( P )-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asthma</td>
<td>CO</td>
<td>0.024</td>
<td>0.017</td>
<td>0.031</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td></td>
<td>NO\textsubscript{x}</td>
<td>0.032</td>
<td>0.017</td>
<td>0.047</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td></td>
<td>PM\textsubscript{2.5}</td>
<td>9.00E-04</td>
<td>-0.012</td>
<td>0.014</td>
<td>0.898</td>
</tr>
<tr>
<td></td>
<td>PM\textsubscript{10}</td>
<td>0.0167</td>
<td>-5.00E-04</td>
<td>0.034</td>
<td>0.057</td>
</tr>
<tr>
<td></td>
<td>SO\textsubscript{2}</td>
<td>0.1169</td>
<td>0.096</td>
<td>0.138</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

\* \( p \)-values give the significance of adjusted associations between zip code level pollutant exposure and the outcome.
Figure 4.1 shows the exposure-response relationship between CAPs and asthma ER visits from 2010 to 2018 by zip code given every 0.05 standard deviation increase in exposure. SO$_2$ showed the largest association with asthma ER visit, followed by NOx and CO. The effect size form PM$_{10}$ is greater than that of PM$_{2.5}$. The figure again indicates the gaseous pollutants showed the largest magnitude effect sizes in association with asthma.

Figure 4.1. Effect sizes for estimated associations for criteria pollutants and asthma

4.5.2. Association Between COPD and Criteria Air Pollutants

Table 4.2 displays the $\beta$ estimates, 95% confidence intervals, and p-values for the CAPs in the study, and their associations with ER visits for COPD. All the pollutants showed positive and statistically significant associations with COPD. Again, the gaseous pollutants showed the most effect, with NOx leading followed by SO$_2$ and CO.
Table 4.2. $\beta$ Estimate, CIs and $P$-values for CAPs and ER visits for COPD

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Pollutant</th>
<th>$\beta$ Estimate</th>
<th>Lower CI</th>
<th>Upper CI</th>
<th>$p$-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>COPD</td>
<td>CO</td>
<td>0.029</td>
<td>0.022</td>
<td>0.037</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td></td>
<td>NOx</td>
<td>0.041</td>
<td>0.029</td>
<td>0.053</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td></td>
<td>PM$_{2.5}$</td>
<td>0.009</td>
<td>0.002</td>
<td>0.018</td>
<td>0.0145</td>
</tr>
<tr>
<td></td>
<td>PM$_{10}$</td>
<td>0.012</td>
<td>0.004</td>
<td>0.021</td>
<td>0.0024</td>
</tr>
<tr>
<td></td>
<td>SO$_2$</td>
<td>0.029</td>
<td>0.021</td>
<td>0.037</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

*P-values give the significance of adjusted associations between zip code level pollutant exposure and the outcome.

Figure 4.2 showed the effect sizes of the pollutants in the study by zip code over the study period, given every 0.02 standard deviation increase in exposure. It can be seen that NOx showed the most effect followed by CO and SO$_2$. The particulates’ sizes are smaller than the gaseous pollutants. And this is consistent for the other diseases in the study.

![Figure 4.2. Effect sizes for estimated associations of criteria pollutants and COPD](82)
4.6. Discussion

Air pollution is a major environmental issue affecting respiratory health globally. This study has demonstrated that there is a significant burden of respiratory diseases when exposed to CAPs from point sources even though point sources are only a minor component of total CAPs.

4.6.1. Criteria Air Pollutants and Respiratory Diseases

The purpose of this study was to assess the associations between CAPs and ER visits for asthma and COPD at zip code levels in NYS from 2010 to 2018, and to identify which of the CAPs increases the risk of an ER visit for both diseases.

The respiratory system is very vulnerable to the hazardous effects of air pollution, and respiratory diseases are significant causes of hospital visits. Air pollution, including CAPs, has been extensively studied and proven to be a major risk factor that leads to significant adverse health outcomes. Both short- and long-term exposures to air pollutants can adversely affect respiratory health leading to ER visits, hospitalization, and in some cases even death by inducing airway inflammation, even at very low concentrations (Maio et al., 2023; Park et al., 2022). ER visits for asthma and COPD in this study showed significant associations with CAPs exposure when considering CAPs exposure coming only from point sources. This association was observed for all the years in this study even after adjusting for poverty and smoking in mixed effects regression models that allow for county level variation.

Single pollutant adjusted regressions showed that CO, NOx, and SO₂ contributed the largest to both disease outcomes. These are also the pollutants that contribute the largest amount of pollution from point sources. The results of this study are consistent with the findings of most of
the literature cited, suggesting that exposure to CAPs is a risk factor associated with an increase in the number of ER visits for both asthma and COPD.

4.6.1.1. CAPs and Asthma

Studies have indicated that air pollution contributes to increased asthma prevalence and symptom onset (Tiotiu et al., 2020; Delfino et al., 2014; Khreis et al., 2019) and asthma exacerbations (Orellano et al., 2017). This study adds to the many research studies that report that exposure to the CAPs increases the risk of ER visits for asthma, and that among the pollutants in this study, NOx and CO have the largest effects followed by SO₂. PM₂.₅, however, did not show any significant association with asthma. This may be because the amount of PM₂.₅ coming from point sources is very small relative to the amount coming from other sources, because there is other evidence showing clearly that PM₂.₅ does contribute to asthma attacks. It was a surprise to find a significant association with PM₁₀ but not PM₂.₅. However similar results have been previously reported, as mentioned above. Even though most larger particulates are trapped and removed by ciliary action and mucosa, they still may trigger irritation and inflammation. The effects of all of these pollutants on the onset and or exacerbation of asthma were confirmed in previous epidemiologic studies (Tiotiu et al., 2020; Delfino et al., 2014; Khreis et al., 2019). For instance, Gorai et al., (2014) in their GIS based approach for assessing the association between air pollution and asthma in NYS, found significant associations between exposure to CAPs with asthma prevalence rate in NYS, US.

4.6.1.2. CAPs and COPD

COPD is a common respiratory disease, affecting 5-10% of the US population. Smoking is known to be a major cause of development of COPD, and when an individual already has impaired respiratory function, it is not surprising that superimposed exposure to CAPs increases
the need for treatment in the ER. COPD related death has continued to increase, and it is one of the leading health burdens worldwide that accounts for almost 3 million deaths annually, and outdoor air pollution has contributed to its increased incidence and prevalence (Eisner et al., 2010; Song et al., 2014). From the results in table 3.2 of this study, there is strong positive and statistically significant association between the pollutants and ER visits. As was the case with asthma, the associations were strongest with the gaseous pollutant, which also were the largest component of pollutants coming from point sources. For COPD both PM$_{10}$ and PM$_{2.5}$ showed significant associations. These associations are confirmed by published associations between exposure to these air pollutants and ER visits for COPD (Li et al., 2016; Moore et al., 2016). For example, Cirera et al., (2013) reported that ambient air levels of SO$_2$ and NO$_2$ relate positively and significantly with a substantial increase in asthma and COPD ER visits.

4.7. Conclusion

Most pollutants in the study were positive and statistically significant with asthma, indicating a detrimental effect for relatively local point sources of pollution. All pollutants showed associations with asthma ER visits except PM$_{2.5}$. For COPD, all the pollutants showed significant positive associations with the outcome. The gaseous pollutants (CO, NOx, and SO$_2$) showed consistent positive associations and showed the most effects. For the particulates, PM$_{10}$ showed positive associations with asthma and COPD but with smaller effect size, while PM$_{2.5}$ also showed positive association with COPD but not asthma. Cirera et al. (2013) confirmed in their study that ambient air levels of SO$_2$ and NOx related positively and significantly with a substantial increase in asthma and COPD ER visits.
Chapter 5


5.1. Abstract

Cardiovascular disease is a public health problem contributing to 30% of mortality and 10% of disease burden globally and is considered the leading cause of death according to the World Health Organization (WHO). Cardiovascular disease prevalence nearly doubled from 271 million in 1990 to 523 million in 2019, and its related deaths increased from 12.1 million in 1990 to approximately 19.7 million in 2019 representing 32% of all global deaths according to the global burden of disease (GBD) study 2019. Cardiovascular diseases are a group of disorders of the heart and blood vessels such as ischemic heart disease (IHD), myocardial infarction (MI), cerebrovascular disease, stroke, peripheral arterial disease, and other conditions. The prevalence of cardiovascular diseases is rising both in high-income countries and low- and middle-income countries, in great part because of increased success in preventing death from other causes.

The financial burden associated with cardiovascular diseases is also growing at an alarming rate. The American Heart Association (AHA) in 2017 indicated that the yearly costs for both direct and indirect cardiovascular disease expenditure to Americans is in several billions of dollars and is expected to exceed one trillion dollars by 2035.

There is strong scientific evidence of an association between increasing exposure to criteria air pollutants (CAPs) (both short-term and long-term) and elevated risk of incidence, exacerbation, and mortality of cardiovascular diseases in certain high-risk populations and throughout different geographic regions according to de Bont et al. (2022)
This study focuses on two major cardiovascular diseases, IHD and MI and their association with CAPs. MI is defined by pathology as myocardial cell death due to prolonged ischemia. It is usually a result of a blood clot travelling to the heart and occluding one of the cardiac arteries. Or atherosclerotic build up within a cardiac artery that finally occludes blood flow. This is largely due to an imbalance between oxygen supply and demand. IHD on the other hand refers to heart weakening caused by reduced blood flow to the heart. It is caused by narrowing of the heart arteries caused by lipid build up, causing an inadequate supply of blood to the heart.

The present study assessed the association between emergency room (ER) visits for both IHD and MI and exposure to the CAPs in New York State (NYS) between 2010 and 2018. Records of ER visit for both IHD and MI were obtained from Statewide Planning and Research Cooperative System (SPARCS) dataset, and the exposure data at zip code level for point sources were retrieved from the United States Environmental Protection Agency (USEPA) National Emission Inventory (NEI) dataset. The statistical method used was the log linear mixed effect model.

