Title
Investigating the Association of Wildfire Specific Fine Particulate Matter Air Pollution Exposure on Respiratory Health Risk

Author
Ramsey, Erika

Publication Date
2024

Peer reviewed|Thesis/dissertation

UNIVERSITY OF CALIFORNIA,
IRVINE

Investigating the Association of Wildfire Specific Fine Particulate Matter Air Pollution Exposure on Respiratory Health Risk

THESIS

submitted in partial satisfaction of the requirements
for the degree of

MASTER OF SCIENCE

in Epidemiology

by

Erika Ramsey

Thesis Committee:
Professor Jun Wu, Chair
Professor Andrew Odegaard
Professor Luohua Jiang

DEDICATION

To

my relatives, especially my late grandmother, Fumiko Kinjo, and friends

in recognition of their worth

an apology

my little dragonfly hunter
I wonder how far
he has gone today...

"Kaga No Chiyo"
Fukuda Chiyo-ni

and hope

It does not matter how slowly you go as long as you do not stop.

Confucius

TABLE OF CONTENTS

LIST OF TABLES

ACKNOWLEDGEMENTS

I would like to express the deepest appreciation to my committee chair, Professor Jun Wu, for their invaluable support, honesty, and kindness throughout the journey of working on my thesis. Professor Wu's guidance and encouragement have been instrumental in shaping my research and academic development. Their unwavering dedication and insightful feedback have truly enriched my learning experience. I am deeply thankful for Professor Wu's mentorship and generosity.

I would like to thank my committee members, Professor Andrew Odegaard and Professor Luohua Jiang, whose unwavering support, kindness, and inspiration throughout the process of working on my thesis. Their guidance, encouragement, and expertise have been invaluable assets to my academic journey. I am truly fortunate to have had the opportunity to learn from such esteemed mentors. Their dedication and passion for their work have inspired and motivated me to strive for excellence. I extend my heartfelt appreciation to Professor Odegaard and Professor Jiang for their mentorship and encouragement.

In addition, a thank you to Professor Rufus Edwards, who introduced me to Dr. Jun Wu and provided me with the necessary guidance and support as I navigated my graduate school experience.

I would like to express my sincere gratitude to the University of California, Irvine, for providing me with the opportunity to pursue my Master of Science degree. I am immensely grateful for the invaluable support, guidance, and resources offered by the faculty, staff, and fellow students throughout my academic journey. The enriching experience at UC Irvine has significantly contributed to my personal and professional growth, and I am truly thankful for the knowledge and skills gained during my time at this esteemed institution.

ABSTRACT OF THE THESIS

Wildfire Air Pollution $PM_{2.5}$ Exposure Impact on Respiratory Health
by

Erika Ramsey

Master of Science in Epidemiology

University of California, Irvine, 2024

Professor Jun Wu, Chair

Introduction: Wildfires, intensified by climate change, emit diverse pollutants, including $PM_{2.5}$, fine particulate matter, which are implicated in respiratory health effects. The pollutant, fine particulate matter, refers to particles with an aerodynamic diameter of 2.5 micrometers or less ($PM_{2.5}$). $PM_{2.5}$ particles from wildfires can deeply penetrate the respiratory system and bloodstream, presenting substantial health hazards. Current regulatory frameworks often fail to differentiate between wildfire specific and ambient $PM_{2.5}$, despite evidence indicating elevated health risks from wildfires. The concept of "smoke waves," representing periods of varying durations and heightened $PM_{2.5}$ concentrations resulting from wildfires, offers a novel approach to characterizing exposure. This study seeks to examine the association between wildfire specific $PM_{2.5}$ exposure and respiratory health outcomes.

Methods: A time series analysis was conducted to assess the association of wildfire-specific $PM_{2.5}$ exposure with respiratory health risk by examining respiratory-related hospitalizations and emergency department visits across various zip codes in the years 2017, 2018, and 2020. Daily concentrations of $PM_{2.5}$ were analyzed alongside daily hospitalization and emergency visit data. The Generalized Estimating Equations (GEE) model with Poisson regression was employed, with the primary exposure variable being wildfire specific $PM_{2.5}$ exposure and the outcome variable being respiratory health risk. An autoregressive covariance structure (AR (1)) was included, and an offset term was incorporated by taking the logarithm of the total population. Demographic, temporal, and meteorological covariates were accounted for in the main analysis. All statistical analyses were conducted using SAS 9.4 (SAS Institute Inc.).

Results: In the primary investigation, a notable positive association was observed between overall respiratory diseases and the presence of wildfire specific $PM_{2.5}$ particulate matter. This association persisted across various lag periods with relative risk estimates ranging from 1.022 to 1.048 across various lag times. Upon disaggregating the data to examine disease-specific outcomes like asthma and chronic obstructive pulmonary disease (COPD), a consistent positive relationship emerged with wildfire-specific $PM_{2.5}$ levels for emergency department visits and hospitalizations across all lag periods with relative risk estimates ranging from 1.025 to 1.048 across various lag times.

Conclusion: We observed a strong association between wildfire specific $PM_{2.5}$ exposure and respiratory health outcomes, showing a consistent positive association across different lag periods. Elevated risks were observed for overall respiratory disease, including asthma and COPD. It was also found that personal behaviors may assist in mitigating risk during smoke waves with increased intensity and similar duration. These results support discerning wildfire $PM_{2.5}$ from ambient levels and highlight the need to further understand this association and its potential consequences.

CHAPTER 1. INTRODUCTION

Overview

As climate change persists, wildfires have increased in both frequency and intensity. These uncontrolled fires can originate from diverse sources, including natural causes like lightning strikes, unauthorized human activities, and accidental escapes from prescribed burn initiatives (Burke et al., 2021; Congressional Research Service, 2023). Fine particulate matter, specifically particles with an aerodynamic diameter of 2.5 micrometers or less ($PM_{2.5}$), is a significant constituent of wildfire smoke and profoundly impacts public health (Interagency Working Group on Climate Change and Health, 2010; Liu et al., 2015; Reid et al., 2016). While $PM_{2.5}$, levels have generally declined across the United States due to strict environmental regulations, exceptions are noted in regions prone to wildfires (McClure & Jaffe, 2018). Projections indicate that wildfire specific $PM_{2.5}$ concentrations in the US are expected to rise in response to climate change (Ford et al., 2018; Stowell et al., 2019; Liu et al., 2016). Unlike non-wildfire $PM_{2.5}$, which may originate from sources like industrial plants and traffic emissions with chronic emissions, wildfire specific $PM_{2.5}$ can experience sudden and substantial increases within short time frames, particularly following the onset of wildfires (Aguilera et al., 2021a; Liu et al., 2017a; Stowell et al., 2019).

Despite variations in emission sources and prevailing air quality standards outlined in regulations like the Clean Air Act Amendments and the World Health Organization Air Quality Guidelines, distinctions between wildfire specific $PM_{2.5}$ and other $PM_{2.5}$ sources are not typically made (World Health Organization, 2005). Wildfire smoke comprises a complex mixture of pollutants that can be deeply inhaled, potentially entering the bloodstream. Pollutants such as $PM_{2.5}$ from wildfires have been implicated in respiratory health risks (Gao et al., 2023; Liu et al., 2015; Reid et al., 2016; Youssouf et al., 2014; Kiser et al., 2020).

Other pollutants, such as PM_{10} (particulate matter with diameters ≤ 10 micrometers, including $PM_{2.5}$), have been implicated in air quality issues. PM_{10} and $PM_{2.5}$ are among the extensively studied pollutants, particularly prevalent after wildfires (Wong et al., 1999; Areal et al., 2022; Faustini et al., 2015; Chen et al., 2006; Henderson et al., 2011). There is speculation about the interaction between particulate matter pollution from wildfires and other environmental factors. Wildfires often occur during the warm season, leading to increased levels of extreme heat and other pollutants such as carbon monoxide, nitrogen oxides, and ozone (Areal et al., 2022; Dong et al., 2017; Heaney et al., 2022; Jiao et al., 2024; Kiser et al., 2020; Xu et al., 2020; Cobelo et al., 2023).

Nitrogen dioxide (NO_2), a hazardous gas, originates from sources like traffic emissions and gas cooking (Huangfu & Atkinson, 2020). In urban areas, NO_2 primarily forms through the oxidation of nitric oxide (NO), a major traffic-related pollutant. Ozone (O_3), a highly reactive oxidative gas, is formed through atmospheric reactions involving nitrogen oxides, volatile organic compounds, and solar radiation. Both NO_2 and O_3 are linked to adverse health effects, including respiratory issues, hospital admissions, and premature mortality (Nuvolone et al., 2018; Strickland et al., 2010; Malig et al., 2016; Urman et al., 2014; Peel et al., 2005; Wong et al., 1999; Aguilera et al., 2021; Areal et al., 2022). Due to its high oxidizing properties, ozone may damage respiratory tissues, leading to respiratory strain and contributing to illness and mortality (Kazemiparkouhi et al., 2019; Diaz et al., 2018; Guo et al., 2017).

While specific studies on carbon monoxide (CO) exposure are limited, various organizations highlight its detrimental impact on respiratory health (Ryter et al., 2018; Jang et al., 2021). CO poisoning is a leading cause of poisoning-related fatalities globally, often linked to house fires (Jang et al., 2021). CO enters the body through the lungs, directly harming lung tissue independently of hemoglobin transport. Elevated levels of carboxyhemoglobin (COHb) due to toxic concentrations impede gas exchange, leading to hypoxemia (Jang et al., 2021; Hanley & Patel, 2023). Given its harmful effects on respiratory health, CO exposure likely increases the risk of respiratory conditions such as acute respiratory distress syndrome (Jang et al., 2021). These factors are significant in research on wildfire air pollution and respiratory health.

Wildfire Specific Particulate Matter and Respiratory Health Risk

Wildfire smoke contains particulate matter that can trigger systemic inflammation, oxidative stress, and vascular dysfunction upon deep penetration into the respiratory system (Franzi et al., 2011; Liu et al., 2017a; Sorensen et al., 2021; Xing et al., 2016). Due to this reason, it is highly suspected that fine particulate matter contributes to increased respiratory health risk.

Despite global regulatory frameworks treating wildfire specific and non-wildfire $PM_{2.5}$ equally in terms of health impact, other studies have demonstrated that $PM_{2.5}$ from wildfires poses a health risk up to tenfold greater than $PM_{2.5}$ from other sources (Aguilera et al., 2021a; de Oliveira Alves et al., 2014; Franzi et al., 2011; Pavagadhi et al., 2013; Wegesser et al., 2010). This underscores the substantial burden wildfire specific $PM_{2.5}$ may impose on respiratory health (Aguilera et al., 2021a; Aguilera et al., 2021b; Stowell et al., 2019; Yuchi et al., 2016). Exposure to $PM_{2.5}$ has been linked to various respiratory ailments, including asthma, chronic obstructive pulmonary disease (COPD), bronchitis, and exacerbation of existing conditions (Cascio et al., 2018; Gan et al., 2017; Magzamen et al., 2021; Stowell et al., 2019). Of particular concern is the association between wildfire specific $PM_{2.5}$ and respiratory health, as it exacerbates respiratory symptoms and increases the risk of hospitalizations and emergency department visits (Sorensen et al., 2021; Rappold et al., 2012; Henderson et al., 2011).

The intensification and increased frequency of wildfires raise concerns about the health impacts of wildfire smoke toxicity and pollution. Climate change-induced exacerbation of severe wildfire smoke incidents is anticipated to result in approximately 178 additional respiratory hospital admissions in the Western US (95% confidence interval: 6.2, 361) (Liu et al., 2016), particularly affecting the elderly population (Le et al., 2014; Liu et al., 2016, 2019; Reid et al., 2019; Lin, 2023). Moreover, climate change is expected to contribute to an additional 4990 days of high-pollution smoke (Liu et al., 2016). Regions such as Central Colorado, Washington, Southern California (included in the study area), and Canada are projected to experience the most substantial percentage increase in respiratory admissions due to wildfire smoke under climate change scenarios (Liu et al., 2016; Kondo et al., 2019).

In a study by Liu et al. (2019), the term "smoke wave" was introduced as part of the investigation into the nexus between wildfires and public health. A "smoke wave" is defined as two or more days of elevated $PM_{2.5}$ levels (daily wildfire specific $PM_{2.5}$ > 15 $\mu g/m^3$) resulting from wildfire smoke (Burrows, 2016; Liu et al., 2019; World Health Organization, 2021). This concept of a "smoke wave" will be employed in this study to aid in defining $PM_{2.5}$ exposure.

Exposure Assessment Methods of Wildfire Smoke

Previously, $PM_{2.5}$ concentrations were gauged using either an aerosol sampler or a $PM_{2.5}$ monitor, both of which draw in air and evaluate $PM_{2.5}$ concentration on a filter. Findings are expressed as micrograms per cubic meter of air (µg/m3) (Airly, 2012). The World Health Organization (WHO) defines acceptable $PM_{2.5}$ levels as 5 $\mu g/m^3$ annually and 15 $\mu g/m^3$ over a 24-hour period in their 2021 Global Air Quality Guidelines (World Health Organization, 2021).

Table 1. The WHO's 2021 Air Quality Guidelines

Pollutant	Average Time	2021 AQG
$PM_{2.5}$,$\mu g/m^3$	Annual	5
	24 - hour	15
PM_{10}, $\mu g/m^3$	Annual	15
	24 - hour	45
O_3, $\mu g/m^3$	Peak Season	60
	8 - hour	100
NO_2, $\mu g/m^3$	Annual	10
	24 - hour	25
CO, mg/m^3	24 - hour	4

Source: World Health Organization, "What are the WHO Air Quality Guidelines?", 2021. Accessed via https://www.who.int/news-room/feature-stories/detail/what-are-the-who-air-quality-guidelines.

Various methods were employed for exposure assessment, including subtracting background PM from all-source PM using measured concentrations from ground monitoring stations and modeling. While the primary focus of this study is the association between $PM_{2.5}$ exposure and respiratory health risk, exposure assessment remains integral to this research and will be briefly addressed.

Exposure assessment methodologies for fine particulate matter concentration during wildfire events vary in the literature. Some studies estimated wildfire-specific PM by subtracting background PM from overall PM concentrations measured by ground monitoring stations (Aguilera et al., 2021a; Aguilera et al., 2021b; Casey et al., 2021; Gan et al., 2020; Hahn et al., 2021; Lipner et al., 2019; Magzamen et al., 2021; Morgan et al., 2010). Background PM levels were typically determined as the long-term average or median concentrations of PM on non-wildfire days within a specific area. While this method simplifies the process and does not require extensive computational or modeling efforts, it relies heavily on the availability of ground-based monitoring station data, which may be limited in rural or suburban regions or during wildfire events. Moreover, subtracting background PM from total PM may not fully distinguish PM originating from wildfires versus other human activities, potentially leading to exposure misclassification (Gan et al., 2020; Hahn et al., 2021; Lipner et al., 2019).

Alternatively, other studies employed atmospheric transport models to differentiate wildfire-specific PM from PM originating from other sources. These models estimate pollutant dispersion in the atmosphere by integrating emission data, meteorological parameters, and physical principles. Eight of these studies calculated wildfire-specific PM concentrations through model simulations of two scenarios: one with fire emissions included and one without. They utilized models such as the Goddard Earth Observing System-Chem model (GEOS-Chem), the Weather Research and Forecasting with Chemistry model (WRF-Chem), or the Community Multiscale Air Quality Modeling System (CMAQ) (Burke et al., 2021; Chen et al., 2021b; Heaney et al., 2022; Liu et al., 2017a; Liu et al., 2017b; Ye et al., 2021; Ye et al., 2022; Gan et al., 2017; Stowell et al., 2019).

Additionally, some studies employed atmospheric dispersion models, such as the CALPUFF dispersion model and the Hybrid Single Particle Lagrangian Integrated Transport model (HYSPLIT), to estimate wildfire-specific emission dispersion (Henderson et al., 2011; Hutchinson et al., 2018). These methods offer potentially more accurate estimates of wildfire-specific PM by considering direct wildfire emissions and meteorology for atmospheric composition simulation. They may also provide higher spatiotemporal resolution estimates compared to ground-based measurements relying on limited monitoring stations. However, accurately simulating emissions, wildfire smoke movement, and chemical processing poses challenges, requiring detailed knowledge, complex model inputs, and rigorous evaluation. The reliability of these models hinges on input data quality and model validity in simulating physical processes. Uncertainties in emission data, such as the amount of dry matter burned and emission factors, can be significant due to their strong dependence on meteorological conditions, fuel characteristics, combustion stages, and fire containment activities, for which accurate data are often elusive.

Other studies obtained estimates of wildfire-specific particulate matter from prediction models, such as the U.S. National Oceanic and Atmospheric Administration (NOAA) Smoke Forecasting System (Rappold et al., 2012; Tinling et al., 2016) and the BlueSky Western Canada Wildfire Smoke Forecasting Framework (Yuchi et al., 2016). Forecasting models introduce greater uncertainties in biomass burning and smoke emissions compared to models that retrospectively estimate wildfire smoke based on known burning areas. The unpredictable nature of wildfires, combined with the assumption of consistent biomass burning emissions in predictive models, limits smoke forecast accuracy, particularly for large wildfires characterized by significant day-to-day behavioral fluctuations.

Furthermore, a study utilized smoke plume density data from the Hazard Mapping System (HMS) provided by the U.S. National Oceanic and Atmospheric Administration (NOAA) (Wettstein et al., 2018). While the HMS combines satellite imagery from multiple NOAA and National Aeronautics and Space Administration (NASA) instruments to generate smoke products, it cannot differentiate whether the smoke plume is at ground level or at a higher elevation (Aguilera et al., 2021a; Lipner et al., 2019; Ruminski et al., 2006). Additionally, the smoke plume is categorized as a binary variable rather than providing continuous PM concentration estimates, limiting its utility in estimating the dose-response relationship, particularly for $PM_{2.5}$ concentrations.

These studies collectively enhance our comprehension of $PM_{2.5}$ exposure during wildfire incidents, providing valuable insights into methodological advancements and their repercussions on health outcome evaluations. Among the existing literature, numerous papers employed a hybrid approach involving modeling and subtraction of background PM levels from total PM concentrations, utilizing data sourced from ground monitoring stations to evaluate overall wildfire specific $PM_{2.5}$. In this study, $PM_{2.5}$ concentration data derived from modeling conducted by Shupeng Zhu, a colleague at the University of California Irvine, with whom we collaborate for this research, will be utilized.

Review of Literature: Inhalation of Wildfire Emissions on Respiratory Health

This literature review extends a systematic review of wildfire particulate matter and respiratory outcomes conducted by our colleague, Anqi Jiao, at the University of California, Irvine (Jiao et al., 2024). Paper inclusion and exclusion criteria were established based on outcome classification (e.g., discussion of respiratory related hospital and emergency department visits) and exposure focus (e.g., specifically addressing wildfire specific $PM_{2.5}$).

The literature consistently reports adverse respiratory outcomes linked to exposure to fine particulate matter. Eleven studies investigated the relationship between emergency department visits and exposure to wildfire specific $PM_{2.5}$. Two studies specifically focused on emergency department visits related to asthma (Gan et al., 2020; Rappold et al., 2012), while the remaining nine studies examined all-cause respiratory emergency department visits across various age groups, consistently reporting adverse effects of $PM_{2.5}$ (Aguilera et al., 2021b; Arriagada et al., 2019; Casey et al., 2021; Hahn et al., 2021; Hutchinson et al., 2018; Tinling et al., 2016; Wettstein et al., 2018; Doubleday et al., 2023; Stowell et al., 2019).

Nine studies investigated hospital admissions, with four focusing specifically on emergency or urgent care admissions to exclude scheduled hospitalizations (Gan et al., 2017; Liu et al., 2017a; Magzamen et al., 2021; Alman et al., 2016). Among the studies examining wildfire specific $PM_{2.5}$, one analyzed admission related to asthma (Gan et al., 2020), while two others estimated admissions for COPD and respiratory tract infections (Liu et al., 2017b; Pothirat et al., 2019). In terms of hospital admissions associated with all-cause respiratory outcomes, four studies indicated a 5%–10% increased risk or odds of respiratory admissions per 10 μg/m3 increase in wildfire-specific $PM_{2.5}$. These results were derived from two time-series studies (Aguilera et al., 2021a; Ye et al., 2021) and two case-crossover studies (Gan et al., 2017; Magzamen et al., 2021). Additionally, a case-crossover study among Medicare enrollees aged 65 years and above in the Western United States yielded positive findings by employing a binary exposure to a smoke event defined based on wildfire-specific $PM_{2.5}$ pollution levels (Liu et al., 2017a).

Fourteen papers examined hospital visits or hospitalizations attributed to specific respiratory diseases, with asthma being the most frequently studied condition (Aguilera et al., 2021b; Gan et al., 2017; Gan et al., 2020; Hahn et al., 2021; Heaney et al., 2022; Henderson et al., 2011; Hutchinson et al., 2018; Magzamen et al., 2021; Morgan et al., 2010; Rappold et al., 2012; Stowell et al., 2019; Wettstein et al., 2018; Yuchi et al., 2016; Tinling et al., 2016). Other respiratory conditions investigated included COPD (Magzamen et al., 2021; Wettstein et al., 2019; Gan et al., 2017; Heaney et al., 2022; Morgan et al., 2010; Wettstein et al., 2018; Stowell et al., 2019; Hahn et al., 2021), bronchitis (Gan et al., 2017; Magzamen et al., 2021; Hahn et al., 2021; Stowell et al., 2019), and various other ailments.

Most studies demonstrated positive associations with asthma-related visits/hospitalizations (Gan et al., 2017; Gan et al., 2020; Hahn et al., 2021; Heaney et al., 2022; Henderson et al., 2011; Hutchinson et al., 2018; Magzamen et al., 2021; Morgan et al., 2010; Rappold et al., 2012; Stowell et al., 2019; Wettstein et al., 2018; Yuchi et al., 2016). However, one study found no significant associations across different age groups (Tinling et al., 2016), and another study focusing on pediatric visits (≤19 years) also did not find an association (Aguilera et al., 2021b). Associations with COPD were reported both in the general population and in specific age groups, with only one study reporting no significant associations (Magzamen et al., 2021). The associations with bronchitis-related visits/hospitalizations were inconsistently reported across studies (Gan et al., 2017; Hahn et al., 2021; Stowell et al., 2019).

Identified Gaps in the Literature

Following an extensive literature review, a consensus has emerged regarding the relationship between wildfire air pollution exposure and respiratory health risk. However, common limitations persist, notably the unavailability and uncertainty of wildfire specific $PM_{2.5}$ measurements in most studies (Lipner et al., 2019; Li et al., 2023; Kiser et al., 2020). To address this gap, our study integrates daily wildfire specific $PM_{2.5}$ data, providing real-time measurements directly attributable to wildfire events. Unlike previous research relying on generalized $PM_{2.5}$ estimates, this methodology enhances the accuracy and granularity of our analysis, offering valuable insights into the intricate dynamics between wildfire emissions and human health.

To address a gap in the literature concerning wildfire-related air pollution dynamics at a fine spatial resolution, this study adopts a methodological approach with higher spatial granularity compared to previous research (Heaney et al., 2022; Alman et al., 2016; Rappold et al., 2012). While previous studies focused on broader geographical units like cities or counties, our investigation analyzes population-weighted data at the level of individual zip codes across California, utilizing high-resolution exposure data at a 1x1 km scale. This approach enables a more elaborate understanding of wildfire-related air pollution dynamics and their impact on respiratory health outcomes, capturing variations in exposure levels and demographic characteristics more accurately within smaller geographic areas. Additionally, we utilize census-level data for exposure assessment, enhancing the precision and granularity of our analyses. Addressing limitations identified in prior research regarding exposure classification precision due to spatial resolution, our study uses zip code-level data to mitigate exposure misclassification risks associated with broader geographical units. By adopting this finer spatial resolution, our research aims to provide a more accurate portrayal of wildfire-related air pollution exposure in California, contributing to a deeper understanding of its effects on respiratory health outcomes.

This study addresses the gap in literature by conducting a comprehensive examination of wildfire-related air pollution dynamics and their impact on respiratory health outcomes across California's expansive geographical area of 423,970 square kilometers. California's diverse population, including a significant Latinx population (40.3%) and sizable Asian population (16.3%), alongside other ethnicities such as White, Black, and Indigenous populations, provides a rich tapestry for analysis (United States Department of Commerce, 2023). Additionally, California exhibits considerable socioeconomic diversity, with an estimated 12.2% living below the poverty line (United States Department of Commerce, 2023). By encompassing this demographic diversity, our study aims to explore the interplay between wildfire specific $PM_{2.5}$ and respiratory health outcomes across varied population subgroups, contributing valuable insights to the existing literature.