The study found criteria pollutant exposures to be significantly associated with IHD but not MI. This does not in any way suggest that air pollution is not a risk factor for MI, because there is no safe level of air pollution according to Centers for Disease Control and Prevention (CDC). However, patients with an MI are usually immediately hospitalized, and therefore are not reported as an ER admission. The results indicate that air pollution is an even more pressing global health challenge in current times, even at zip code levels. These results underscore the relevance of air pollution as a global health concern that affects cardiovascular health.
5.2. Introduction

Cardiovascular disease is an umbrella term for a broad range of diseases that affect the heart and blood vessels and are the leading cause of mortality and morbidity in the United States (US), and the world over (Campbell et al., 2008; Gastaldelli & Basta, 2010; Allarakha, Yadav, & Yadav, 2022). Cardiovascular disease is responsible for approximately one-third of deaths worldwide (Khan et al. 2020). Cardiovascular diseases include ischemic heart disease (IHD), myocardial infarction (MI), hypertension, stroke, peripheral arterial disease, and heart failure (HF) and remain major world health problems (Ruan et al., 2018; Bowry et al., 2015). The World Health Organization (WHO) noted that cardiovascular disease has no geographic, socioeconomic, or sex boundaries according to Deaton et al. (2011), and half of all US adults have some form of cardiovascular problem (Ward et al., 2014). In 2016, alone, more than 840,000 people died from cardiovascular related illnesses in the US and about 17.6 million deaths worldwide (Yan et al., 2019). This rate increases steadily year by year (Yan et al., 2019; Klompmaker et al., 2021; Allarakha, Yadav, & Yadav, 2022), and it is estimated that by the year 2030, around 23.6 million people will die of cardiovascular diseases per year globally (Francula-Zaninovic & Nola, 2018). In part this is a reflection of reduced deaths from other causes and an increase in life expectancy. Hyperlipidemia, diabetes, hypertension, sedentary lifestyle, high blood pressure, unhealthy diet, physical inaction, and tobacco smoking remain leading risk factors (Gastaldelli & Basta, 2010; Thomas et al., 2018; Allarakha, Yadav, & Yadav, 2022). In addition to the list of risk factors above, air pollution has also been found to contribute to cardiovascular disease burden (Gastaldelli & Basta, 2010; Thomas et al., 2018).

The association between air pollution and cardiovascular related problems has gained considerable attention in recent years (Bhatt, 2024), and so is the body of knowledge linking
ambient air pollution and cardiovascular related ER visits and deaths (Dehghani et al., 2022). This point was further stressed by Miller (2022) where he maintained that both acute and chronic exposure to air pollutants have been implicated in a wide range of cardiovascular conditions, including IHD, MI, HF, hypertension, and stroke, and these diseases contribute to approximately 4 million deaths with 140 million disability-adjusted life-years (DALYs) each year (Bi et al., 2023). Cardiovascular diseases also result in increased medication usage and reductions in life expectancy (Hanigan et al., 2021).

Atherosclerosis, caused by lipid accumulation within both peripheral and heart arteries, is the primary cause of IHD and MI (Jebari-Benslaiman et al., 2022; Herrington et al., 2016). Atherosclerosis is a result of excessive consumption of fats, lack of exercise and a sedentary lifestyle (Salekeen et al., 2022). It reflects systemic oxidative stress and inflammatory responses that impair endothelial function, leading to lipid plaques that occlude arteries and can break free and travel to occlude arteries in the heart or brain. Air pollution is one major source of oxidative stress and inflammation (Albano et al., 2022; Dehghani et al., 2022).

The increase in the concentration of criteria air pollutants (CAPs) and its correlation with the rates of cardiovascular related ER visits, hospitalization, and mortality (Yang et al., 2023; Hoek et al., 2013) has been found to be a major source of financial burden and distress (Slavin et al., 2021). This could be in the form of psychological distress, cost-related care, and tradeoffs with basic non-medical needs, and are all found to be associated with poor outcomes for patients with cardiovascular conditions, including poorer mental health and quality of life, more frequent hospitalization, and increased cardiovascular mortality (Slavin et al., 2021; Hanigan et al., 2021). Cardiovascular related financial burden was around 863 billion US Dollars (USD) in 2010.
globally, and it is estimated to increase by 22 percent by 2030 (Allarakha, Yadav, & Yadav, 2022).

Although road traffic and residential and commercial heating have the largest impact on outdoor air pollution-related morbidity and mortality (Khreis et al., 2020; Chowdhury et al., 2023), industry and power generation using fossil fuels are also important sources of criteria pollutants (Bourdrel et al., 2017). This study therefore was conducted to assess the association, if any, between point source CAPs exposure and ER visits for IHD and MI as reported in the SPARCS dataset for New York State (NYS) from 2010 to 2108.

5.3. Ischemic Heart Disease

Among cardiovascular illnesses, IHD ranks as the most prevalent (Khan et al. 2020), and it is predicted to be the leading cause of death in the world by 2030 (Deaton et al., 2011). IHD, also known as coronary artery disease, is the result of a limited blood supply to the heart muscle, or a condition in which heart muscle is damaged or ineffective due to absence or reduced blood supply (Szyszkowicz, 2007). It is a group of clinical syndromes or an imbalance between myocardial blood supply and demand caused by plaque buildup on the walls of the heart’s arteries, called atherosclerosis (Severino et al., 2020). The plaque prevents sufficient blood circulation, resulting in inadequate amounts of oxygen being delivered to the heart (Khan et al. 2020). The increasing incidence of IHD is expected to continue, due not only to the increased prevalence of obesity, diabetes, hypertension, and hyperlipidemia (also called the metabolic syndrome) but also to population aging and increased air pollution (Christoffersen et al., 2014). The number of patients diagnosed with IHD increased over the past 27 years and this increase has serious implications for health systems’ capacity and planning (Khan et al. 2020; Nowbar et al., 2019). IHD accounted for more than 9 million deaths in 2016 according to WHO (Nowbar et
al., 2019; Khan et al. 2020), and affected around 126 million individuals globally in 2017, estimated to be 1.72% of the world’s population (Khan et al. 2020).

There is strong evidence that the criteria pollutants are major risk factors for IHD ER visits and death. Beckerman et al., (2012) investigated the association between IHD prevalence and exposure to nitrogen dioxide (NO$_2$), fine particulate (PM$_{2.5}$), and ozone (O$_3$) in a population of susceptible subjects in Toronto, Canada. The study results showed NO$_2$ was significantly associated with increased IHD relative risk (RR)=1.33 (1.2, 1.47), especially among subjects near major roads and highways with RR = 1.08 (0.99, 1.18). Kim et (2021) explored short-term and long-term effects of air pollutants on the risk of IHD in a cohort of 2155 participants with the disease and 8620 control participants from 2002 to 2013. Exposure to SO$_2$ for one month showed an OR=1.36 (1.06-1.75) for IHD. Twelve months exposure to SO$_2$ resulted in an OR=1.58 (1.01-2.47), while for O$_3$ OR=1.53(1.27-1.84), and PM$_{10}$ OR=1.14 (1.02-1.26) for IHD. The study concluded that short-term exposure to SO$_2$ and long-term exposure to SO$_2$, O$_3$, and PM$_{10}$ increased risk of IHD.

5.4. Myocardial Infarction

In recent years, the prevalence of MI has increased globally, and is found to be the key component of cardiovascular related illnesses and is the foremost cause of mortality globally (Fathima, 2021; Farhadi et al., 2020). MI, or a heart attack occurs when blood stops flowing properly to the heart and causes death of heart muscle due to lack of oxygen supply (Lu et al., 2015). It is an acute event leading to immediate death or survival but with some death and damage to heart muscle fibers. Survival of acute MI often leads to chronic IHD and HF and/or a secondary MI (Yu et al., 2018; Zou et al., 2021).
Studies have recently linked air pollution to MI ER visits, hospitalization, and death. A time-series study conducted by Yu et al. (2018) investigated the association between criteria pollutants and MI. The study found short-term exposure to particulates was associated with increased MI risks. Every 10-μg/m³ increase in PM$_{2.5}$ was associated with increases of 1.636% (0.537–2.740%) in MI. The study demonstrated that short-term exposure to PM$_{2.5}$ and PM$_{10}$ were associated with MI. Additionally, population and individual level exposures to air pollution have also been associated with MI (Shah et al., 2013). A recent meta-analysis of 26 published studies found that each 10μg/m³ increase in PM$_{2.5}$ was associated with 1.02 times higher risk of MI (Tao et al., 2023).

5.5. Criteria Air Pollutants and Cardiovascular Diseases

5.5.1. Effects of Carbon Monoxide on Cardiovascular Diseases

CO is a colorless and odorless toxic gas that is produced as a byproduct of incomplete combustion of carbon-based fuels and substances (Samuel & Barik, 2020; Ryter et al., 2018). Common sources include fire, engine exhaust, and faulty furnaces (Rose et al., 2017). The United States Environmental Protection Agency (USEPA) National Ambient Air Quality Standards (NAAQS) for the general population is 9 ppm over 8 hours. Occupational Safety and Health Administration (OSHA) suggests limiting CO exposure to 50 ppm for 8 hours, whiles NIOSH recommends a time-weighted limit of 35 ppm over 8 hours, and the American Conference of Governmental Industrial Hygienists (ACGIH) recommends limiting CO exposure to 25 ppm for 8 hours (Levy, 2016).