To address the literature gap, this study adopts a comprehensive approach, examining both continuous wildfire specific $PM_{2.5}$ exposure and smoke waves. Prior research often focuses on either long-term $PM_{2.5}$ exposure or acute smoke events separately. Our methodology aims to understand the interplay between sustained $PM_{2.5}$ exposure and episodic smoke events on respiratory health outcomes by integrating continuous exposure assessments with smoke wave characterization. This multifaceted analysis enhances the granularity of investigation and enables delineation of distinct health implications associated with different temporal patterns of wildfire smoke exposure.

CHAPTER 2. METHODS

Respiratory Outcome Data Source and Collection

Respiratory health outcome data utilized in this investigation were obtained from the Department of Health Care Access and Information (HCAI), formerly known as the Office of Statewide Health Planning and Development (OSHPD) data. HCAI serves as a centralized repository responsible for collecting and disseminating insights on California's healthcare system infrastructure, focusing primarily on surveillance and management of healthcare-associated infections (HCAIs). The data collection process involves systematic aggregation from various sources, including electronic health records, laboratory reports, and infection control databases. The dataset encompasses patient demographics, medical interventions, laboratory findings, and infection details. Specifically, the dataset consists of daily entries documenting respiratory health outcomes and environmental parameters by zip codes within California, covering the years 2017, 2018, and 2020.

Study Design

This study employs a retrospective time series analysis to investigate the association between exposure to wildfire specific $PM_{2.5}$ and respiratory health risks, including hospitalizations and emergency department visits due to respiratory conditions. The Generalized Estimating Equations (GEE) model, employing Poisson regression and incorporating an autoregressive covariance structure (AR(1)), serves as the primary statistical method for modeling the relationship between exposure and outcomes while controlling for various covariates. This approach allows us to address the correlation of repeated measures within each zip code, with zip code no longer treated as a random effect. By adopting the AR structure, we effectively account for the temporal autocorrelation inherent in the data, ensuring that the longitudinal nature of the data is appropriately captured in our analysis. The population sample was constrained to comprise solely of zip codes with populations numbering 20 or greater, a measure undertaken to address concerns pertaining to statistical robustness. An offset term of the logarithm of the total population was also included in the models to account for differences in population size across different units.

Exposure Assessment Methods

As stated previously, the $PM_{2.5}$ exposure data was obtained in collaboration with a research team led by Dr. Zhu Shupeng at University of California, Irvine (Zhu et al., 2024). Exposure data for wildfire specific $PM_{2.5}$ concentrations were obtained through a two-phase modeling approach: downscaling non-wildfire air quality data and refining wildfire smoke filtering techniques. Extensive investigation identified the most effective downscaling method, utilizing multiple machine learning approaches and a dataset with 41 input parameters, including air pollutant concentrations, non-fire CMAQ-derived meteorological conditions, purple air measurements, satellite-based reanalysis data, and vegetation coverage.

Exposure Variables for Wildfire Specific $PM_{2.5}$

I will investigate two $PM_{2.5}$ exposure metrics: continuous $PM_{2.5}$ exposure, comprising total $PM_{2.5}$ concentration with lagged effects, and smoke waves. Incorporating both metrics serves multiple pivotal purposes in this study. Firstly, their inclusion ensures the robustness of our estimates, guaranteeing the reliability and stability of the findings. By assessing the association between continuous PM exposure and adverse health outcomes, we aim to elucidate the potential impact of sustained $PM_{2.5}$ exposure on respiratory health outcomes, addressing one of our primary hypotheses. Furthermore, investigating smoke wave episodes allows for exploration of an additional hypothesis: the influence of acute exposure to elevated $PM_{2.5}$ levels across varying durations, characteristic of wildfire smoke events, on respiratory health outcomes. Through this dual approach, I aim to comprehensively evaluate the diverse pathways through which $PM_{2.5}$ exposure may affect respiratory health, enhancing the depth and breadth of our analysis.

From Liu et al.'s (2019) study, the term "smoke wave" was introduced to explore the association between wildfires and public health. It represents a consecutive series of two or more days with elevated $PM_{2.5}$ levels, specifically daily wildfire-specific $PM_{2.5}$ exceeding 15 $\mu g/m^3$, due to wildfire smoke (Burrows, 2016; Liu et al., 2019; Word Health Organization, 2021). Previous research has shown an increased risk of respiratory-related hospital admissions during days characterized by smoke waves and heightened levels of wildfire-specific $PM_{2.5}$ (Liu et al., 2019; Reid et al., 2019; Lin, 2023). In this study, smoke wave occurrences are identified using binary variables for each smoke wave definition. Observations are categorized into the exposed group if any smoke wave event occurred during specified consecutive days with $PM_{2.5}$ concentrations surpassing predefined thresholds.

In the methodological framework, the generation of smoke wave episodes begins by creating binary indicators denoting $PM_{2.5}$ concentration levels surpassing predefined thresholds, such as the 75th, 90th, and 95th percentiles. These indicators, taking values of 0 or 1, signify whether the $PM_{2.5}$ concentration on a given day exceeds the designated threshold. Subsequently, lagged indicators are established for each threshold level, reflecting whether the $PM_{2.5}$ concentration on the preceding day surpassed the specified threshold. Utilizing the "sum" function, the cumulative count of days exhibiting $PM_{2.5}$ concentrations surpassing each threshold level, encompassing lagged days, is computed. Lastly, smoke wave episodes are discerned based on specific sequences of consecutive days with $PM_{2.5}$ concentrations surpassing designated thresholds. For instance, if $PM_{2.5}$ concentrations exceed the 75th percentile threshold for two successive days, it initiates the identification of a smoke wave episode.

Table 2. Definition of Smoke Wave Severity Levels Based on Daily Average $PM_{2.5}$ Concentrations

Smoke Wave	**Criteria**
Smoke Wave 1	Daily average $PM_{2.5}$ concentration ≥ 3.56 μg/m^3 for 2 consecutive days
Smoke Wave 2	Daily average $PM_{2.5}$ concentration ≥ 3.56 μg/m^3 for 3 consecutive days
Smoke Wave 3	Daily average $PM_{2.5}$ concentration ≥ 3.56 μg/m^3 for 4 consecutive days
Smoke Wave 4	Daily average $PM_{2.5}$ concentration ≥ 5.33 μg/m^3 for 2 consecutive days
Smoke Wave 5	Daily average $PM_{2.5}$ concentration ≥ 5.33 μg/m^3 for 3 consecutive days
Smoke Wave 6	Daily average $PM_{2.5}$ concentration ≥ 5.33 μg/m^3 for 4 consecutive days
Smoke Wave 7	Daily average $PM_{2.5}$ concentration ≥ 9.05 μg/m^3 for 2 consecutive days
Smoke Wave 8	Daily average $PM_{2.5}$ concentration ≥ 9.05 μg/m^3 for 3 consecutive days
Smoke Wave 9	Daily average $PM_{2.5}$ concentration ≥ 9.05 μg/m^3 for 4 consecutive days

Outcome Variables for Respiratory Health Risk Assessment

Daily hospitalizations and emergency department visits served as primary indicators for assessing respiratory health risk, encompassing aggregated data on respiratory-related hospitalizations and emergency department visits for the years 2017, 2018, and 2020. The study investigated disease-specific outcomes, encompassing conditions such as asthma (ICD code J45), chronic obstructive pulmonary disease (COPD) (ICD codes J41, J42, J43, J44), and bronchitis and bronchiolitis (ICD codes J20, J21), to evaluate the impact of wildfire-specific $PM_{2.5}$ exposure on these specific health conditions and determine potential variations among them.

Covariates

Covariates, including day of the week, month, holiday indicators, and year, are included to capture potential temporal patterns and trends in both wildfire-specific $PM_{2.5}$ exposure levels and respiratory health risk, as measured by daily hospitalization and emergency room data. Additionally, meteorological variables such as humidity, precipitation, temperature, and wind velocity are incorporated to address the influence of weather conditions on both exposure and outcome variables. These meteorological factors can impact the dispersion and concentration of airborne pollutants as well as respiratory health outcomes (Pothirat et al., 2019; Doubleday et al., 2020; Elliott et al., 2013).

In this investigation, sociodemographic covariates such as the percentage of Hispanic population, income group, median age, and female population percentage were incorporated into the analytical model to address potential confounding factors affecting the relationship between $PM_{2.5}$ exposure and respiratory health outcomes. The inclusion of these covariates is particularly relevant considering the analysis is conducted at the zip code level, providing insights into the sociodemographic structure of each area. By integrating these sociodemographic covariates, the model enhances robustness and validity, ensuring a more comprehensive understanding of the association between $PM_{2.5}$ exposure and respiratory health outcomes. The data utilized for these demographic covariates were obtained from the US Census Bureau 2020, ensuring the accuracy and reliability of the sociodemographic information incorporated into the analysis.

Offset Variable

Furthermore, to mitigate disparities in population size among various zip codes within California, I integrated a log-transformed, zip code-specific population estimate into the analytical framework. This adjustment was imperative to normalize the rates of respiratory health outcomes across heterogeneous zip code populations. By introducing an offset term denoting the logarithm of the total population, this approach effectively adjusted for population size discrepancies, thereby enhancing the precision and validity of comparisons of health outcomes across zip codes.

Statistical Analysis

Descriptive Analysis

The preliminary stage of the analysis involved descriptive examination, which entailed summarizing the distribution of pertinent variables. These variables encompassed wildfire specific $PM_{2.5}$ levels, emergency department visits and hospitalizations related to respiratory issues, as well as demographic factors such as age, ethnicity, and gender. Descriptive statistics, including measures such as mean, median, maximum, and interquartile range, were computed to characterize the dataset. This descriptive analysis was performed using Statistical Analysis Software, specifically SAS 9.4 (SAS Institute Inc.).

Time Series Statistical Analysis

Time series analysis was conducted using SAS 9.4 (SAS Institute Inc.). Poisson regression models were employed to assess the relationship between wildfire $PM_{2.5}$ exposure and respiratory health outcomes while adjusting for covariates. An autoregressive covariance structure was applied to address potential temporal autocorrelation within the dataset. This methodology was chosen based on prior studies within the same research domain (Bobb et al., 2014; Bhaskaran et al., 2013; Ciciretti et al., 2022; Gasparrini et al., 2016; Guo et al., 2017; Morgan et al., 2010; Reid et al., 2016; Reid et al., 2019). Alternative approaches were explored, including log rates via the PROC MIXED function in SAS, but were deemed unsuitable given the dataset's characteristics. Consequently, the most appropriate method selected was to proceed with the generalized estimating equations (GEE) model employing a Poisson distribution.

The primary model employs total wildfire-specific $PM_{2.5}$ exposure as the independent variable and total respiratory health-related admissions, categorized by visit type (hospitalization or emergency department visit), as the dependent measure. Disease-specific outcomes, including asthma, COPD, acute bronchitis and bronchiolitis, were also examined to provide a more detailed understanding of the health effects of wildfire-specific $PM_{2.5}$ exposure. By considering disease-specific outcomes, the aim was to cover a range of respiratory conditions and assess their individual contributions to the overall health effects of wildfire-specific $PM_{2.5}$ exposure. Additionally, analyzing disease-specific outcomes allowed for an evaluation of the consistency of associations across different respiratory conditions, thereby offering insights into which ailments are most vulnerable to the impacts of wildfire smoke.

In time-series air pollution research, it is customary to explore the temporal relationship between daily health outcomes and ambient concentrations of fine particulate matter (Vedal et al., 2009; Kim et al., 2012). This approach, utilized in numerous studies, typically considers associations over the same day and a few preceding days (Dominici et al., 2006; Lippmann et al., 2000; Samet et al., 2000; Gan et al., 2017; Hahn et al., 2021). Examining lag effects within this study is crucial as it allows for exploration of the diverse biological mechanisms governing acute responses to particulate matter pollution, as highlighted by Zanobetti et al. (2003). Previous literature has suggested stronger association estimates for emergency department visits for asthma and hospital admissions for respiratory-related conditions at lags of 0-4 days (Gan et al., 2017; Magzamen et al., 2021; Morgan et al., 2010; Wettstein et al., 2018). Therefore, this investigation will analyze lag effects from lag 0 through lag 7 for all respiratory-related illness cases. For disease-specific analysis, focus will be placed solely on lag 0 and the cumulative lag, aiming to scrutinize the magnitude of lagged effects on respiratory health risk.