CO binds with hemoglobin to form carboxyhemoglobin (COHb) leading to decreased oxygen-carrying capacity into tissues resulting in tissue hypoxia and ischemia (Samuel & Barik, 2020). CO also binds with many heme-containing proteins, eventually interrupting oxidative
metabolism, leading to the formation of free radicals causing increased oxidative stress and cellular inflammation (Rose et al., 2017; Ryter et al., 2018). WHO has suggested that levels greater than 6 ppm are potentially toxic over a longer period and can cause profound cardiovascular effects (Rose et al., 2017). However, research has also shown that prolonged exposure to even low levels of CO may have adverse effects, particularly on the cardiovascular and nervous systems (Ramirez et al., 2014). Also, CO exposures at elevated concentrations even accidentally can cause asphyxiation and death (Ryter et al., 2018). Up to one-third of patients with moderate to severe CO poisoning or higher levels of COHb suffer from both acute and long-term development of IHD and MI (Rose et al., 2017). And the clinical toxicology of CO poisoning involves severe neurocognitive effects, cardiac dysfunction, and potential death, and has been reviewed extensively elsewhere (Ryter et al., 2018). Castner et al. (2015) believe that exposure to high outdoor levels of CO, especially during exertion, can lead to chest pain, shortness of breath, and can affect mental alertness in otherwise healthy individuals.

Epidemiological studies have also reported associations of short-term exposure to ambient CO with mortality and morbidity from cardiovascular diseases (Liu et al., 2018), including asphyxia-related deaths, myocardial ischemia, impaired neuropsychological performance, and rhythm disturbance even at lower concentrations (Liu et al., 2018; Bell et al., 2009). This is especially important for individuals who already have preexisting cardiovascular disease due to atherosclerosis. An example of such studies is the one conducted by You et al., (2023). They examined the relationship between ambient CO and daily ER visits for total and cause-specific cardiovascular conditions in Lanzhou, China. Their results showed that for every 1 mg/m³ increase in CO concentration, RRs for daily ER visits were 1.041 (1.017, 1.065) for total cardiovascular diseases, RR =1.065 (1.018, 1.114) for IHD, RR =1.083 (1.020, 1.149) for heart
rhythm disturbances (HRD), \( RR = 1.062 \ (1.011, 1.115) \) for HF, and \( RR = 1.057 \ (1.017, 1.098) \) for cerebrovascular diseases. The study concluded that short-term exposure to ambient CO increases the risks of ER visits for total and cause-specific cardiovascular diseases, especially in the cold season.

Another classic example was a multisite time-series study conducted by Bell et al., (2009) to estimate risk of cardiovascular hospitalization associated with short-term CO exposure in 126 US urban counties, 1999-2005 for over 9 million older Medicare enrollees. The study found a significant association between same-day CO exposure and increased risk of hospitalization for multiple cardiovascular outcomes including IHD, HRD, HF, cerebrovascular disease, and total cardiovascular disease. The results also showed that every 1ppm increase in the same day daily 1-hour maximum CO exposure was associated with an increased risk of cardiovascular admission. The authors concluded that there was enough evidence of an association between short-term exposure to ambient CO and risk of cardiovascular related hospitalizations, even at levels well below current US health-based regulatory standards.

5.5.2. Effects of Particulate Matter on Cardiovascular Diseases

Epidemiological, biomedical and clinical studies have found ambient particulates air pollution to be strongly associated with increased cardiovascular diseases such as MI, cardiac arrhythmias, ischemic stroke, vascular dysfunction, hypertension and atherosclerosis (Du et al., 2016). Particulates are classified as \( \text{PM}_{10} \), \( \text{PM}_{2.5} \) and ultrafine particles (\( \text{PM}_{0.1} \)) according to their diameter. Consistent evidence has demonstrated that daily and seasonal variations of particulates concentrations have been associated with increased cardiovascular mortality and higher hospitalization rates for several cardiovascular conditions (Fang et al., 2010; Martinelli et al., 2013; Martinelli et al., 2013; Abrams et al., 2017; Du et al., 2016).
Studies have indicated that even a few hours to weeks (short-term) of exposure to particulates (PM$_{2.5}$ and PM$_{10}$) can trigger cardiovascular-related mortality events, especially among the susceptible individuals at elevated risk including the elderly or the patients with preexisting conditions (Du et al., 2016). Increases in ER visits for cardiac arrest, general cardiac and ischemic heart and cerebrovascular events, thromboembolism, dysrhythmia, hypertension, have been linked to increases in outdoor levels of particulate matter (PM) (Castner et al., 2015). A study carried out by Xu et al., (2017) in Shanghai, China found strong association between hospitalizations for IHD with short-term exposure to high levels of particulate. Every 10μg/m$^3$ increase in particulates (PM$_{2.5}$ and PM$_{10}$), coincided with an increase in IHD hospitalizations.

Prenatal and postnatal PM$_{2.5}$ exposure can result in HF later in life (de Bont et al., 2022). A large prospective cohort study and meta-analysis in 11 European cohorts confirmed that long term exposure to PM is associated with incidence of coronary events. The authors concluded that with a 5 μg/m$^3$ increase in estimated annual mean PM$_{2.5}$ was associated with a 13% increased risk of coronary events [hazard ratio (HR)=1.13 (0.98 to 1.30)], and a 10μg/m$^3$ increase in estimated annual mean PM$_{10}$ was associated with a 12% increased risk of coronary events [1.12 (1.01 to 1.25)] (Cesaroni et al., 2014).

PM$_{2.5}$ is particularly harmful due to its size (Tao et al., 2023; Al-Kindi et al., 2020). Studies such as the one conducted by Zanobetti et al., (2005) found an increase of 1.89% in cardiovascular conditions, 2.25% in MI, and 1.85% in congestive heart failure admissions for every 10μg/m$^3$ increase in 2-day averaged PM$_{2.5}$ concentration in 21 US communities. Long-term exposure to PM$_{2.5}$ has previously been associated with progression in atherosclerosis (Kaufman et al., 2016), the pathophysiological process behind IHD (Ljungman et al., 2019) and acute exposure increases the rate of cardiovascular deaths (Fiordelisi et al., 2017). Long-term exposure to high
concentrations of PM$_{2.5}$ has been associated with serious health impacts including IHD according to Song et al. (2017), while for a short-term exposure, a 2013 meta-analysis found that an average increase of 11% in cardiovascular mortality was associated with a 10μg/m$^3$ increase in annual PM$_{2.5}$ concentration (Bourdrel et al., 2017). Several studies reported a strong association between long-term exposure to air pollution and AMI. For example, in a large-scale prospective European study, annual increases of 5 μg/m$^3$ in PM$_{2.5}$ were associated with increased risks of MI of 13% (Bourdrel et al., 2017). A multicity case-crossover study conducted by Zanobetti & Schwartz (2005) found an increased risk of hospitalization for MI for every 10μg/m$^3$ increase in ambient PM$_{10}$ concentration among elderly residents of 21 US cities.

A retrospective cohort study by Zhang et al., (2014) containing 39,054 subjects from four cities in northern China, was conducted for mortality of all-cause and specific cardiovascular diseases from 1998 to 2009. The study found that for each 10 μg/m$^3$ increase in PM$_{10}$, mortality risk ratios (RRs) for all-cause cardiovascular diseases, IHD, HF, and cerebrovascular disease increased by 1.24, 1.23, 1.37, 1.11, and 1.23%, respectively.

5.5.3. Effects of Sulfur Dioxide on Cardiovascular Diseases

Sulfur dioxide (SO$_2$) is a colorless toxic gas with a pungent odor resulting primarily from activities associated with the burning of fossil fuels such as at power plants (Reno et al., 2015). SO$_2$ can also be released into the air through natural means such as volcanic eruptions (Liu et al., 2019). In 2010, the USEPA replaced the existing primary SO$_2$ standards of annual and 24-hour with a new 1-hour standard set at a level of 75 ppb. The acceptable standard sets by NIOSH vary from 5000 ppb (5 ppm) for 15 minutes work period of SO$_2$ exposure to 2000 ppb (2 ppm) for 10-hour work shift of exposure. OSHA has set a permissible exposure limit (PEL) of 5 ppm SO$_2$ averaged over an 8-hour work shift. ACGIH goes one step further, setting its threshold limit
value (TLV) at 0.25 ppm averaged over an 8-hour work shift. Which can still prove to be problematic for those living with asthma (Lee et al., 2019).

SO₂ has been found to trigger endothelial dysfunction, oxidative stress, and systemic inflammation, all of which can affect blood pressure and heart rate variability, leading to the development and progression of cardiovascular diseases (Bhatt, 2024; Kim et al., 2016; Ma et al., 2021). In their retrospective cohort study, Ma et al. (2021) found an association between SO₂ and cardiovascular diseases and concluded that the risk of coronary heart disease (CHD) increased by 2.5% for every 10μg/m³ increase in SO₂ concentration. Amsalu et al., (2019) also examined the short-term associations between SO₂ and cause specific cardiovascular HAs in Beijing. About 460,938 hospitalizations for total cardiovascular diseases were obtained for the periods 2013 to 2017. This was a time series study conducted to investigate the association between SO₂ exposure and hospitalizations for total cardiovascular diseases, CHD, atrial fibrillation (AF), and HF. The results showed that every 10 μg/m³ increase in a two-day average concentration (lag0-1) of SO₂ was associated with an increase of 1.38% (0.99%; 1.77%) in HAs for total cardiovascular diseases, 1.58% (1.16%; 2%) for CHD and 1.69% (0.41%; 2.99%) for AF. The authors concluded that the significant association between hospitalizations and SO₂ provides evidence of an immediate effects of SO₂ on HAs of total and cause-specific diseases.

5.5.4. Effects of Nitrogen Oxide on Cardiovascular Diseases

Nitrogen dioxide (NO₂) gas is one of the components of nitrogen oxides (NOx) that represents an important urban pollutant because of its massive discharge from vehicle exhausts, electrical utilities, and industrial boilers (Zhu et al., 2012). NO and NO₂ are often grouped together as NOx because they are simultaneously emitted from combustion sources and react to produce each
other. Oxides of nitrogen, or NOx, are poisonous, highly reactive gases, and are formed when fuel is burned at elevated temperatures. In the workplace the time-weighted 8-hour average is 3ppm, and the short-term emergency concentration is 5ppm according to the Occupational Safety and Health Administration (OSHA). The USEPA has set 0.053 ppm, averaging annually, and 0.100 ppm, averaging more than 1 hour, as the two primary NOx levels that are regulated in the US. NOx, or its chemical derivatives, when inhaled can either remain within the lung or be transported to extrapulmonary sites through the bloodstream and react with hemoglobin to form methemoglobin which is an ineffective oxygen carrier. This increases health risks to vulnerable individuals who have hypoxia associated with pulmonary and cardiac disease. NOx exposures show effect in pulmonary metabolism, pulmonary structure, pulmonary function, airway inflammation, and susceptibility to bacterial and viral infections (Petit et al., 2017). Rasche et al. (2018) in a case-crossover study to investigate the association between rapid changes in major air pollutants and the risk for MI concluded that rapid increase in NO2 as well as in NOx exposures is associated with increased risk of MI. Also, exposure to air pollution, mainly PM2.5 and NOx, is associated with the development of atherosclerosis, hypertension, stroke, and HF (Konduracka & Rostoff, 2022). César et al. (2015) estimated association between exposure to NOx and HAs for cardiovascular diseases in adults aged over 40 years, living in Piracicaba, Brazil. The study found cardiovascular admissions to be associated with exposure to NOx at lag 3 \([RR = 1.003 (1.000; 1.005)]\), for men lag 3 \([RR=1.004 (1.000; 1.007)]\) and for women lag 2 \([RR=1.004 (1.000; 1.008)]\). An increase of 10µg/m³ NOx led to an increase in 2.8 % risk of hospitalizations, 3.4 % for men and 4.1 % women, respectively. The conclusion is that exposure to NOx can lead to hospitalizations for cardiovascular disease independent of gender.
Although most exposures to air pollutants are from non-point sources, point sources constitute a localized source of air toxics and thus allow one to examine whether individuals living near these point sources experience greater exposure and more disease as a result. The goal of this study was to assess the association between ER visits for both MI and IHD, and exposure to point source CAPs. Previous studies have reported elevated rates of hospitalization and ER visits for cardiovascular diseases and living near pollution points sources (Rodopoulou et al., 2014; Castner, Guo & Yin., 2018).

5.6. Materials and Method

5.6.1. Study Area

The study area encompasses all zip codes that the United States Environmental Protection Agency (USEPA) National Emission Inventory (NEI) and the New York State Department of Health (NYSDOH) Statewide Planning and Research Cooperative System (SPARCS) cover. This study focused on the records collected between 2010 and 2018. The SPARCS data records contain information on admission date, discharge date, date of birth, 5-digit zip code of residence and demographic information (age, gender, ethnicity, and race) of individuals, while the NEI data has information on the pollutants.

5.6.2. Emergency Room Visit Data

The individual-level data were aggregated into daily counts for the outcomes of interest that are identified using the International Classification of Diseases (ICD), 9th and 10th revisions, Clinical Modification (CM) codes. The outcome diseases considered in this study included visits for IHD (ICD-9-CM codes 410–414, and ICD-10-CM codes I20-I25), and MI (ICD-9-CM codes 410, and ICD-10- codes I21-I22) as defined by the SPARCS data dictionary. The study only focused on ER visits and narrowed it to primary diagnosis of each disease of interest. For each
disease and year, the study looked at variables of concern using the longitudinal patient identifier. All diagnoses made in NYS regulated hospitals ER visits and acute treatment facilities are reported to the NYSDOH upon discharge. This diagnostic reporting system is called SPARCS. Based on SPARCS data for 2010-2018, the study determined the number of ER visits for IHD and MI. To get the crude numbers of ER visits for each of the diseases by zip code, patients were grouped by their residential zip codes and the rate of ER visits in each zip code was calculated using the total number of ER visits and the population count by zip code. Data was then stratified by sex (male and female), and age categorized as 0-5, 6-19, 20-44, 45-64, 65-74 and 75+ for both diseases.

5.6.3. Criteria Air Pollutants Data

Exposure data was obtained for CAPs from the USEPA’s NEI dataset which is a comprehensive and detailed estimate of air emissions of criteria pollutants, including precursors, and hazardous air pollutants. The NEI is released every three years based primarily upon data provided by State, local, and tribal air agencies for sources in their jurisdictions and supplemented by data developed by the USEPA. Since this dataset only has data for point sources at the zip code level, the study focused only on the point sources of pollution. A point source is emission produced by large stationary sources, such as industrial facilities, electrical power plants, solid waste landfills, sewage treatment facilities, breweries and airports, or smaller non-industrial sources.

Point source pollution information for the years 2011, 2014, and 2017 was downloaded from the USEPA NEI site. Pollutant site latitude and longitude locations were then associated with the zip code in which the facility was located using a scheme that minimized the absolute great circle distance between the zip code centroid and the site location. Data from the United State Census Bureau (USCB) was used to determine the land area in each zip code (square miles). Pollution
per square mile for each pollutant at the zip code was calculated by summing all point source contributions of the pollutant and dividing it by the land area of each zip code.

Pollution from other sources, such as on-road, non-road, and non-point sources, was not studied because data at the zip code level is not available. To address this limitation, the adjusting variables were added for total CAPs from all sources of pollution at the county level.

5.6.4. **Data on Poverty**

The USCB dataset on poverty was used in this study. Since the 1960s, the USCB has produced poverty estimates to measure the economic well-being of households, families, and individuals in the US. The official poverty measure defines poverty by comparing pretax money income to a poverty threshold that is adjusted by family composition. The Census Bureau provides poverty data from several household surveys and programs and defines poverty by considering families’ income thresholds and these vary based on family composition and size. Data from the small area income and poverty estimates (SAIPE) program at the USCB website was used for this study. These estimates are based on several data sources, such as aggregate tax, supplemental nutrition assistance program (SNAP) benefits, and poverty incidence data. In this data, poverty is defined based on the family’s income. For instance, a family is considered poor when their total income is less than the threshold set by SAIPE.

5.6.5. **Data on Tobacco Smoking**

The behavioral risk factor surveillance system (BRFSS) is a system of health-related telephone surveys that collect state data about US residents regarding their health-related risk behaviors, chronic health conditions, and use of preventive services. The BRFSS database was used to determine the crude rate of smoking for this study. Smoking data was not available at the zip code level in the BRFES dataset and county level data was used as a confounder in the models.
Surveys are conducted using landline telephones as well as cellular telephones. For each county, the crude smoking rates were averaged and used in this study.

5.6.6. Control Variables

Different adjusted variables that can influence the outcomes of interest were considered, they included sex (male or female) with female as the reference level, age category with varied reference levels based on disease type, a poverty category variable with the reference level being below median poverty, average county level smoking, study years from 2010 to 2018 with reference level been 2010, county level VOCs, and county level CAPs from all pollutant sources.

5.6.7. Statistical Analysis

Analyses were performed with the use of R programming software, version 4.2.2. In this ecological study, the correlation between air pollutant exposures was estimated by Spearman’s correlation coefficients. Log linear mixed effects models were implemented to quantify the exposure-response associations between criteria pollutants and ER visits for IHD and MI and calculated the incidence rates for each of the outcomes per 100,000 person-years.

5.6.7.1. Imputation of Missing Exposure Data

The exposure data for this study covers 2011, 2014, and 2017, and for these years, there were disparities in reporting emissions across zip codes because some emitting units did not report in some of the given years. This is likely due to the fact that while reporting is mandatory in NYS for emissions from large point sources, both at site and unit levels, they are often not enforced. Also, reporting standards were dropped for certain polluters based on the title V requirements. It is reasonable to assume that these stationary sources are operating over all of the period used in this study, and that they are still producing emissions even though they were not reported. Therefore, missing data for those years were inputted using emitting site IDs and unit IDs per zip
code. For each zip code and site ID, missing unit IDs and their emissions were replaced by assuming emissions were the same for the years not reported as for those that were reported. A reference set of codes for 2011 was used to resolve changes in zip codes during the study period. The total number of zip codes in NYS is estimated at 1792, and a little less than that reported some point source pollution for at least one of the target pollutants in 2011, 2014, and 2017, which also had cases of the diseases in this study. Those zip codes with disease cases but without point source data over the study period were given a point source emission rate of zero. Zip codes with zero population were assumed to be post office boxes and were not considered in the analysis.

5.6.7.2. Single Pollutant Models

To create datasets for each of the pollutants in this study, data were merged across years for each pollutant and all years were analyzed together. 2011 pollutant data was associated with 2010, 2011, and 2012 zip code disease rates. For 2014, pollutant data were joined to disease data from 2013, 2014, and 2015, while 2017 pollutant data were also matched with disease data from 2016, 2017, and 2018. These were then assembled to get a complete workable dataset needed for the study. To accurately estimate pollutants at the zip level, and account for within county variability, the log-linear mixed effects model with a random effect was used. Adjusted associations between the rates of ER visits were scaled to 100,000 population. This study models were adjusted for sex using female as the reference level, age level category was determined by disease type based on previous studies. For the poverty level category, below median poverty was used as the reference, while 2010 was used as the reference for the study years. Average county level smoking, county level VOCs, and CAPs from point, non-point, onroad, and non-road sources were considered as covariates and all results were adjusted for
these factors. Covariates that are numeric were standardized and disease rates at the zip codes were log-transformed for normality. Standardized effect sizes were created to compare across outcomes and exposures.

5.7. Results for the Association Between Criteria Pollutants and Cardiovascular Diseases

This study investigated the associations between CAPs and ER visits for MI and IHD at zip code levels in NYS from 2010 to 2018. The results for this analysis are shown in the following tables and explained thereafter.