In the sensitivity analysis models, alongside the primary model, a supplementary exposure variable was integrated to ascertain the resilience of the conclusions. This encompassed smoke wave episodes, delineated by nine occurrences identified via $PM_{2.5}$ threshold criteria for smoke days. Through the inclusion of these parameters in the sensitivity analysis, the objective was to appraise the potential influence of alterations in exposure definitions and temporal windows on the outcomes. This method facilitated an evaluation of the coherence and durability of the primary model's findings across diverse modeling assumptions and exposure delineations, thereby augmenting the study's overall dependability.

Subgroup Analysis

Subgroup analysis was conducted to discern potential differences among various subgroups, encompassing factors such as sex (male/female), age categories (>18, 18-44, 45-64, and ≥65), and ancestry/ethnicity (non-Hispanic Asian, non-Hispanic Black, Hispanic, non-Hispanic White, and other). Binary variables were employed to represent each subgroup, with respective numerical values assigned to denote specific groups within each category. Furthermore, subgroup analysis focused on disease-specific considerations within age groups, acknowledging that certain age demographics may exhibit heightened susceptibility to particular health conditions (e.g., children displaying increased vulnerability to asthma, while elderly populations may be more prone to COPD) (Delfino et al., 2009; Heaney et al., 2020; Stowell et al., 2019; Lipner et al., 2019; Wettstein et al., 2018; Arriagada et al., 2019; Liu et al., 2017b).

In our study, we employed the Cochran Q test to assess the variability between groups within each subgroup, aiming to evaluate whether the observed differences among these groups were statistically significant. This statistical test enabled us to determine if there was heterogeneity in the treatment effect across demographic subgroups. Specifically, we utilized the Cochran Q test to scrutinize potential variations in the impact of the independent variable, such as exposure to $PM_{2.5}$, on the outcome variable within distinct subgroups. The significance of the Cochran Q test results provided crucial insights into the presence of statistically significant differences in the effect sizes among the subgroups, thereby informing our understanding of how demographic or clinical characteristics may modify the relationship between exposure and outcome.

CHAPTER 3. RESULTS

Descriptive Statistics

There were 626,219 hospitalizations with all cause respiratory related visits, 44,148 with asthma (7.05%), 111,279 with COPD (17.77%), and 34,586 with acute bronchitis and bronchiolitis (5.52%). In terms of emergency department visits, there were 3,526,358 participants with all cause respiratory related visits, 415,683 with asthma, 292,382 with COPD (8.29%), and 306,228 with acute bronchitis and bronchiolitis (8.68%). Age specific results showed that for hospitalizations older individuals (e.g. 45-64 years and ≥ 65 years) were more likely to be hospitalized for respiratory related outcomes. However, for respiratory related emergency department visits, the results indicated an opposite trend with the younger age group (e.g. < 18 years and 18-44 years) having increased visits in comparison to the older age group (e.g. 45-64 years and ≥ 65 years). In the hospitalizations there was no significant difference between sex, however in emergency department visits those who identified as female had higher numbers compared to their male counterparts.

Table 3. Hospitalizations Related to Respiratory Outcomes (2017, 2018, and 2020)

			Percentile				
	Total	Mean ± SD	Min	25th	50th	75th	Max
All cause respiratory	626,219 (100)	571 ± 243	15	370	527	720	1,557
Disease specific							
Chronic Obstructive Pulmonary Disease	111,279 (17.77)	102 ± 47	1	61	102	127	269
Asthma	44,148 (7.05)	40 ± 20	2	21	44	56	89
Bronchitis and Bronchiolitis	34,586 (5.52)	32 ± 33	0	6	18	46	156
Age-specific							
< 18	96,186 (15.36)	88 ± 63	1	31	80	127	282
18 - 44	55,765 (8.91)	51 ± 15	0	40	50	61	105
45 - 64	151,848 (24.25)	139 ± 47	2	104	132	168	317
≥ 65	322,420 (51.49)	294 ± 130	8	202	267	363	978
Ancestry-specific							
AAPI	56,338 (8.64)	51 ± 24	0	33	47	65	156
Black	65,398 (10.44)	60 ± 22	1	43	58	74	140
Hispanic	162,304 (25.92)	148 ± 71	4	92	132	188	395
Non-Hispanic White	307,247 (49.06)	280 ± 120	8	187	258	354	834
Other	30,549 (4.88)	28 ± 13	0	19	24	33	79
Sex at birth							
Female	313,305 (50.03)	286 ± 130	7	180	262	361	838
Male	312,818 (49.95)	285 ± 115	8	193	263	356	734

Table 4. Emergency Room Visits Related to Respiratory Outcomes (2017, 2018, and 2020)

			Percentile				
	Total	Mean ± SD	Min	25th	50th	75th	Max
All cause respiratory	3,526,358 (100)	3,218 ± 1,890	790	1,625	2,920	4,352	10,207
Disease specific							
Chronic Obstructive Pulmonary Disease	292,382 (8.29)	267 ± 130	68	154	246	359	763
Asthma	415,683 (11.79)	379 ± 149	116	243	410	489	870
Acute Bronchitis and Bronchiolitis	306,228 (8.68)	279 ± 223	13	86	226	432	1,305
Age-specific							
< 18	1,446,503 (41.02)	1,320 ± 953	105	398	1,224	1,932	4,001
18 - 44	1,105,378 (31.35)	1,009 ± 495	323	626	897	1,285	3,029
45 - 64	588,119 (16.68)	537 ± 296	171	312	445	701	1,934
≥ 65	386,357 (10.96)	353 ± 211	119	209	292	450	1,697
Ancestry-specific							
Asian/Pacific Islander	200,074 (5.67)	183 ± 121	29	87	154	244	689
Black	423,097 (12.00)	386 ± 198	98	211	375	522	1,024
Hispanic	1,633,766 (46.33)	1491 ± 947	303	677	1,343	2,009	4,612
Non-Hispanic White	1,036,335 (29.39)	946 ± 513	264	526	851	1,283	3,305
Other	193,131 (5.48)	176 ± 108	38	91	148	227	570
Sex at birth							
Female	1872541 (53.10)	1709 ± 1015	400	863	1525	2326	5642
Male	1653687 (46.90)	1509 ± 877	374	763	1382	2029	4564

Associations Between Wildfire Specific $PM_{2.5}$ and Respiratory Health Risk

Prior to presenting these results, it should be noted that the reported relative risks (RR) and confidence intervals (CIs) are based on a 10-unit increase in wildfire specific $PM_{2.5}$. This clarification is important as it specifies whether the effects are per fixed unit or per interquartile range, which may influence the absolute values. We found significantly positive associations in both emergency department visits (RR=1.022, 95% CI, 1.019-1.025) and hospitalizations (RR=1.021, 95% CI, 1.017, 1.025) for all respiratory related health outcomes when looking at wildfire specific $PM_{2.5}$. Similar results were found for different lag time periods, with RR ranging from 1.022 to 1.048 (Table 5).

Table 5. Risk Ratios (RRs) With 95% CIs of All Respiratory Related Emergency Department Visits and Hospitalizations Associated with $PM_{2.5}$ Exposure with Lagged Effects

Lag	Emergency Department Visits (RR, 95% CI)	Hospitalizations (RR, 95% CI)
Lag 0	1.022 (1.019-1.025)	1.021 (1.017-1.025)
Lag 1	1.025 (1.022-1.027)	1.022 (1.018-1.026)
Lag 2	1.024 (1.022-1.027)	1.024 (1.020-1.028)
Lag 3	1.026 (1.023-1.029)	1.024 (1.021-1.028)
Lag 4	1.029 (1.027-1.032)	1.025 (1.021-1.029)
Lag 5	1.031 (1.028-1.033)	1.025 (1.021-1.029)
Lag 6	1.028 (1.026-1.031)	1.025 (1.021-1.029)
Lag 7	1.028 (1.025-1.030)	1.022 (1.018-1.026)
Cumulative Lag 0-3	1.033 (1.030-1.036)	1.029 (1.024-1.033)
Cumulative Lag 0-7	1.048 (1.044-1.051)	1.038 (1.033-1.043)

$y=\beta_0+\beta_1$ (wildfire specific $PM_{2.5}$ exposure)$+\beta_2$ (day of the week)$+\beta_3$ (month)$+\beta_4$ (holiday)$+\beta_5$ (year)$+\beta_6$ (humidity)$+\beta_7$ (precipitation)$+\beta_8$ (temperature)$+\beta_9$ (wind velocity)$+\beta_{10}$ (Hispanic percentage)$+\beta_{11}$ (income group)$+\beta_{12}$ (median age)$+\beta_{13}$ (female percentage)$+\epsilon$

Y representing sum of all hospitalizations and emergency department visits related to respiratory conditions

Relative risks (RR) and confidence intervals (CIs) are based on a 10-unit increase in wildfire specific $PM_{2.5}$

Disease Specific

Looking at disease specific outcomes for emergency department visits and hospitalizations, it was found that both asthma and COPD indicated a higher risk compared to those who are not exposed to wildfire specific $PM_{2.5}$ with RR estimates ranging from 1.025 to 1.074 (Table 5). However, for acute bronchitis and bronchiolitis the results showed a negative association in terms of wildfire specific $PM_{2.5}$ exposure in both emergency department visits (RR=0.991, 95% CI, 0.984, 0.999).

Upon scrutiny of disease-specific emergency department visit and hospitalization lag effects, both asthma and COPD showed similar outcomes, featuring noteworthy positive estimates ranging between RRs of 1.025 and 1.096 (Table 5). These findings underscore a consistent association between smoke exposure and an increased risk of emergency department and hospitalization admission for asthma and COPD-related ailments. Our analysis revealed that at lag 0, chronic obstructive pulmonary disease (COPD) yielded a statistically significant negative association, with a RR of 0.991 (95% CI, 0.984, 0.999). Moreover, analysis of emergency department visits related to bronchitis and bronchiolitis revealed that solely the cumulative lag of 0 to 7 days demonstrated a positive and statistically significant association. Specifically, a cumulative lag of 7 days yielded an RR of 1.02 (95% CI, 1.01, 1.03), thereby accentuating the association of wildfire specific $PM_{2.5}$ exposure on these respiratory conditions.

Table 6. Risk Ratios (RRs) With 95% CIs of Disease Specific Emergency Department Visits and Hospitalizations Associated with $PM_{2.5}$ Exposure With Lagged Effects

Disease	Lag	Emergency Department Visits (RR, 95% CI)	Emergency Department Cases N=3,526,358	Hospitalizations (RR, 95% CI)	Hospital Cases N=626,219
Asthma	Lag 0	1.074 (1.070-1.079)	415,683	1.025 (1.011-1.039)	44,148
	Cumulative Lag 0-3	1.084 (1.079-1.089)		1.031 (1.016-1.047)	
	Cumulative Lag 0-7	1.096 (1.090-1.102)		1.029 (1.011-1.047)	
COPD	Lag 0	1.036 (1.031-1.042)	292,382	1.034 (1.025-1.043)	111,279
	Cumulative Lag 0-3	1.046 (1.039-1.05)		1.044 (1.034-1.055)	
	Cumulative Lag 0-7	1.066 (1.059-1.074)		1.060 (1.048-1.071)	
Bronchitis Bronchiolitis	Lag 0	0.991 (0.984-0.999)	306,228	0.987 (0.961-1.013)	34,586
	Cumulative Lag 0-3	1.004 (0.996-1.013)		0.991 (0.963-1.019)	
	Cumulative Lag 0-7	1.021 (1.012-1.030)		0.990 (0.959-1.021)	

$y=\beta_0 + \beta_1$ (wildfire specific $PM_{2.5}$ exposure)$+\beta_2$ (day of the week)$+\beta_3$ (month)$+\beta_4$ (holiday)$+\beta_5$ (year)$+\beta_6$ (humidity)$+\beta_7$ (precipitation)$+\beta_8$ (temperature)$+\beta_9$ (wind velocity)$+\beta_{10}$ (Hispanic percentage)$+\beta_{11}$ (income group)$+\beta_{12}$ (median age)$+\beta_{13}$ (female percentage) $+\epsilon$

Y representing sum of all hospitalizations and emergency department visits related to specific conditions (e.g. Asthma, COPD, Bronchitis and Bronchiolitis)

Relative risks (RR) and confidence intervals (CIs) are based on a 10-unit increase in wildfire specific $PM_{2.5}$

Smoke Wave

I further examined the association between exposure to wildfire specific $PM_{2.5}$ smoke waves and the incidence of respiratory health issues. The severity levels of smoke waves were evaluated based on predefined criteria established in the analysis (Table 2). Smoke waves were classified into nine distinct periods, each reflecting varying intensities of smoke exposure and durations. When examining smoke waves with consistent durations but differing intensities (e.g., smoke waves 1, 4, and 7; smoke waves 2, 5, and 8; smoke waves 3, 6, and 9) concerning both hospitalizations and emergency department visits, we observe an initial increase from SW1 (RR=1.082, 95% CI: 1.077-1.087) to SW4 (RR=1.141, 95% CI: 1.134-1.148). However, there is a subsequent decrease for SW7 (RR=1.100, 95% CI: 1.089-1.110). Similar trends are noted across the remaining smoke waves with comparable durations but differing intensities (Table 7).

Table 7. Risk Ratios (RRs) With 95% CIs of All Respiratory Related Emergency Department Visits and Hospitalizations Associated with Exposure to Smoke Waves (SW) Under Different Definitions

Smoke Wave	Emergency Department Visits (RR, 95% CI)	Hospitalizations (RR, 95% CI)
SW1	1.082 (1.077-1.087)	1.098 (1.090-1.107)
SW2	1.062 (1.056-1.067)	1.102 (1.093-1.111)
SW3	1.063 (1.057-1.069)	1.110 (1.100-1.119)
SW4	1.141 (1.134-1.148)	1.143 (1.132-1.155)

$y=\beta_0 + \beta_1$ (wildfire specific $PM_{2.5}$ exposure smoke wave)+β_2 (day of the week)+β_3 (month)+β_4 (holiday)+β_5 (year)+β_6 (humidity)+β_7 (precipitation)+β_8 (temperature)+β_9 (wind velocity)+β_{10} (Hispanic percentage)+β_{11} (income group)+β_{12} (median age)+β_1+(female percentage)+ϵ

Y representing sum of all hospitalizations and emergency department visits related to respiratory conditions

Relative risks (RR) and confidence intervals (CIs) are based on a 10-unit increase in wildfire specific $PM_{2.5}$

Table 7. Risk Ratios (RRs) With 95% CIs of All Respiratory Related Emergency Department Visits and Hospitalizations Associated with Exposure to Smoke Waves (SW) Under Different Definitions (Continued)

SW5	1.133 (1.125-1.14)	1.149 (1.135-1.163)
SW6	1.102 (1.092-1.112)	1.124 (1.108-1.141)
SW7	1.100 (1.089-1.110)	1.127 (1.111-1.143)
SW8	1.076 (1.064-1.089)	1.099 (1.080-1.118)
SW9	1.036 (1.021-1.051)	1.060 (1.038-1.082)

y=β_0 +β_1 (wildfire specific $PM_{2.5}$ exposure smoke wave)+β_2 (day of the week)+β_3 (month)+β_4 (holiday)+β_5 (year)+β_6 (humidity)+β_7 (precipitation)+β_8 (temperature)+β_9 (wind velocity)+β_{10} (Hispanic percentage)+β_{11} (income group)+β_{12} (median age)+β_1+(female percentage)+ϵ

Y representing sum of all hospitalizations and emergency department visits related to respiratory conditions

Relative risks (RR) and confidence intervals (CIs) are based on a 10-unit increase in wildfire specific $PM_{2.5}$

Subgroup Analysis

In evaluating the relationship between wildfire-specific $PM_{2.5}$ exposure and respiratory-related hospitalizations and emergency department visits, we employed the Cochran Q test to examine subgroup heterogeneity. Our results demonstrated significant heterogeneity within subgroups for both hospitalizations and emergency department visits, indicating diverse associations across subgroups.

General estimating equation models showed various associations with wildfire specific $PM_{2.5}$ exposure. In the analysis of wildfire specific $PM_{2.5}$ exposure and respiratory-related risk, similar statistically significant associations were observed for both females and males regarding daily emergency department visits and hospitalizations for respiratory conditions with RRs ranging from 1.017 to 1.027 (Table 8). When looking at age specific association, results reported younger individuals (< 18 years) exposed to wildfire specific $PM_{2.5}$ have a statistically significant negative association with daily respiratory related hospitalizations. In contrast, statistically significant positive associations with daily respiratory-related emergency department visits and hospitalizations were observed across all remaining age groups, with RR estimates ranging from 1.017 to 1.040 (Table 8). Ethnicity based subgroup analysis results revealed similar positive estimates across all ethnic groups except the other racial group, with RRs ranging from 1.016 to 1.034 (Table 8).

Table 8. Subgroup Analysis of Association Between Wildfire Specific $PM_{2.5}$ and All Respiratory Related Emergency Department Visits and Hospitalizations

Subgroup	Emergency Department Visits (RR, 95% CI)	P-value Cochran Q Test	Hospitalizations (RR, 95% CI)	P-value Cochran Q Test
Sex				
Female	1.027 (1.023-1.030)	< 0.001	1.024 (1.019-1.029)	0.078
Male	1.017 (1.014-1.021)		1.018 (1.012-1.023)	
Age Group				
< 18	1.003 (0.999-1.007)	< 0.001	0.979 (0.966-0.991)	< 0.001
18-44	1.029 (1.025-1.032)		1.017 (1.005-1.030)	
45-64	1.040 (1.036-1.044)		1.024 (1.016-1.031)	
≥ 65	1.038 (1.034-1.043)		1.025 (1.020-1.031)	
Ancestry/Ethnicity				
Non-Hispanic Asian	1.030 (1.022-1.038)	< 0.001	1.034 (1.021-1.048)	0.003
Non-Hispanic Black	1.026 (1.021-1.031)		1.030 (1.019-1.042)	
Hispanic	1.016 (1.012-1.020)		1.016 (1.007-1.025)	
Non-Hispanic White	1.028 (1.024-1.031)		1.023 (1.018-1.028)	
Other	0.995 (0.987-1.003)		0.995 (0.978-1.013)	

$y=\beta_0+\beta_1$ (wildfire specific $PM_{2.5}$ exposure)$+\beta_2$ (day of the week)$+\beta_3$ (month)$+\beta_4$ (holiday)$+\beta_5$ (year)$+\beta_6$ (humidity)$+\beta_7$ (precipitation)$+\beta_8$ (temperature)$+\beta_9$ (wind velocity)$+\beta_{10}$ (Hispanic percentage)$+\beta_{11}$ (income group)$+\beta_{12}$ (median age)$+\beta_{13}$ (female percentage)$+\epsilon$

Y representing sum of all hospitalizations and emergency department visits related to respiratory conditions in each respective subgroup (e.g. sex at birth, age group, ancestry/ethnicity)

Relative risks (RR) and confidence intervals (CIs) are based on a 10-unit increase in wildfire specific $PM_{2.5}$

Table 9. Age Specific Subgroup Analysis of Association Between Wildfire Specific $PM_{2.5}$ and Disease Specific Outcomes in Emergency Department Visits and Hospitalizations

Disease by Age Group	Emergency Department Visits (RR, 95% CI) N=3,526,358	P-value Cochran Q Test	Hospitalizations (RR, 95% CI) N=626,219	P-value Cochran Q Test
Asthma	(N=415, 683)		(N=44,148)	
< 18	1.042 (1.035-1.050)	< 0.001	0.985 (0.961-1.010)	< 0.001
18-44	1.084 (1.078-1.090)		1.033 (1.004-1.062)	
45-64	1.095 (1.087-1.103)		1.072 (1.046-1.099)	
≥ 65	1.090 (1.077-1.103)		1.055 (1.024-1.087)	
COPD	(N=292,382)		(N=111,279)	
>18	1.004 (0.974-1.034)	< 0.001	MODEL DID NOT CONVERGE	0.106
18-44	1.007 (0.993-1.021)		1.007 (0.946-1.072)	
45-64	1.040 (1.031-1.049)		1.032 (1.016-1.048)	
≥ 65	1.041 (1.034-1.049)		1.034 (1.024-1.045)	
Bronchitis Bronchiolitis	(N=306,228)		(N=34,586)	
>18	0.972 (0.960-0.983)	< 0.001	0.998 (0.970-1.028)	< 0.001
18-44	0.998 (0.984-1.011)		1.028 (0.934-1.133)	
45-64	1.010 (0.994-1.025)		0.959 (0.879-1.046)	
≥ 65	1.009 (0.991-1.028)		0.981 (0.933-1.030)	

$y=\beta_0+\beta_1$ (wildfire specific $PM_{2.5}$ exposure)$+\beta_2$ (day of the week)$+\beta_3$ (month)$+\beta_4$ (holiday)$+\beta_5$ (year)$+\beta_6$ (humidity)$+\beta_7$ (precipitation)$+\beta_8$ (temperature)$+\beta_9$ (wind velocity)$+\beta_{10}$ (Hispanic percentage)$+\beta_{11}$ (income group)$+\beta_{12}$ (median age)$+\beta_{13}$ (female percentage)$+\epsilon$

Y representing sum of all hospitalizations and emergency department visits related to specific conditions (e.g. Asthma, COPD, Bronchitis and Bronchiolitis in each respective age group)

Relative risks (RR) and confidence intervals (CIs) are based on a 10-unit increase in wildfire specific $PM_{2.5}$

CHAPTER 4. DISCUSSION

Main Results

The analysis revealed that individuals exposed to wildfire specific $PM_{2.5}$ exhibited a heightened risk for respiratory-related health outcomes. These results are consistent with multiple published studies (Aguilera et al., 2021a; Aguilera et al., 2021b; Alman et al., 2016; Kiser et al., 2020; Ye et al., 2021; Casey et al., 2021; Hahn et al., 2021; Mahsin et al., 2022; Hutchinson et al., 2018; Tinling et al., 2016; Wettstein et al., 2018; Doubleday et al., 2023; Stowell et al., 2019). Several factors likely contribute to this consistency. Firstly, the well-established physiological mechanisms explaining the detrimental health impacts of $PM_{2.5}$ exposure are likely uniform across populations. Additionally, our methodological approach, including the use of generalized estimating equations (GEE) to control for confounding variables and repeated measures, aligns with approaches employed in prior research, fostering comparability. Overall, the congruence between our study outcomes and existing literature highlights the robust association between wildfire specific $PM_{2.5}$ exposure and respiratory health risks.

Disease Specific

The analysis of disease-specific outcomes related to emergency department visits and hospitalizations revealed associations between wildfire specific $PM_{2.5}$ exposure and respiratory health risks. Specifically, individuals exposed to wildfire specific $PM_{2.5}$ exhibited heightened risks for asthma and COPD. These findings align with existing literature documenting the adverse respiratory effects of $PM_{2.5}$ exposure (Arriagada et al., 2019;

Heaney et al., 2022; Henderson et al., 2011; Hutchinson et al., 2018; Wettstein et al., 2019; Gan et al., 2017). However, a negative association was observed for acute bronchitis and bronchiolitis in both emergency department visits. This differs from previous studies that have found increased risk for bronchitis from exposure to $PM_{2.5}$ during wildfire period (Gan et al., 2017; Magzamen et al., 2021; Stowell et al., 2019). This unexpected finding warrants further investigation to elucidate potential mechanisms underlying the observed inverse association and to determine whether it reflects true biological phenomena or methodological artifacts. Possible explanations may include individuals delaying seeking medical assistance until symptoms significantly worsen, or they may not seek hospital care at all due to the availability of home treatments for bronchitis. In addition, cumulative lag of 0 to 7 days was found to have a positive association. This could be due to the nature of bronchitis progression taking a longer period to develop due to continuous exposure to respiratory irritants. Further research incorporating longitudinal data and detailed exposure assessment methods could provide valuable insights into the complex relationships between wildfire specific $PM_{2.5}$ exposure and specific respiratory outcomes.