5.7.1. Results for the Association Between Criteria Air Pollutants and IHD

Table 5.1 summarizes the beta estimates, 95% CIs, and p-values for CAPs regressed against ER visits for IHD. With $p < 0.05$ considered statistically significant association, all the pollutants showed significant positive associations with IHD ER visits. CO showed the highest impact followed by NOx, SO$_2$, and then PM$_{2.5}$, and PM$_{10}$.

Table 5.1. Estimates, confidence intervals and p-values for the criteria air pollutants and IHD

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Pollutant</th>
<th>$\beta$ Estimate</th>
<th>Lower CI</th>
<th>Upper CI</th>
<th>$p$-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>IHD</td>
<td>CO</td>
<td>0.049</td>
<td>0.025</td>
<td>0.072</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td></td>
<td>NO$_x$</td>
<td>0.043</td>
<td>0.019</td>
<td>0.067</td>
<td>0.0004</td>
</tr>
<tr>
<td></td>
<td>PM$_{2.5}$</td>
<td>0.028</td>
<td>0.005</td>
<td>0.050</td>
<td>0.0155</td>
</tr>
<tr>
<td></td>
<td>PM$_{10}$</td>
<td>0.026</td>
<td>0.003</td>
<td>0.049</td>
<td>0.0271</td>
</tr>
<tr>
<td></td>
<td>SO$_2$</td>
<td>0.028</td>
<td>0.006</td>
<td>0.049</td>
<td>0.011</td>
</tr>
</tbody>
</table>

*P-values give the significance of adjusted associations between zip code level pollutant exposure and the outcome.
Figure 5.1 shows the estimated associations between each criteria pollutant and IHD, with 95% CIs, and the effect sizes for the pollutants in the study against IHD by zip code over the study period, given one standard deviation increase in exposure. Estimated effect sizes are significant for all the pollutants. CO appears to have the largest effect, followed by NOx, PM_{2.5}, SO_{2}, and PM_{10} showed the smallest effect.

![Effect sizes for estimated associations between criteria air pollutants and IHD](image)

**Figure 5.1.** Effect sizes for estimated associations between criteria air pollutants and IHD

### 5.7.2. Results for the Association Between Criteria Pollutants and Myocardial Infarction

Table 5.1 shows the estimate, 95% CIs and \( p \)-values for the criteria pollutants and their association with ER visits for MI. The results did not show any significant association between any of the pollutants and the outcome. This is likely because people with an MI who come to the ER for a MI are immediately transferred to inpatient and no longer show up as an ER patient. While the associations are positive, none of the pollutants showed any statistically significant association with the outcome of interest.
<table>
<thead>
<tr>
<th>Outcome</th>
<th>Pollutant</th>
<th>$\beta$ Estimate</th>
<th>Lower CI</th>
<th>Upper CI</th>
<th>$P$-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>MI</td>
<td>CO</td>
<td>0.132</td>
<td>-0.019</td>
<td>0.283</td>
<td>0.086</td>
</tr>
<tr>
<td></td>
<td>NOx</td>
<td>0.045</td>
<td>-0.062</td>
<td>0.152</td>
<td>0.409</td>
</tr>
<tr>
<td></td>
<td>PM$_{2.5}$</td>
<td>0.107</td>
<td>-0.099</td>
<td>0.312</td>
<td>0.309</td>
</tr>
<tr>
<td></td>
<td>PM$_{10}$</td>
<td>0.126</td>
<td>-0.042</td>
<td>0.294</td>
<td>0.141</td>
</tr>
<tr>
<td></td>
<td>SO2</td>
<td>0.022</td>
<td>-0.011</td>
<td>0.054</td>
<td>0.186</td>
</tr>
</tbody>
</table>

* $P$-values give the significance of adjusted associations between zip code level pollutant exposure and the outcome

Figure 5.2 shows the estimated associations between each criteria pollutant and MI, with 95% CIs, and the effect sizes for the pollutants in the study against MI by zip code over the study period, given 0.1 standard deviation increase in exposure. Estimated effect sizes are not significant for any of the pollutants, although CO and PM$_{10}$ appear to have the largest effect, closely followed by PM$_{2.5}$, NOx, and SO$_2$ showed the smallest effect.
Figure 5.2. Comparing effect sizes for associations between CAPs and myocardial infarction.

5.8. Discussion

Air pollution is a serious global problem. It has been reported that 91% of the world’s population cannot breathe clean air, and more than half of the urban population is exposed to outdoor air pollution levels at least 2.5 times higher than international safety standards (Chen et al., 2020). More than 2,150 Americans die of cardiovascular diseases every day, and in China, about 3 million Chinese die of it every year (Chen et al., 2017). More specifically, it is estimated that CAPs account for over 25% of the total burden of IHD, and previous population-based studies have linked outdoor air pollution with increased hospital visits (Chen et al., 2020; Li et al., 2015). This current study observed statistically significant effects of CO, NOx, PM and SO\textsubscript{2} on the rate of ER visits for IHD.

One of the most surprising observations from this study is the finding that the gaseous pollutants were much more strongly associated with IHD than the particulates. In part this may reflect the fact that there has been much more attention to the adverse effects of particulates than of CO, SO\textsubscript{2} and NOx. Many studies don’t even measure the gaseous pollutants and it is always difficult
to separate which CAP causes which disease because they are almost always emitted together. However, the NEI data shows that the gaseous pollutants dominate (Figure 2.4) in the emissions from point sources, consistent with the finding that they show the greatest risk for IHDs.

However, none of the pollutants showed any statistically significant association with MI. This is similar to a study by Cramer et al., (2020), where they found no association between long-term exposure to PM$_{2.5}$, PM$_{10}$, NO$_2$, or NOx and overall MI incidence. As with other studies, the association between air pollutants and the risk of MI remains controversial. Some studies have shown an association, while other studies have found either no association, or association only for selected pollutants (Mustafić et al., 2012). A study conducted in Canada found no association between PM$_{2.5}$, PM$_{10}$, or NO$_2$ with hospitalizations for MI (Wang et al., 2015). The lack of a statistically significant association does not mean that these pollutants do not increase risk of MI, because other studies were able to establish such associations at point and non-point sources (Cramer et al., 2020; Poulsen et al., 2023). For example, Mustafić et al. (2012) in their meta-analysis demonstrated an increase in near-term risk of MI associated with short-term exposure to criteria pollutants. Zou et al. (2021) also identified long-term exposure to PM$_{2.5}$ and PM$_{10}$ as significant risk factors for MI. The lack of a significant association here is almost certainly due to the fact that when someone comes to an ER with an MI they are immediately admitted as an inpatient to the hospital, and thus are not included as an ER admission. This is likely a consideration for IHD as well. In further studies I will use the SPARCS data to explore HA data in relation to CAPs exposures.
5.9. Conclusion

Air pollution negatively impacts many aspects of health, particularly when exposed to these pollutants at an early age (Clark et al., 2010; Currie et al., 2014; Garcia, Rice, & Gold, 2021). The hypothesis for this dissertation research was that exposure to the CAPs would be associated with increased ER visits for cardiovascular diseases in this case IHD and MI. This is an ecological study assessing the effects of the CAPs on ER visits for MI and IHD for the period 2010 to 2018 at zip code levels in NYS. All the pollutants in the study were positively associated with ER visits for IHD, even after adjusting other variables. This adds to the evidence that even point source CAPs pollution that might be considered small relative to total CAPs from all sources, can contribute in a significant way to cardiovascular disease-related ER visits. CO and NOx consistently contributed the largest relative effect sizes followed by SO₂, PM_{2.5}, and PM_{10}. However, none of the pollutants showed any association with MI. The number of ER visits for MI was very small compared to the other diseases in the study (Table 4.S1). The reason for this is almost certainly that an MI is a serious acute event for which patients are immediately admitted to the hospital and therefore are not captured by ER data.
Chapter Six


This is an ecological study that was performed using quasi poisson and the log linear mixed effects models to assess the associations ($p$-value <0.05 at 95% CIs) between respiratory and cardiovascular diseases and CAPs at zip code levels in NYS from 2010 to 2018. Air pollution is a great environmental threat to public health globally and accounts for an estimated 7 million premature deaths every year (Valavanidis, 2023). The adverse impacts of air pollution on health are enormous, and health impact assessments are useful for governments and other decision-makers to determine the need for action and address potential public health problems arising from exposure to air pollution.

Many people live and work near to air pollution point source areas such as industrial and waste disposal sites. People living near such sites are at elevated risk of diseases due to the activities around them, and public health authorities and research communities continue to push for detailed disease research and investigations. To investigate such clusters is often difficult because of limited reliable and accurate population exposure data. This often leads to the key question of whether releases from point sources which are small compared to the other sources can result in significant exposure. Research has shown that many pollutants arise from a wide range of sources other than point sources and are ubiquitous in the environment. So, releases from point sources may result in only a negligible increase in exposure. This study is therefore important because it has shown that even the small exposures at the point sources contribute to air pollution related ER visits at zip code levels in NYS. The present study was conducted primarily to assess the health impacts of CAPs at zip code levels in NYS, and the main aim was to investigate
associations between CAPs and ER visits for two respiratory diseases (asthma and COPD) and two cardiovascular diseases (MI and IHD), and to determine which component of the CAPs has the most adverse effects.

The results of this study are consistent with previous epidemiologic studies that found positive associations between most of the CAPs and ER visits, and no associations in some cases. Other interesting findings of this study point to the fact that while air pollution is considered a tangible and measurable risk factor for disease outcomes, several other factors such as smoking (Polosa and Thomson, 2013) and low income or poverty (Grant and Wood, 2022) can contribute to disease development and exacerbation.

This study has demonstrated the health effects of ambient air pollution from point sources and the findings provide additional evidence that poor air quality is harmful to human health. And the primary criteria pollutants produce adverse health effects to human beings after short-term or long-term exposure. This is a confirmation to Byrwa-Hill et al. (2020) who indicated that exposure to CAPs due to burning of fossil fuels and industrial emissions trigger disease exacerbations and result in increased ER admissions in both children and adults.

6.1. PM$_{2.5}$, Smoking, Poverty, and Asthma

PM$_{2.5}$, smoking and poverty were assessed individually and then jointly to establish their associations with ER visits for asthma. When assessed individually and unadjusted, all three variables showed significant positive associations with asthma, poverty showed the highest association with a $p$-value of $< 0.0001$, followed by smoking ($p$-value $< 0.0001$) and PM$_{2.5}$ ($p$-value 0.003). When assessed jointly, all the three variables retained positive and significant associations with asthma. Again, poverty showed the highest effect. Although this is not uncommon, it can be explained that such association may have resulted from high ER visits by
people of low SES. Minority populations are more likely to reside in poor communities and are mostly believed to visit the nearest ER, even for their routine checkups because they often do not have a primary care physician nor medical insurance. This reflects the reality that many poor people get all of their health care in the emergency room. This study cannot distinguish an added health care burden due to greater CAPs exposure among poor people from the fact that poor people use the ER much more frequently than people with access to other sites of treatment, such as primary care physicians. However poor people often live at sites where all kinds of environmental exposure are greater than those seen among the more affluent. Other population-level characteristics known as social determinants of health (SDoH) can contribute to the exacerbation of diseases (Grant, Croce, & Matsui, 2022; Emeny, Carpenter & Lawrence, 2021). SDoH are defined by the World Health Organization as the non-medical factors that influence health outcomes.

6.2. Effects of Criteria Air Pollutants on Respiratory and Cardiovascular Diseases

Air pollution is undoubtedly associated with a variety of diseases including respiratory and cardiovascular diseases. Numerous studies, mainly in the developed countries, have evaluated the relationships between air pollution and ER visits or deaths due to respiratory and cardiovascular infections, and have established such associations (Anderson et al., 2012; Perez et al., 2015; Pope et al., 2015).


CO was found to be strongly associated with ER visits for asthma with a statistically significant $p<0.0001$. The same analysis also found CO to have a positive and statistically significant association with ER visit for COPD ($p < 0.0001$).
The results of this study showed positive and statistically significant associations between exposure to CO and the risks of hospital ER visits for asthma and COPD. This is similar to the result by Zhao et al. (2019) in which they also found significant associations between CO and respiratory health impacts with asthma and COPD. Other studies carried out in different parts of the world also found such associations (Duan, Hao, and Yang, 2020; Zhao et al., 2019b; Almetwally et al., 2020).

In examining the rates of ER visits for asthma due to NOx and to access their association, this study found a positive and statistically significant association between the two ($p < 0.0001$). Also, result of this study showed a significant association between NOx and ER visits for COPD with a $p < 0.0001$. This result is similar to the one by Andersen et al (2011).

PM$_{2.5}$ showed a statistically significant association with asthma when unadjusted with a $p$-value of 0.003. When adjusted for smoking, the association was again statistically significant, with a $p$-value of 0.0004. A $p$-value of 0.073 registered for PM$_{2.5}$ when adjusted for poverty. Finally, when PM$_{2.5}$ was regressed with asthma and adjusted for both smoking and poverty, the study found significant associations for all three variables, with poverty showing the most effect ($p$-value $= < 0.0001$), followed by smoking ($p = < 0.0001$) and then PM$_{2.5}$ ($p = 0.036$).

When analyzed for asthma and adjusted for other covariates including county level CAPs and PM$_{2.5}$ for all sources, PM$_{2.5}$ had a $p$-value of 0.898 while PM$_{10}$ showed a $p$-value of 0.057, indicating that both results are positive but only PM$_{10}$ showed significant association. When analyzed for COPD and adjusted for other covariates, both PM$_{2.5}$ and PM$_{10}$ were positive and statistically significant. PM$_{2.5}$ had a $p$-value $= 0.015$ and PM$_{10}$ had $p$-value of 0.002. This may be due in part to the percentage exposure of each pollutant. PM$_{10}$ formed 4% of the total CAPs
emission, while PM$_{2.5}$ contributed only 3% of the total emission. Since PM$_{2.5}$ is part of PM$_{10}$, one would expect PM$_{10}$ exposure to be higher.

SO$_2$, which is a bronchoconstrictor that promotes systemic inflammation and oxidative stress, has not been extensively studied as a risk to human health. It is mainly generated from coal and oil combustion and believed to be a significant cause of respiratory damage (Zhu et al., 2014). Analysis between the effects of SO$_2$ on asthma ER visits in this study found a strong and significant positive association between the two with $p < 0.0001$. SO$_2$ was also found to be significantly associated with ER visits for COPD with $p < 0.0001$.

SO$_2$ was found to be significantly associated with ER visits for both asthma and COPD, and the result is consistent with other studies (Bălă et al., 2021; Mo et al., 2018; Wang et al., 2018). Also, a case-crossover study carried out in southeast China by Smargiassi et al (2009) found an increased number of asthma episodes and ER visits associated with elevated exposure to SO$_2$ emitted from refineries.

6.2.2. Criteria Air Pollutants and Cardiovascular Diseases.

In the analysis between CO and IHD and to assess if there is any statistically significant association, it was established that there was indeed such an association with $p < 0.0001$. However, when CO was regressed for its association with MI, there was no statistically significant association although the association was positive with a $p$-value = 0.086.

There was an association found between NOx exposure and ER visits for IHD ($p$-value = < 0.0004). When analyzed for its association with MI, NOx did not show any significant association, although a $p$-value of 0.409 shows a positive association.
Also, the association between PM$_{2.5}$ and IHD was analyzed, and the result showed a positive and statistically significant association with a $p$-value of 0.016. But when analyzed for MI, the association between PM$_{2.5}$ and MI was insignificant with a $p$-value = 0.727. PM$_{10}$ was also found to be significantly associated with IHD ($p$-value = 0.027) but had no significant association with MI ($p$-value of 0.141). This result shows that PM exposure poses increased risk of ER visits for IHD. That cannot be said for MI, at least in this current study. This does not in any way exclude PM from being a risk factor for MI in general.

When a person with MI appears at an ER they will usually be immediately admitted as an inpatient, and therefore do not get listed in SPARCS as an ER patient. This is probably also true for many individuals appearing at the ER with IHD. It is noteworthy that the numbers of admissions for both IHD and MI are much smaller than those for asthma and COPD. To adequately determine the associations between the cardiovascular diseases and CAPs exposure it is necessary to consider both ER and HA admissions. This I plan to do after completion of the PhD program, as we have just received the HA data from the SPARCS program.

Furthermore, the analysis reported significant effects of SO$_2$ exposure on IHD with a $p$-value of 0.011 but shows insignificant result for MI with $p$-values of 0.186. This was also confirmed by Pope, (2015). The current study in the same analysis resulted in a positive but not significant association for MI. This is possibly hinged on the fact that a very small number of ER visits for MI (tables 5S1 and 5S2) was found in the outcome data by SPARCS, as discussed above.

### 6.3. Contributions of this Investigation

Multiple studies have focused on particulates, especially PM$_{2.5}$ and this has led to particulates been moved in the last decades on the top list of polluting factors as an important toxic risk for human health, especially for the respiratory and cardiovascular systems. These particulates have
been considered the most influential environmental risk factors contributing to global respiratory and cardiovascular morbidity, disability, and mortality (Valavanidis, 2023; Cheng et al., 2021). There is overwhelming evidence for PM$_{2.5}$ as an air pollutant posing a threat to global public health (Moradi et al., 2019; Rajagopalan, Al-Kindi, & Brook., 2018; Cohen et al., 2005). However, this is at least in part due to the fact that studies have focused on particulates, especially PM$_{2.5}$ and this has led to particulates being moved in the last decades on the top list of polluting factors as an important toxic risk for human health, especially for the respiratory and cardiovascular systems (Valavanidis, 2023; Cheng et al., 2021).

One of the most important conclusions from this study is the clear evidence that at least for the diseases I have studied that the gaseous pollutants, CO, NOx and SO$_2$, have a greater impact of ER visits than do the particulates. This is in agreement with some previous studies (Smargiassi et al., 2009; Cheng et al., 2018; Tajudin et al., 2019; Gao et al., 2022). Ibrahim et al., (2022) found short-term exposure to SO$_2$ to be associated with a higher risk of respiratory hospitalizations among children than PM$_{2.5}$.

Another major contribution of this study is that I have focused on only point source air pollution, which is only a minor part of total pollution with CAPs and have demonstrated that even the contribution from point sources increases risk of seeking ER care for respiratory and cardiovascular diseases. Air pollution is a major threat to global health and prosperity, and in all its forms, is responsible for millions of deaths each year globally (Arab, Saltzman, & Jacobs, 2024). The significance of this research project is that even though the point source CAPs do not contribute a large part of total emissions, they still contribute to both respiratory and cardiovascular illnesses. These results provide additional support for a relationship between environmental exposure to CAPs and the rate of ER visits for asthma, COPD, IHD and MI.
Before publication of the results for specific aim three, I will utilize the SPARCS inpatient data and examine the effects of CAPs on both the ER and inpatient hospitalization for cardiovascular diseases using more sophisticated study designs.

6.4. **Strengths and Weaknesses**

A strength of this study is that the databases used are credible and cover a considerable period of time, hence gave a high statistical power. These databases have been used by governments and non-governmental organizations, and formidable research institutions.

The NEI is a comprehensive and detailed estimate of specific air emissions from air emissions sources. While the EPA is a primary user of the NEI, the comprehensive nature of NEI makes it an important tool for government agencies, the general public, research institutions, and other countries.

SPARCS has been in existence for over 35 years, and the data files are refreshed on a monthly basis to keep it updated. SPARCS has been and continues to be committed to reliable data. Consequently, questions about data quality are looked upon as positive steps to improve the data, because the more data is used and scrutinized, the better it becomes.