Smoke wave

Upon examination of the results and considering smoke waves with differing durations but consistent intensity levels (e.g., smoke waves 1-3, 4-6, and 7-9), a notable trend emerges revealing a decline in estimates as the duration extends. This observation contrasts with the anticipated outcome, as an increase in estimate was expected with prolonged duration under similar intensity conditions. We posit that this discrepancy may stem from alterations in personal behavior influenced by individuals' risk perceptions. For instance, heightened intensity and prolonged duration of smoke waves may prompt individuals to adopt precautionary measures such as wearing masks or remaining indoors, thereby potentially mitigating the anticipated increase in respiratory health risks.

Following the discussion of the relationship between smoke waves and respiratory health outcomes, it is pertinent to acknowledge the insights provided by another study, which emphasized an augmented risk of respiratory issues associated with the occurrence of smoke waves (Liu et al., 2017a). Furthermore, this study and another study documented a discernible escalation in hospital admissions for respiratory ailments corresponding to the intensification of smoke wave days (Liu et al., 2017a; Liu et al., 2017b). For instance, during days characterized by exceedingly high levels of smoke (exceeding 37μg/m3), a notable 7.2% increase in respiratory admissions was observed in comparison to non-smoke wave days. This highlights the pronounced impact of heightened intensity in smoke wave days on respiratory health within the studied populations.

A smoke wave is typically defined as a consecutive period of days with elevated levels of particulate matter, often associated with wildfire smoke. In contrast, a smoke wave day refers to an individual day within a smoke wave period characterized by heightened $PM_{2.5}$ concentrations. The distinction between these terms is crucial as it allows for a more delicate examination of the temporal dynamics and intensity levels of wildfire smoke exposure. By scrutinizing individual smoke wave days alongside broader smoke wave occurrences, researchers can gain deeper insights into the differential impacts of varying exposure durations and intensities on respiratory health outcomes. This approach may facilitate more targeted mitigation strategies and interventions to mitigate the adverse effects of wildfire smoke on public health.

Lag Effects

The lagged effect was observed for all respiratory-related health conditions, aligning with findings in other studies of air pollution (Gan et al., 2017; Magzamen et al., 2021; Wettstein et al., 2018). Estimates were similar across all lag days including cumulative lag, which differs from previous studies that have suggested that lags for ambient $PM_{2.5}$ exposure (not necessarily wildfire specific PM) tend to 0-4 days in terms of respiratory health risk (Morgan et al., 2010; Aguilera et al., 2021b; Hahn et al., 2021). The similar lagged effects observed in Table 5 may be due to the stable levels of wildfire-specific $PM_{2.5}$ over time. Consistent $PM_{2.5}$ concentrations could explain the minimal variation in risk ratios across different lag days. Testing extreme cases with long lags, such as 15 or 30 days, could serve as a negative control to clarify these patterns. Further exploration of $PM_{2.5}$ variability over time might provide additional insights into the observed lack of distinct lag effects. Wildfire smoke, containing a complex mixture of particulate matter and chemical compounds, can persist in the atmosphere for extended periods, potentially resulting in prolonged and sustained exposure compared to ambient $PM_{2.5}$. Consequently, estimates remained similar across all lag days, including cumulative lag, in our analysis, suggesting a distinct temporal relationship between wildfire specific $PM_{2.5}$ exposure and respiratory health outcomes.

Disease specific lagged results varied by the type of ailment under investigation. For bronchitis, there was no discernible difference in risk for emergency department visits associated with the cumulative lag spanning days 0 to 3; however, a positive association was found for the cumulative lag covering days 0 through 7. The lack of discernible difference in risk for emergency department visits associated with the cumulative lag spanning days 0 to 3 may suggest that the short-term impact of $PM_{2.5}$ exposure on bronchitis development is not immediately evident. Additionally, the positive association shown for the cumulative lag covering days 0 through 7 implies that the respiratory effects of prolonged exposure to elevated $PM_{2.5}$ levels may become more pronounced over time, leading to an increased likelihood of emergency department visits for bronchitis-related symptoms.

Population Vulnerabilities and Disparities

The sex-specific subgroup analysis revealed that women faced a 0.979% higher risk of respiratory health outcomes compared to men in both emergency admissions when exposed to wildfire-specific $PM_{2.5}$, aligning with findings from previous studies (Gan et al., 2020; Hahn et al., 2021; Liu et al., 2017b; Tinling et al., 2016). Additionally, age-specific subgroup analysis indicated that older individuals (e.g., 45-64 years and ≥ 65 years) exhibited the highest risk in both emergency department visits and hospitalizations, consistent with prior research (Heaney et al., 2022; Morgan et al., 2010; Wettstein et al., 2018; Arriagada et al., 2019; Le et al., 2014; Liu et al., 2017b; Gan et al., 2020; Hahn et al., 2021; Henderson et al., 2011; Stowell et al., 2019). However, existing literature offers inconclusive evidence regarding vulnerable subpopulations in terms of all-cause respiratory hospital visits/admissions across various age groups.

Several studies have identified elevated risks among children aged under 19 years (Gan et al., 2017; Tinling et al., 2016; Hutchinson et al., 2018; Holm et al., 2021; Mahsin et al., 2022). Additionally, a nationwide study in Brazil reported higher attributable fractions of respiratory-specific hospitalizations associated with wildfire-specific $PM_{2.5}$ among children aged 0–9 years (Ye et al., 2021a). These findings diverge from our own, which demonstrated that older individuals had the highest risk. However, it is important to note that existing literature also acknowledges variability in the identified vulnerable age groups. While these results provide insights into age-specific vulnerability to respiratory health outcomes, further research is warranted to elucidate the nuanced associations across different age groups.

Furthermore, older age groups, particularly those aged 45-64 years and 65 years and above, exhibited a slightly elevated risk in asthma-related emergency department visits and hospitalizations. Consistent with this, one study reported a significant 10.1% increase in asthma risk per 10 μg/m3 increment of $PM_{2.5}$ among individuals aged 65-99 years (Delfino et al., 2009). However, some studies indicated a higher susceptibility to asthma among younger populations (Heaney et al., 2022; Stowell et al., 2019). It is important to note that these studies focused on age groups younger than 5 years or employed a more detailed age breakdown, while our study considered individuals aged 18 years and younger as the youngest cohort (Aguilera et al., 2022; Li et al., 2023; Lipner et al., 2019). This highlights the potential value of further disaggregating age groups and investigating younger cohorts to gain insights into age-specific asthma risks associated with wildfire-specific $PM_{2.5}$ exposure.

Based on the results of the Cochran Q test, there is significant heterogeneity among the five racial groups; however, we cannot confidently conclude that any one group has a higher risk than the others. Previous investigations primarily focused on Black, White, and Indigenous populations, with limited exploration of Hispanic or Asian populations (Hahn et al., 2021; Liu et al., 2019; Liu et al., 2017b; Batdorf and McGee, 2023; Casey et al., 2008).

However, it is noteworthy that geographic location may contribute to differences in the ethnic groups included in the analysis. Among the studies that included Black individuals in their subgroup analysis, results varied, with one study showing no association (Lipner et al., 2019) and another showing a positive association between Black populations and a greater risk compared to White individuals (Liu et al., 2017b). Therefore, further research is warranted to investigate the impact of wildfire specific $PM_{2.5}$ on respiratory health risks and its variability among different ethnic groups.

Strengths and Limitations

This study has several strengths. Firstly, its comprehensive coverage of the entire State of California provides a robust foundation for analysis, considering the state's pronounced vulnerability to wildfire effects (Fann et al., 2018; Ford et al., 2018; Jaffe et al., 2020). California's diverse geographical landscape, encompassing various wildfire intensities and frequencies, offers a rich tapestry of exposure variability essential for thorough dose-response assessments. Secondly, the state's heterogeneous population composition enables the exploration of demographic disparities in susceptibility to wildfire smoke, including racial and socioeconomic factors. Moreover, the availability of extensive health and wildfire specific $PM_{2.5}$ data bolsters the reliability and validity of the study's findings. Additionally, the recent surge in severe wildfire occurrences has led to heightened levels of wildfire specific PM and increased population exposure, potentially enhancing the study's statistical power for detecting wildfire effects. As wildfire events escalate, the heightened concentrations of wildfire PM and broader population exposure bolster the study's statistical power, facilitating more precise detection and analysis of wildfire impacts on respiratory health.

This study presents several notable limitations. Primarily, it focuses on investigating the association between wildfire specific $PM_{2.5}$ exposure and respiratory health outcomes, omitting consideration of other pollutants such as PM_{10}, NO_2, and O_3 from the analysis. This exclusion is due to the lack of comprehensive exposure data for these pollutants, hindering their integration into the study's analytical framework. While $PM_{2.5}$ serves as a significant surrogate for other pollutants emitted during wildfires, the exclusion of these pollutants may limit the comprehensiveness of health impact assessments. Relying solely on $PM_{2.5}$ may underestimate the true scope of health effects associated with wildfire emissions. Moreover, the potential for interactions among various pollutants, including synergistic effects, necessitates further investigation. Future research efforts should strive to address these limitations by incorporating a broader range of pollutants and exploring potential interactions, thereby enhancing understanding of the health implications linked to wildfire exposures.

Further limitations necessitate consideration, notably the omission of analyses regarding indigenous populations and socioeconomic status. Presently, the dataset lacks granularity in distinguishing indigenous populations, grouping them under broader classifications, potentially masking any distinctive vulnerabilities they may harbor. Additionally, while income serves as a covariate to address socioeconomic status, this study does not explore divergent impacts among specific income groups due to the dataset's neighborhood-level nature rather than individual-level granularity. Previous research underscores the potential vulnerability of these groups to the health effects of wildfire specific $PM_{2.5}$ exposure, underscoring the need for further exploration of maternal, indigenous, and socioeconomic factors (Chen et al., 2021a; Rappold et al., 2012; Batdorf & McGee, 2023; Hanigan et al., 2008; Hahn et al., 2021). Such investigations may unveil health outcome disparities and guide targeted interventions to mitigate risks within these populations.

Future Directions

Expanding the analysis to encompass additional respiratory related conditions such as pneumonia, influenza, and upper respiratory infections would provide a more comprehensive understanding of the health effects associated with wildfire specific $PM_{2.5}$ exposure. This broader investigation into respiratory conditions could offer refined insights into the intricate relationship between wildfire events and health outcomes. Moreover, conducting subgroup analysis on age groups with a more refined breakdown to assess age-specific variation would allow for a deeper exploration of the effects across different age demographics. Additionally, incorporating individual smoke days alongside smoke waves in the analysis could bolster these findings. By examining both short-term and prolonged smoke exposure events, a more refined understanding of the acute and cumulative impacts of wildfire smoke on respiratory health can be attained. This dual approach would facilitate a more thorough comprehension of the temporal patterns of health effects associated with wildfires, thereby enhancing the accuracy and precision of this research.

Conclusion

In conclusion, this study suggests that both continuous exposure and smoke wave-based exposure to wildfire specific $PM_{2.5}$ may impact respiratory health risk. These findings are predominantly consistent with existing literature. Future research should continue investigating the link between respiratory health outcomes and wildfire specific $PM_{2.5}$ exposure to deepen the understanding of these relationships.

REFERENCES

Aguilera, R., Corringham, T., Gershunov, A., Benmarhnia, T., (2021a). Wildfire smoke impacts respiratory health more than fine particles from other sources: observational evidence from Southern California. Nat. Commun. 12, 1493.

Aguilera, R., Corringham, T., Gershunov, A., Leibel, S., Benmarhnia, T., (2021b). Fine particles in wildfire smoke and pediatric respiratory health in California. Pediatrics 147.

Airly - Air Quality Monitor in UK & Europe, (2012). How is $PM_{2.5}$ measured?. How is $PM_{2.5}$ measured? - Explained - Airly WP | Air Quality Monitoring. Airly Data Platform and Monitors.

Alman, B. L., Pfister, G., Hao, H., Stowell, J., Hu, X., Liu, Y., & Strickland, M. J., (2016). The association of wildfire smoke with respiratory and cardiovascular emergency department visits in Colorado in 2012: a case crossover study. Environ Health 15, 64.

Areal, A.T., Zhao, Q., Wigmann, C., Schneider, A., Schikowski, T., (2022). The effect of air pollution when modified by temperature on respiratory health outcomes: a systematic review and meta-analysis. Sci. Total Environ. 811, 152336.

Arriagada, N.B., Horsley, J.A., Palmer, A.J., Morgan, G.G., Tham, R., Johnston, F.H., (2019). Association between fire smoke fine particulate matter and asthma-related outcomes: systematic review and meta-analysis. Environ. Res. 179.