However, there are also significant weaknesses in this study. In order to examine ER admissions at the zip code it was necessary to study only point source emissions of air pollutants. Point source emissions are only a small portion of total air pollutants, but the emissions from road, non-road and non-point are available only at a county level. In addition some point source emission information was not available in each of the three years for which EPA reports point source emissions. This suggests that the federal requirement for industries to report emission is not always enforced. While I have inputted information for years for which emissions were not
reported, based on the assumption that point sources are not going away over this period of time, this indicates some inadequacies in the NEI data. In addition, the exposure data is limited to once every three years, but annual and daily levels are not available. As a result, the misclassification of exposure may be non-differential and the bias would be towards the null. For instance, we didn’t find any positive association between PM$_{2.5}$ and asthma and none of the air pollutants were positively associated with MI in the current study while other studies have observed significant effects. Most previous studies have been able to examine daily air pollutant exposure on health outcomes which could reduce exposure misclassification bias. Additionally, This is an ecological study that only relates exposure and disease at the region and population level, rather than at the individual level. The bias with this study design is ecological fallacy. This may have impacted my study results because the association identified was only for group level, and not the individual level.

In addition, this study was focused mainly on disease exacerbation and ER visits that did not result in hospitalization, not the cause of diseases. The use of only ER data is a weakness in this study. I used only the ER data because that was the only available data when I was running my analysis. This may have impacted my results because when patients with cardiovascular conditions, especially IHD and MI, most of them go to the ER first, and they usually end up to be admitted as inpatients, and therefore these cases do not get listed as ER patients anymore in the SPARCS. For this reason, substantial number of cardiovascular disease cases may have been missed by using the ER data only in this study. Furthermore, the complete ER data should include those cases with ER and then admitted to hospitals. Due to non-access to admission data, the current study only caught the cases with ER. Therefore, incomplete case ascertainment would be a major concern, especially for cardiovascular cases. This selection bias of ER cases may lead
to including relatively mild cardiovascular cases, as the severe cases would be admitted to hospitals who have not been included in this study.

The generalizability of this study may be limited, since it is necessary to consider both ER and HA admissions. In my study, I assumed that most patients that visited the ER for cardiovascular diseases were registered as inpatient instead of outpatients. This could have been the reason for the decreased observed association between CAPs and the cardiovascular diseases. Furthermore, multiple residual confounders, including temperature, relative humidity, neighborhood greenness coverage, and indoor environment have not been controlled. These variables have been found to be associated with respiratory and cardiovascular diseases, and the associations found could be explained by these variables. NEI dataset does not contain emission data on ozone which is one of the main criteria air pollutants. Pb exposure was very low and variable, and thus I decided not to include it in this study. Future research should analyze in-patient data using more sophisticated study designs to further assess the research questions of this study.

6.5. Conclusions

This statewide study assessed the associations of exposure to CAPs and ER visits for respiratory and cardiovascular diseases at zip code levels in NYS from 2010 to 2018. The results showed that the gaseous pollutants, CO, NOx, and SO\textsubscript{2} were more strongly associated with ER visits that did not result in hospitalization for asthma, COPD, and IHD than were particulates. Although most of the pollutants in the study were positively associated and some were significantly associated with risk of ER visits for most of the diseases in the study, their effects however differed in magnitude, gaseous pollutants with the most effects.

This study adds to the many research studies that report that exposure to the CAPs increases the risk of ER visits for respiratory and cardiovascular diseases. PM\textsubscript{2.5}, however, did not show any
significant association with asthma. This may be because the amount of PM$_{2.5}$ coming from point sources is very small relative to the amount coming from other sources, because there is other evidence showing clearly that PM$_{2.5}$ does contribute to asthma attacks. The significance of this research project is that even though the point source CAPs do not contribute a large part of total emissions, they still contribute to both respiratory and cardiovascular illnesses. These results provide additional support for a relationship between environmental exposure to CAPs and the rate of ER visits for asthma, COPD, IHD and MI. Before publication of the results for specific aim three, I will utilize the SPARCS inpatient data and examine the effects of CAPs on both the ER and inpatient hospitalization for cardiovascular diseases using more sophisticated study designs.
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Centers for Disease Control and Prevention. *Most Recent National Asthma Data*. Accessed May 2, 2024. [https://www.cdc.gov/asthma/most_recent_national_asthma_data.htm](https://www.cdc.gov/asthma/most_recent_national_asthma_data.htm)


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Appendix A: Chapter 4 Supplementary Materials for Asthma and Chronic Obstructive Pulmonary Disease.

Table 4.S1. Crude Number of ER Visits for Asthma and COPD

<table>
<thead>
<tr>
<th>Year</th>
<th>Asthma</th>
<th>COPD</th>
</tr>
</thead>
<tbody>
<tr>
<td>2010</td>
<td>137,756</td>
<td>43,460</td>
</tr>
<tr>
<td>2011</td>
<td>141,816</td>
<td>47,346</td>
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</tr>
<tr>
<td>2013</td>
<td>143,225</td>
<td>47,608</td>
</tr>
<tr>
<td>2014</td>
<td>146,120</td>
<td>49,923</td>
</tr>
<tr>
<td>2015</td>
<td>143,120</td>
<td>51,211</td>
</tr>
<tr>
<td>2016</td>
<td>135,123</td>
<td>51,003</td>
</tr>
<tr>
<td>2017</td>
<td>126,400</td>
<td>51,487</td>
</tr>
<tr>
<td>2018</td>
<td>123,303</td>
<td>49,718</td>
</tr>
</tbody>
</table>

Table 4.S2. Deduplicated Number of ER Visits for Asthma and COPD from 2010 to 2018

<table>
<thead>
<tr>
<th>Year</th>
<th>Asthma</th>
<th>COPD</th>
</tr>
</thead>
<tbody>
<tr>
<td>2010</td>
<td>72,832</td>
<td>25,963</td>
</tr>
<tr>
<td>2011</td>
<td>74,630</td>
<td>28,784</td>
</tr>
<tr>
<td>2012</td>
<td>76,673</td>
<td>29,873</td>
</tr>
<tr>
<td>2013</td>
<td>73,149</td>
<td>27,901</td>
</tr>
<tr>
<td>2014</td>
<td>74,429</td>
<td>29,108</td>
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<tr>
<td>2015</td>
<td>72,958</td>
<td>28,870</td>
</tr>
<tr>
<td>2016</td>
<td>68,123</td>
<td>28,386</td>
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<tr>
<td>2017</td>
<td>66,830</td>
<td>28,997</td>
</tr>
<tr>
<td>2018</td>
<td>63,442</td>
<td>26,667</td>
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</tbody>
</table>
### Table 4.S3. Distribution of Respiratory Diseases over the Study Period, 2010 to 2018

<table>
<thead>
<tr>
<th>Year</th>
<th>Asthma crude visit</th>
<th>Asthma visit</th>
<th>COPD crude visit</th>
<th>COPD visit</th>
</tr>
</thead>
<tbody>
<tr>
<td>2010</td>
<td>137,756</td>
<td>72,832</td>
<td>43,460</td>
<td>25,963</td>
</tr>
<tr>
<td>2011</td>
<td>141,816</td>
<td>74,630</td>
<td>47,346</td>
<td>28,784</td>
</tr>
<tr>
<td>2012</td>
<td>149,010</td>
<td>76,673</td>
<td>51,124</td>
<td>29,873</td>
</tr>
<tr>
<td>2013</td>
<td>143,225</td>
<td>73,149</td>
<td>47,608</td>
<td>27,901</td>
</tr>
<tr>
<td>2014</td>
<td>146,120</td>
<td>74,429</td>
<td>49,923</td>
<td>29,108</td>
</tr>
<tr>
<td>2015</td>
<td>143,120</td>
<td>72,958</td>
<td>51,211</td>
<td>28,870</td>
</tr>
<tr>
<td>2016</td>
<td>135,123</td>
<td>68,123</td>
<td>51,003</td>
<td>28,386</td>
</tr>
<tr>
<td>2017</td>
<td>126,400</td>
<td>66,830</td>
<td>51,487</td>
<td>28,997</td>
</tr>
<tr>
<td>2018</td>
<td>123,303</td>
<td>63,442</td>
<td>49,718</td>
<td>26,667</td>
</tr>
</tbody>
</table>

### Table 4.S4. Crude Number of ER Visits Stratified by Sex from 2010 to 2018

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
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<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Asthma</td>
<td>Female</td>
<td>68,973</td>
<td>74,89</td>
<td>83,42</td>
<td>75,03</td>
<td>81,41</td>
<td>90,02</td>
<td>77,38</td>
<td>65,28</td>
<td>63,47</td>
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<tr>
<td></td>
<td>Male</td>
<td>68,783</td>
<td>66,92</td>
<td>65,58</td>
<td>68,18</td>
<td>64,70</td>
<td>53,09</td>
<td>57,73</td>
<td>61,11</td>
<td>59,82</td>
</tr>
<tr>
<td>COPD</td>
<td>Female</td>
<td>24,784</td>
<td>26,65</td>
<td>28,37</td>
<td>26,75</td>
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<td>29,18</td>
<td>27,25</td>
<td>27,74</td>
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<tr>
<td></td>
<td>Male</td>
<td>18,676</td>
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<td>20,85</td>
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<td>22,02</td>
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</tr>
<tr>
<td>Disease</td>
<td>Age</td>
<td>2010</td>
<td>2011</td>
<td>2012</td>
<td>2013</td>
<td>2014</td>
<td>2015</td>
<td>2016</td>
<td>2017</td>
<td>2018</td>
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<td>-------</td>
<td>-------</td>
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<td>-------</td>
</tr>
<tr>
<td>Asthma</td>
<td>0-5</td>
<td>7,979</td>
<td>15,596</td>
<td>12,136</td>
<td>14,790</td>
<td>24,167</td>
<td>19,458</td>
<td>18,684</td>
<td>14,233</td>
<td>21,822</td>
</tr>
<tr>
<td></td>
<td>6-14</td>
<td>21,836</td>
<td>16,344</td>
<td>21,328</td>
<td>18,412</td>
<td>22,206</td>
<td>19,904</td>
<td>21,657</td>
<td>16,739</td>
<td>14,578</td>
</tr>
<tr>
<td></td>
<td>15-19</td>
<td>19,524</td>
<td>18,993</td>
<td>23,151</td>
<td>22,289</td>
<td>8,670</td>
<td>8,081</td>
<td>14,290</td>
<td>6,839</td>
<td>6,066</td>
</tr>
<tr>
<td></td>
<td>20-44</td>
<td>60,852</td>
<td>66,450</td>
<td>62,816</td>
<td>61,749</td>
<td>50,781</td>
<td>48,495</td>
<td>41,811</td>
<td>52,770</td>
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<tr>
<td></td>
<td>45-64</td>
<td>21,655</td>
<td>22,356</td>
<td>24,349</td>
<td>22,576</td>
<td>31,109</td>
<td>41,264</td>
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<td>29,115</td>
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<td>4,689</td>
<td>1,617</td>
<td>4,663</td>
<td>2,236</td>
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<tr>
<td></td>
<td>85+</td>
<td>695</td>
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<td>113</td>
<td>149</td>
<td>410</td>
<td>432</td>
<td>421</td>
<td>115</td>
<td>284</td>
</tr>
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</table>