Batdorf B, McGee TK., (2023). "Wildfire Smoke and Protective Actions in Canadian Indigenous Communities" Atmosphere 14, no. 8: 1204.

Bobb, J. F., Obermeyer, Z., Wang, Y., & Dominici, F., (2014). Cause-specific risk of hospital admission related to extreme heat in older adults. JAMA, 312(24), 2659–2667.

Bhaskaran, K., Gasparrini, A., Hajat, S., Smeeth, L., & Armstrong, B., (2013). Time series regression studies in environmental epidemiology. International journal of epidemiology, 42(4), 1187–1195.

Burke, M., Driscoll, A., Heft-Neal, S., Xue, J., Burney, J., Wara, M., (2021). The changing risk and burden of wildfire in the United States. Proc. Natl. Acad. Sci. U. S. A. 118.

Burrows , L., (2016). "Smoke Waves" Will Affect Millions In Coming Decades. Researchers identify western US counties with the highest risk of exposure to pollution from wildfires. News.

Cascio, W.E., (2018). Wildland fire smoke and human health. Sci. Total Environ. 624, 586–59.

Casey, J.A., Kioumourtzoglou, M.A., Elser, H., Walker, D., Taylor, S., Adams, S., Aguilera, R., Benmarhnia, T., Catalano, R., (2021). Wildfire particulate matter in Shasta County, California and respiratory and circulatory disease-related emergency department visits and mortality, 2013–2018. Environ. Epidemiol. 5, e124.

Chen, H., Samet, J.M., Bromberg, P.A., Tong, H., (2021a). Cardiovascular health impacts of wildfire smoke exposure. Part Fibre Toxicol 18, 2.

Chen, G., Guo, Y., Yue, X., Tong, S., Gasparrini, A., Bell, M.L., Armstrong, B., Schwartz, J., Jaakkola, J.J.K., Zanobetti, A., Lavigne, E., Nascimento Saldiva, P.H., Kan, H., Roye, D., Milojevic, A., Overcenco, A., Urban, A., Schneider, A., Entezari, A., Vicedo-Cabrera, A.M., Zeka, A., Tobias, A., Nunes, B., Alahmad, B., Forsberg, B., Pan, S.C., Iniguez, C., Ameling, C., De la Cruz Valencia, C., Astrom, C., Houthuijs, D., Van Dung, D., Samoli, E., Mayvaneh, F., Sera, F., Carrasco-Escobar, G., Lei, Y., Orru, H., Kim, H., Holobaca, I.H., Kysely, J., Teixeira, J.P., Madureira, J., Katsouyanni, K., Hurtado-Diaz, M., Maasikmets, M., Ragettli, M.S., Hashizume, M., Stafoggia, M., Pascal, M., Scortichini, M., de Sousa Zanotti Stagliorio Coelho, M., Valdes Ortega, N., Ryti, N.R.I., Scovronick, N., Matus, P., Goodman, P., Garland, R. M., Abrutzky, R., Garcia, S.O., Rao, S., Fratianni, S., Dang, T.N., Colistro, V., Huber, V., Lee, W., Seposo, X., Honda, Y., Guo, Y.L., Ye, T., Yu, W., Abramson, M.J., Samet, J.M., Li, S., (2021b). Mortality risk attributable to wildfire-related PM(2.5) pollution: a global time series study in 749 locations. Lancet Planet. Health 5, e579–e587.

Chen, L., Verrall, K., Tong, S., (2006). Air particulate pollution due to bushfires and respiratory hospital admissions in Brisbane, Australia. Int. J. Environ. Health Res. 16, 181–191.

Ciciretti, R., Barraza, F., De la Barrera, F., Urquieta, L., Cortes, S., (2022). Relationship between Wildfire Smoke and Children's Respiratory Health in the Metropolitan Cities of Central-Chile. Atmosphere. 13, 58.

Cobelo, I., Castelhano, F.J., Borge, R., Roig, H.L., Adams, M., Amini, H., Koutrakis, P., Requia, W.J., (2023). The impact of wildfires on air pollution and health across land use categories in Brazil over a 16-year period. Environ. Res. 224, 115522.

Congressional Research Service, (2023). Wildfire Statistics.

de Oliveira Alves, N., de Souza Hacon, S., de Oliveira Galvao, M.F., Simoes Peixotoc, M., Artaxo, P., de Castro Vasconcellos, P., de Medeiros, S.R., (2014). Genetic damage of organic matter in the Brazilian Amazon: a comparative study between intense and moderate biomass burning. Environ. Res. 130, 51–58.

Delfino, R. J., Brummel, S., Wu, J., Stern, H., Ostro, B., Lipsett, M., Winer, A., Street, D. H., Zhang, L., Tjoa, T., & Gillen, D. L., (2009). The relationship of respiratory and cardiovascular hospital admissions to the southern California wildfires of 2003. Occupational and Environmental Medicine 66, 189-197.

Diaz, J., Ortiz, C., Falcon, J., Salvador, C., Linares, C., (2018). Short-term effect of tropospheric ozone on daily mortality in Spain. Atmospheric Environment 187, 107-116.

Dominici F., Peng, R.D., Bell, M.L., Pham, L., McDermott, A., Zeger, S.L., Samet, J.M., (2006). Fine particulate air pollution and hospital admission for cardiovascular and respiratory diseases. JAMA. 295:1127–1134.

Dong, T.T.T., Hinwood, A.L., Callan, A.C., Zosky, G., Stock, W.D., (2017). In vitro assessment of the toxicity of bushfire emissions: a review. Sci. Total Environ. 603- 604, 268–278.

Doubleday, A., Schulte, J., Sheppard, L., Kadlec, M., Dhammapala, R., Fox, J., Busch Isaksen, T., (2020). Mortality associated with wildfire smoke exposure in Washington state, 2006–2017: a case-crossover study. Environ. Health 19, 4.

Doubleday, A., Sheppard, L., Austin, E., Busch Isaksen, T., (2023). Wildfire smoke exposure and emergency department visits in Washington State. Environ. Res. Health 1, 025006.

Fann, N., Alman, B., Broome, R.A., Morgan, G.G., Johnston, F.H., Pouliot, G., Rappold, A. G., (2018). The health impacts and economic value of wildland fire episodes in the U. S.: 2008–2012. Sci. Total Environ. 610–611, 802–809.

Faustini, A., Alessandrini, E.R., Pey, J., Perez, N., Samoli, E., Querol, X., Cadum, E., Perrino, C., Ostro, B., Ranzi, A., Sunyer, J., Stafoggia, M., Forastiere, F., group, M.-P. s., (2015). Short-term effects of particulate matter on mortality during forest fires in Southern

Europe: results of the MED-PARTICLES Project. Occup. Environ. Med. 72, 323–329.

Ford, B.,Val Martin, M., Zelasky, S., Fischer, E., Anenberg, S., Heald, C., Pierce, J., (2018). Future fire impacts on smoke concentrations, visibility, and health in the contiguous United States. GeoHealth **2**, 229–247.

Franzi, L.M., Bratt, J.M., Williams, K.M., Last, J.A., (2011). Why is particulate matter produced by wildfires toxic to lung macrophages? Toxicol. Appl. Pharmacol. 257, 182–188.

Gan, R.W., Ford, B., Lassman, W., Pfister, G., Vaidyanathan, A., Fischer, E., Volckens, J., Pierce, J.R., Magzamen, S., (2017). Comparison of wildfire smoke estimation methods and associations with cardiopulmonary-related hospital admissions. GeoHealth 1, 122–136.

Gan, R.W., Liu, J., Ford, B., O'Dell, K., Vaidyanathan, A., Wilson, A., Volckens, J., Pfister, G., Fischer, E.V., Pierce, J.R., Magzamen, S., (2020). The association between wildfire smoke exposure and asthma-specific medical care utilization in Oregon during the 2013 wildfire season. J. Expo. Sci. Environ. Epidemiol. 30, 618–628.

Gao, Y., Huang, W., Yu, P., Xu, R., Yang, Z., Gasevic, D., Ye, T., Guo, Y., Li, S., (2023). Long-term impacts of non-occupational wildfire exposure on human health: a systematic review. Environ. Pollut. 320, 121041.

Gasparrini, A., Guo, Y., Hashizume, M., Kinney, P. L., Petkova, E. P., Lavigne, E., Zanobetti, A., Schwartz, J. D., Tobias, A., Leone, M., Tong, S., Honda, Y., Kim, H., & Armstrong, B. G., (2015). Temporal Variation in Heat-Mortality Associations: A Multicountry Study. Environmental health perspectives, 123(11), 1200–1207.

Guo, Y., Gasparrini, A., Armstrong, B. G., Tawatsupa, B., Tobias, A., Lavigne, E., Coelho, M. S. Z. S., Pan, X., Kim, H., Hashizume, M., Honda, Y., Guo, Y. L., Wu, C. F., Zanobetti, A., Schwartz, J. D., Bell, M. L., Scortichini, M., Michelozzi, P., Punnasiri, K., Li, S., … Tong, S., (2017). Heat Wave and Mortality: A Multicountry, Multicommunity Study. Environmental health perspectives, 125(8), 087006.

Hahn, M.B., Kuiper, G., O'Dell, K., Fischer, E.V., Magzamen, S., (2021). Wildfire smoke is associated with an increased risk of cardiorespiratory emergency department visits in Alaska. Geohealth 5, e2020GH000349.

Hanley, M.E., Patel, P.H., (2023). Carbon Monoxide Toxicity. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing.

Hanigan, I.C., Johnston, F.H., Morgan, G.G., (2008). Vegetation fire smoke, indigenous status and cardio-respiratory hospital admissions in Darwin, Australia, 1996–2005: a time-series study. Environ. Health 7.

Heaney, A., Stowell, J. D., Liu, J. C., Basu, R., Marlier, M., & Kinney, P., (2022). Impacts of fine particulate matter from wildfire. AGU Advancing Earth and Space Sciences.

Henderson, S.B., Brauer, M., Macnab, Y.C., Kennedy, S.M., (2011). Three measures of forest fire smoke exposure and their associations with respiratory and cardiovascular health outcomes in a population-based cohort. Environ. Health Perspect. 119, 1266–1271.

Holm, S.M., Miller, M.D., Balmes, J.R., (2021). Health effects of wildfire smoke in children and public health tools: a narrative review. J. Expo. Sci. Environ. Epidemiol. 31, 1–20.

Huangfu, P., & Atkinson, R. (2020). Long-term exposure to no2 and O3 and all-cause and respiratory mortality: A systematic review and meta-analysis. Environment International.

Hutchinson, J.A., Vargo, J., Milet, M., French, N.H.F., Billmire, M., Johnson, J., Hoshiko, S., (2018). The San Diego 2007 wildfires and Medi-Cal emergency department presentations, inpatient hospitalizations, and outpatient visits: an observational study of smoke exposure periods and a bidirectional case-crossover analysis. PLoS Med. 15, e1002601.

Interagency Working Group on Climate Change and Health (U.S.), (2010). A Human health perspective on climate change; a report outlining the research needs on the human health effects of climate change.

Jaffe, D.A., O'Neill, S.M., Larkin, N.K., Holder, A.L., Peterson, D.L., Halofsky, J.E., Rappold, A.G., (2020). Wildfire and prescribed burning impacts on air quality in the United States. J. Air Waste Manage. Assoc. 70, 583–615.

Jang, J. H., Jang, H. J., Kim, H. K., Park, J. H., Kim, H. J., Jo, K. M., Heo, W., Kim, S. H., No, T. H., & Lee, J. H., (2021). Acute respiratory distress syndrome caused by carbon monoxide poisoning and inhalation injury recovered after extracorporeal membrane oxygenation along with direct hemoperfusion with polymyxin B-immobilized fiber column: a case report. Journal of medical case reports, 15(1), 456.

Jiao, A., Headon, K., Han, T., Umer, W., & Wu, J. (2024). Associations between short-term exposure to wildfire particulate matter and respiratory outcomes: A systematic review. Science of The Total Environment, 907, 168134.

Kazemiparkouhi, F., Eum, KD., Wang, B., Manjourides, J., Suh, H.H., (2020). Long-term ozone exposures and cause-specific mortality in a US Medicare cohort. J Expo Sci Environ Epidemiol 30, 650–658.

Kim, S. Y., Peel, J. L., Hannigan, M. P., Dutton, S. J., Sheppard, L., Clark, M. L., & Vedal, S., (2012). The temporal lag structure of short-term associations of fine particulate matter chemical constituents and cardiovascular and respiratory hospitalizations. Environmental health perspectives, 120(8), 1094–1099.

Kiser, D., Metcalf, W.J., Elhanan, G., Schnieder, B., Schlauch, K., Joros, A., Petersen, C., Grzymski, J., (2020). Particulate matter and emergency visits for asthma: a time-series study of their association in the presence and absence of wildfire smoke in Reno, Nevada, 2013–2018. Environ. Health 19, 92.

Kondo, M.C., De Roos, A.J., White, L.S., Heilman, W.E., Mockrin, M.H., Gross-Davis, C.A., Burstyn, I., (2019). Meta-Analysis of Heterogeneity in the Effects of Wildfire Smoke Exposure on Respiratory Health in North America. Int. J. Environ. Res. Public Health. 16, 960.

Le, G.E., Breysse, P.N., McDermott, A., Eftim, S.E., Geyh, A., Berman, J.D., Curriero, F.C., (2014). Canadian forest fires and the effects of long-range transboundary air pollution on hospitalizations among the elderly. ISPRS Int. J. Geoinf. 3, 713–731.

Li, J., Cai, Y.S., Kelly, F.J., Wooster, M.J., Han, Y., Zheng, Y., Guan, T., Li, P., Zhu, T., Xue, T., (2023). Landscape fire smoke enhances the association between fine particulate matter exposure and acute respiratory infection among children under 5 years of age: findings of a case-crossover study for 48 low- and middle-income countries. Environ. Int. 171, 107665.

Lin, E., (2023). Canadian wildfire smoke associated with increased asthma cases in NYC. Yale School of Public Health. https://ysph.yale.edu/news-article/canadian-wildfire-smoke-associated-with-increased-asthma-cases-in-nyc/

Lippmann, M., Ito, K., Nádas, A., Burnett R.T., (2000). Association of particulate matter components with daily mortality and morbidity in urban populations. Research

Report (Health Effects Institute). (95):5-72, discussion 73-82.

Lipner, E.M., O'Dell, K., Brey, S.J., Ford, B., Pierce, J.R., Fischer, E.V., Crooks, J.L., (2019). The associations between clinical respiratory outcomes and ambient wildfire smoke exposure among pediatric asthma patients at National Jewish Health, 2012–2015. Geohealth 3, 146–159.

Liu, J.C., Peng, R.D., (2019). The impact of wildfire smoke on compositions of fine particulate matter by ecoregion in the Western US. J. Expo. Sci. Environ. Epidemiol. 29, 765–776.

Liu, J.C., Mickley, L.J., Sulprizio, M.P., Yue, X., Peng, R.D., Dominici, F., Bell, M.L., (2016). Future respiratory hospital admissions from wildfire smoke under climate change in the Western US. Environ. Res. Lett. 11, 124018.

Liu, J. C., Pereira, G., Uhl, S. A., Bravo, M. A. & Bell, M. L., (2015). A systematic review of the physical health impacts from non-occupational exposure to wildfire smoke. Environ. Res. 136, 120–132.

Liu, J.C., Wilson, A., Mickley, L.J., Dominici, F., Ebisu, K., Wang, Y., Sulprizio, M.P., Peng, R.D., Yue, X., Son, J.Y., Anderson, G.B., Bell, M.L., (2017a). Wildfire-specific fine particulate matter and risk of hospital admissions in URBAN and rural counties. Epidemiology 28, 77–85.

Liu, J.C., Wilson, A., Mickley, L.J., Ebisu, K., Sulprizio, M.P., Wang, Y., Peng, R.D., Yue, X., Dominici, F., Bell, M.L., (2017b). Who among the elderly is most vulnerable to exposure to and health risks of fine particulate matter from wildfire smoke? Am. J. Epidemiol. 186, 730–735.

Magzamen, S., Gan, R.W., Liu, J., O'Dell, K., Ford, B., Berg, K., Bol, K., Wilson, A., Fischer, E.V., Pierce, J.R., (2021). Differential cardiopulmonary health impacts of local and long-range transport of wildfire smoke. Geohealth 5, e2020GH000330.

Mahsin, M.D., Cabaj, J., Saini, V., (2022). Respiratory and cardiovascular condition-related physician visits associated with wildfire smoke exposure in Calgary, Canada, in 2015: a population-based study, International Journal of Epidemiology. Volume 51, Issue 1, Pages 166–178.

Malig, B. J., Pearson, D. L., Chang, Y. B., Broadwin, R., Basu, R., Green, R. S., & Ostro, B., (2015). A Time-Stratified Case-Crossover Study of Ambient Ozone Exposure and Emergency Department Visits for Specific Respiratory Diagnoses in California (2005–2008). Environmental Health Perspectives. Volume 124, Issue 6, Pages 745-753.

McClure, C. D. & Jaffe, D. A., (2018). US particulate matter air quality improves except in wildfire-prone areas. Proc. Natl Acad. Sci. USA 115, 7901–7906.

Morgan, G., Sheppeard, V., Khalaj, B., Ayyar, A., Lincoln, D., Jalaludin, B., Beard, J., Corbett, S., & Lumley, T., (2010). Effects of bushfire smoke on daily mortality and hospital admissions in Sydney, Australia. Epidemiology (Cambridge, Mass.), 21(1), 47–55.

Nuvolone, D., Petri, D. & Voller, F., (2018). The effects of ozone on human health. Environ. Sci. Pollut. Res. 25, 8074–8088.

Pavagadhi, S., Betha, R., Venkatesan, S., Balasubramanian, R., Hande, M.P., (2013). Physicochemical and toxicological characteristics of urban aerosols during a recent Indonesian biomass burning episode. Environ. Sci. Pollut. Res. Int. 20, 2569–2578.

Peel, J. L., Tolbert, P. E., Klein, M., Metzger, K. B., Flanders, W. D., Todd, K., Mulholland, J. A., Ryan, P. B., & Frumkin, H. (2005). Ambient air pollution and respiratory emergency department visits. *Epidemiology (Cambridge, Mass.)*, *16*(2), 164–174.

Pothirat, C., Chaiwong, W., Liwsrisakun, C., Bumroongkit, C., Deesomchok, A., Theerakittikul, T., Limsukon, A., Tajarernmuang, P., & Phetsuk, N., (2019). Acute effects of air pollutants on daily mortality and hospitalizations due to cardiovascular and respiratory diseases. Journal of thoracic disease, 11(7), 3070–3083.

Rappold, A. G., Cascio, W. E., Kilaru, V. J., Stone, S. L., Neas, L. M., Devlin, R. B., & Diaz-Sanchez, D., (2012). Cardio-respiratory outcomes associated with exposure to wildfire smoke are modified by measures of community health. Environ Health 11, 71.

Reid, C. E., Jerrett, M., Tager, I. B., Petersen, M. L., Mann, J. K., & Balmes, J. R., (2016). Differential respiratory health effects from the 2008 northern California wildfires: A spatiotemporal approach. Environmental research, 150, 227–235.

Reid, C. E., Considine, E. M., Watson, G. L., Telesca, D., Pfister, G. G., & Jerrett, M., (2019). Associations between respiratory health and ozone and fine particulate matter during a wildfire event. Environment international, 129, 291–298.

Ruminski, M., Kondragunta, S., Draxler, R., Zeng, J., (2006). Recent changes to the hazard mapping system. In: Proceedings of the 15th International Emission Inventory Conference: National Oceanic and Atmospheric Administration.

Ryter, S. W., Ma, K. C., & Choi, A. M. K., (2018). Carbon monoxide in lung cell physiology and disease. American journal of physiology. Cell physiology, 314(2), C211–C227.

Samet, J.M., Zeger, S.L., Dominici, F., Curriero, F., Coursac, I., Dockery, D.W., Schwartz, J., Zanobetti, A., (2000). The National Morbidity, Mortality, and Air Pollution Study. Part 2: morbidity and mortality from air pollution in the United States. Res Rep

Health Eff Inst. 94(pt 2):5–70.

Sorensen, C., House, J. A., O'Dell, K., Brey, S. J., Ford, B., Pierce, J. R., Fischer, E. V., Lemery, J., & Crooks, J. L., (2021). Associations Between Wildfire-Related $PM_{2.5}$ and Intensive Care Unit Admissions in the United States, 2006-2015. GeoHealth, 5(5), e2021GH000385.

Stowell, J. D., Geng, G., Saikawa, E., Chang, H. H., Fu, J., Yang, C.-E., Zhu, Q., Liu, Y., & Strickland, M. J., (2019). Associations of wildfire smoke $PM_{2.5}$ exposure with cardiorespiratory events in Colorado 2011–2014. Environment International.

Strickland, M. J., Darrow, L. A., Klein, M., Flanders, W. D., Sarnat, J. A., Waller, L. A., Sarnat, S. E., Mulholland, J. A., & Tolbert, P. E., (2010). Short-term associations between ambient air pollutants and pediatric asthma emergency department visits. American journal of respiratory and critical care medicine, 182(3), 307–316.

Tinling, M. A., West, J. J., Cascio, W. E., Kilaru, V., & Rappold, A. G., (2016). Repeating cardiopulmonary health effects in rural North Carolina population during a second large peat wildfire. Environ Health 15, 12.

Urman, R., McConnell, R., Islam, T., Avol, E.L., Lurmann, F.W., Vora, H., Linn, W.S., Rappaport, E.B., Gilliland, F.D., Gauderman, W.J., (2014). Associations of children's lung function with ambient air pollution: joint effects of regional and near-roadway pollutant. Thorax;69:540-547.

U.S. Department of Commerce, (2023). *U.S. Census Bureau quickfacts: California*. California Quick Facts.

Vedal, S., Hannigan, M.P., Dutton, S.J., Miller, S.L., Milford, J.B., Rabinovitch, N., Kim, S.Y., Sheppard, L., (2009). The Denver Aerosol Sources and Health (DASH) study:

overview and early findings. Atmos Environ. 43:1666–1673.

Wegesser, T.C., Franzi, L.M., Mitloehner, F.M., Eiguren-Fernandez, A., Last, J.A., (2010). Lung antioxidant and cytokine responses to coarse and fine particulate matter from the great California wildfires of 2008. Inhal. Toxicol. 22, 561–570.

Wettstein, Z. S., Hoshiko, S., Fahimi, J., Harrison, R. J., Cascio, W. E., & Rappold, A. G., (2018). Cardiovascular and cerebrovascular emergency department visits. JAHA Journal of the American Heart Association.

WHO (2005). Air Quality Guidelines Global Update 2005. Particulate Matter, Ozone, Nitrogen Dioxide and Sulfur Dioxide.

World Health Organization, (2021). World Health Organization Global Air Quality Guidelines.

Xing, Y. F., Xu, Y. H., Shi, M. H. & Lian, Y. X., (2016). The impact of $PM_{2.5}$ on the human respiratory system. J. Thorac. Dis. 8, E69.

Ye, T., Guo, Y., Chen, G., Yue, X., Xu, R., Coelho, M., Saldiva, P.H.N., Zhao, Q., Li, S., (2021a). Risk and burden of hospital admissions associated with wildfire-related PM (2.5) in Brazil, 2000–15: a nationwide time-series study. Lancet Planet. Health 5, e599–e607.

Ye, T., Xu, R., Yue, X., Chen, G., Yu, P., Coelho, M.S.Z.S., Saldiva, P.H.N., Abramson, M.J., Guo, Y., Li, S., (2022). Short-term exposure to wildfire-related $PM_{2.5}$ increases mortality risks and burdens in Brazil. Nat Commun 13, 7651.

Zanobetti A, Schwartz J, Samoli E, Gryparis A, Touloumi G, Peacock J, Anderson, R.H., Le Tertre, A., Bobros, J., Celko, M., Goren, A., Forsberg, B., Michelozzi, P., Rabczenko, D., Hoyos, S.P., Wichmann, H.E., Katsuoyanni, Klea, (2003). The temporal pattern of respiratory and heart disease mortality in response to air pollution. Environ Health Perspect. 111:1188–1193.

Zhu, S., Wu, K., Mac Kinnon, M., Wu, J., & Samuelsen, S., (2024). Modeling polycyclic aromatic hydrocarbons (PAHs) concentrations from wildfires in California. Agricultural and Forest Meteorology.