**Table 4.6. Crude Number of ER Visits or COPD Stratified by Age, from 2010 to 2018**

<table>
<thead>
<tr>
<th>Disease</th>
<th>Age</th>
<th>2010</th>
<th>2011</th>
<th>2012</th>
<th>2013</th>
<th>2014</th>
<th>2015</th>
<th>2016</th>
<th>2017</th>
<th>2018</th>
</tr>
</thead>
<tbody>
<tr>
<td>COPD</td>
<td>0-5</td>
<td>1,927</td>
<td>1,882</td>
<td>1,582</td>
<td>1,409</td>
<td>1,150</td>
<td>1,259</td>
<td>727</td>
<td>434</td>
<td>747</td>
</tr>
<tr>
<td></td>
<td>6-14</td>
<td>769</td>
<td>1,395</td>
<td>1,476</td>
<td>586</td>
<td>392</td>
<td>845</td>
<td>449</td>
<td>665</td>
<td>704</td>
</tr>
<tr>
<td></td>
<td>15-19</td>
<td>1,643</td>
<td>2,252</td>
<td>3,172</td>
<td>2,131</td>
<td>985</td>
<td>826</td>
<td>742</td>
<td>628</td>
<td>253</td>
</tr>
<tr>
<td></td>
<td>20-44</td>
<td>13,440</td>
<td>16,005</td>
<td>16,181</td>
<td>14,389</td>
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<td>8,029</td>
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<td></td>
<td>45-64</td>
<td>15,572</td>
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<td>17,013</td>
<td>18,259</td>
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<td>22,900</td>
<td>22,227</td>
</tr>
<tr>
<td></td>
<td>65-74</td>
<td>4,919</td>
<td>5,562</td>
<td>5,282</td>
<td>6,028</td>
<td>7,240</td>
<td>8,982</td>
<td>8,345</td>
<td>10,192</td>
<td>9,572</td>
</tr>
<tr>
<td></td>
<td>75-84</td>
<td>3,481</td>
<td>2,912</td>
<td>4,703</td>
<td>3,234</td>
<td>4,233</td>
<td>4,631</td>
<td>5,655</td>
<td>5,436</td>
<td>5,276</td>
</tr>
<tr>
<td></td>
<td>85+</td>
<td>1,709</td>
<td>2,017</td>
<td>1,715</td>
<td>1,569</td>
<td>2,614</td>
<td>2,192</td>
<td>3,887</td>
<td>3,203</td>
<td>1,915</td>
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</table>
Appendix B: Chapter 5 Supplementary Materials for Myocardial Infarction and Ischemic Heart Disease.

Table 5.S1. A Crude Number of ER Visits for IHD and MI

<table>
<thead>
<tr>
<th>Patients</th>
<th>IHD</th>
<th>MI</th>
</tr>
</thead>
<tbody>
<tr>
<td>2010</td>
<td>5,889</td>
<td>2,900</td>
</tr>
<tr>
<td>2011</td>
<td>6,152</td>
<td>3,102</td>
</tr>
<tr>
<td>2012</td>
<td>6,410</td>
<td>3,141</td>
</tr>
<tr>
<td>2013</td>
<td>6,464</td>
<td>3,219</td>
</tr>
<tr>
<td>2014</td>
<td>6,033</td>
<td>3,310</td>
</tr>
<tr>
<td>2015</td>
<td>6,332</td>
<td>3,550</td>
</tr>
<tr>
<td>2016</td>
<td>5,485</td>
<td>3,828</td>
</tr>
<tr>
<td>2017</td>
<td>5,240</td>
<td>3,842</td>
</tr>
<tr>
<td>2018</td>
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</table>

Table 5.S2. Actual Number of ER Visits for IHD and MI

<table>
<thead>
<tr>
<th>Patients</th>
<th>IHD</th>
<th>MI</th>
</tr>
</thead>
<tbody>
<tr>
<td>2010</td>
<td>2,611</td>
<td>2,501</td>
</tr>
<tr>
<td>2011</td>
<td>5,652</td>
<td>2,902</td>
</tr>
<tr>
<td>2012</td>
<td>4,347</td>
<td>3,131</td>
</tr>
<tr>
<td>2013</td>
<td>4,512</td>
<td>3,011</td>
</tr>
<tr>
<td>2014</td>
<td>3,231</td>
<td>2,910</td>
</tr>
<tr>
<td>2015</td>
<td>5,430</td>
<td>3,510</td>
</tr>
<tr>
<td>2016</td>
<td>3,485</td>
<td>2,887</td>
</tr>
<tr>
<td>2017</td>
<td>4,240</td>
<td>3,443</td>
</tr>
<tr>
<td>2018</td>
<td>3,435</td>
<td>3,007</td>
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Table 5.S3. Crude Emergency Room Visits by Gender for both MI and IHD

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<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>MI</td>
<td>Female</td>
<td>870</td>
<td>978</td>
<td>1,112</td>
<td>1,178</td>
<td>1,194</td>
<td>1,283</td>
<td>1,394</td>
<td>1,523</td>
<td>1,385</td>
</tr>
<tr>
<td></td>
<td>Male</td>
<td>2,030</td>
<td>2,124</td>
<td>2,029</td>
<td>2,041</td>
<td>2,116</td>
<td>2,267</td>
<td>2,435</td>
<td>2,319</td>
<td>2,403</td>
</tr>
<tr>
<td>IHD</td>
<td>Female</td>
<td>2,622</td>
<td>2,359</td>
<td>2,340</td>
<td>2,789</td>
<td>2,605</td>
<td>2,654</td>
<td>2,440</td>
<td>2,035</td>
<td>1,385</td>
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<td>Male</td>
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<td>3,793</td>
<td>4,070</td>
<td>3,675</td>
<td>3,428</td>
<td>3,678</td>
<td>3,045</td>
<td>3,205</td>
<td>2,403</td>
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Table 5.S4. Age Adjusted Stratification for IHD

<table>
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<th>Disease</th>
<th>Age</th>
<th>2010</th>
<th>2011</th>
<th>2012</th>
<th>2013</th>
<th>2014</th>
<th>2015</th>
<th>2016</th>
<th>2017</th>
<th>2018</th>
</tr>
</thead>
<tbody>
<tr>
<td>IHD</td>
<td>0-19</td>
<td>01</td>
<td>05</td>
<td>32</td>
<td>34</td>
<td>11</td>
<td>00</td>
<td>11</td>
<td>17</td>
<td>05</td>
</tr>
<tr>
<td></td>
<td>20-44</td>
<td>646</td>
<td>789</td>
<td>827</td>
<td>659</td>
<td>450</td>
<td>356</td>
<td>401</td>
<td>389</td>
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</tr>
<tr>
<td></td>
<td>45-64</td>
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<td>3,094</td>
<td>3,355</td>
<td>2,814</td>
<td>2,854</td>
<td>2,581</td>
<td>2,434</td>
<td>1,477</td>
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<td>1,097</td>
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<td>1,281</td>
<td>1,345</td>
<td>1,367</td>
<td>1,213</td>
<td>1,264</td>
<td>967</td>
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<td>75-84</td>
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<td>846</td>
<td>765</td>
<td>742</td>
<td>842</td>
<td>1,187</td>
<td>715</td>
<td>760</td>
<td>726</td>
</tr>
<tr>
<td></td>
<td>85+</td>
<td>347</td>
<td>392</td>
<td>393</td>
<td>393</td>
<td>571</td>
<td>546</td>
<td>564</td>
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Table 5.S5. Age Adjusted Stratification for MI 2010 to 2018

<table>
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<th>2012</th>
<th>2013</th>
<th>2014</th>
<th>2015</th>
<th>2016</th>
<th>2017</th>
<th>2018</th>
</tr>
</thead>
<tbody>
<tr>
<td>MI</td>
<td>0-19</td>
<td>01</td>
<td>00</td>
<td>00</td>
<td>00</td>
<td>14</td>
<td>00</td>
<td>15</td>
<td>03</td>
<td>07</td>
</tr>
<tr>
<td></td>
<td>20-44</td>
<td>235</td>
<td>273</td>
<td>222</td>
<td>01</td>
<td>267</td>
<td>361</td>
<td>238</td>
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</tr>
<tr>
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<td>575</td>
<td>651</td>
<td>1,599</td>
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<td>834</td>
<td>792</td>
<td>667</td>
</tr>
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<td>401</td>
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<td>692</td>
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<td>679</td>
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<td>235</td>
</tr>
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