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Impacts of Fine Particulate Matter From Wildfire Smoke on Respiratory and Cardiovascular Health in California

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Alexandra Heaney and Jennifer D. Stowell contributed equally to this work.

**Key Points:**

- Consecutive days of wildfire smoke PM<sub>2.5</sub> exposure can significantly impact respiratory and cardiovascular health outcomes
- Ischemic heart disease and failure highest in adults 65+; heart failure elevated in non-Hispanic white and non-Hispanic Black populations
- When combined with increase in temperature, wildfire smoke exposure is associated with increased risk of cardiovascular disease

**Supporting Information:**

Supporting Information may be found in the online version of this article.

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# Impacts of Fine Particulate Matter From Wildfire Smoke on Respiratory and Cardiovascular Health in California

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**Abstract** Increases in wildfire activity across the Western US pose a significant public health threat. While there is evidence that wildfire smoke is detrimental for respiratory health, the impacts on cardiovascular health remain unclear. This study evaluates the association between fine particulate matter (PM<sub>2.5</sub>) from wildfire smoke and unscheduled cardiorespiratory hospital visits in California during the 2004–2009 wildfire seasons. We estimate daily mean wildfire-specific PM<sub>2.5</sub> with Goddard Earth Observing System-Chem, a global three-dimensional model of atmospheric chemistry, with wildfire emissions estimates from the Global Fire Emissions Database. We defined a “smoke event day” as cumulative 0–1-day lag wildfire-specific PM<sub>2.5</sub> ≥ 98th percentile of cumulative 0–1 lag day wildfire PM<sub>2.5</sub>. Associations between exposure and outcomes are estimated using negative binomial regression. Results indicate that smoke event days are associated with a 3.3% (95% CI: [0.4%, 6.3%]) increase in visits for all respiratory diseases and a 10.3% (95% CI: [2.3%, 19.0%]) increase for asthma specifically. Stratifying by age, we found the largest effect for asthma among children ages 0–5 years. We observed no significant association between exposure and overall cardiovascular disease, but stratified analyses revealed increases in visits for all cardiovascular, ischemic heart disease, and heart failure among non-Hispanic white individuals and those older than 65 years. Further, we found a significant interaction between smoke event days and daily average temperature for all cardiovascular disease visits, suggesting that days with high wildfire PM<sub>2.5</sub> concentrations and high temperatures may pose greater risk for cardiovascular disease. These results suggest substantial increases in adverse outcomes from wildfire smoke exposure and indicate the need for improved prevention strategies and adaptations to protect vulnerable populations.

**Plain Language Summary** Due to continued climate change, wildfire activity has increased in recent years and poses a significant public health threat. In this study, we investigated the impact of increased wildfire smoke exposure on cardiovascular and respiratory emergency department (ED) visits. We found that smoke events are linked to a > 3% increase of respiratory ED visits with a > 10% increase for asthma specifically, with the largest effect seen in children 0–5 years of age. We did not find an increase in cardiovascular visits for the entire population, but we did observe significant increases in several cardiovascular outcomes for individuals 65 years of age and older as well as for non-Hispanic white individuals.

## 1. Introduction

The frequency, size, and intensity of wildfires in the Western United States have increased over the past 40 years (Ager et al., 2017; Balch et al., 2017; Coogan et al., 2019; Littell et al., 2009; Mueller et al., 2020; Westerling et al., 2006) presenting substantial threat to human health. In particular, the past several fire seasons in the Western United States rank among the most devastating in history and 6 of the 20 largest wildfires ever in California occurred in 2020 alone (Cal Fire, 2020). While extensive research has established the negative effects of particles measuring less than 2.5 μm in aerodynamic diameter (PM<sub>2.5</sub>) on respiratory and cardiovascular health (Dominici et al., 2006; Medina-Ramon et al., 2006), the previous literature focuses mostly on air pollution generated from the burning of fossil fuels (Naeher et al., 2007). However, the composition of PM emitted from wildfire differs from PM generated from fossil fuel combustion (Naeher et al., 2007) and some have suggested that the unique mixture of particulates in smoke may have unique toxicity (Aguilera et al., 2021; Stowell et al., 2019). Given the distinctions between fire-derived PM and other sources of PM, and that wildfires are likely to present an

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**Resources:** Jia Coco Liu, Miriam Marlier

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increasingly greater threat throughout the this century in many fire-prone regions around the world due to climate change (Fried et al., 2004, 2008; Westerling, 2018), further research investigating the health impacts of fire emissions is essential to guide future public health efforts.

While growing evidence from epidemiological studies suggests that wildfire smoke is associated with adverse respiratory health outcomes, the impact of fire emissions on cardiovascular health remains unclear. As with ambient air pollution more broadly, wildfire PM emissions have been linked to declines in lung function of non-asthmatic children (Jacobson et al., 2012), increases in self-reported respiratory symptoms (Frankenberg et al., 2005; Kolbe & Gilchrist, 2009; Mirabelli et al., 2009; Mott et al., 2002; Sutherland et al., 2005), respiratory-related physician visits (Henderson et al., 2011; Mott et al., 2002), respiratory-related emergency department (ED) visits (Rappold et al., 2011), and respiratory-related hospitalizations (Alman et al., 2016; Chen et al., 2006; Delfino et al., 2009; Fann et al., 2018; Henderson et al., 2011; Ignotti, Valente, et al., 2010; Malig et al., 2021; Martin et al., 2013; Morgan et al., 2010; Mott et al., 2005; Stowell et al., 2019). Although extensive work has shown biomass smoke from household cooking or heating adversely affects cardiovascular health (Gouveia & Fletcher, 2000; McCracken et al., 2012), associations between cardiovascular outcomes and exposure to wildfire smoke have been inconsistent across studies (Stowell et al., 2019).

Relatively little is known about the vulnerability of specific sub-populations to wildfire emissions. Some work suggests that older individuals may be particularly susceptible to wildfire PM exposure (Analitis et al., 2012; Gouveia & Fletcher, 2000; Henderson et al., 2011; Ignotti, Hacon, et al., 2010; Le et al., 2014; Liu, Wilson, Mickley, Ebisu, et al., 2017; Morgan et al., 2010; Mott et al., 2005; Reid, 2014). Older individuals may have higher susceptibility to wildfire PM exposure due to declining physiological processes over time, and higher baseline prevalence of cardiovascular and respiratory health problems (Sacks et al., 2011). Studies have shown reduced clearance of ambient PM in the respiratory tract with age (EPA., U.S., 2009), as well as decreased heart rate variability in older individuals following PM exposure (Devlin et al., 2003). Additionally, young children may be more vulnerable to wildfire smoke exposure due to higher rates of respiration and subsequent increase in exposure (Delfino et al., 2009; Kerem, 1996; Kunzli et al., 2006; Morgan et al., 2010; Stowell et al., 2019; Wu et al., 2006). While the ambient PM literature suggests that females may be at higher risk for respiratory health problems due to PM exposure (Bell et al., 2013), potentially due to sex differences in lung airway size, lung function, and absorption of gases through the respiratory system (Sacks et al., 2011), evidence for wildfire exposure is limited and has mixed results (Reid, 2014; Reid et al., 2016). More work is needed to identify and clarify which sub-populations may be particularly vulnerable to wildfire smoke exposure to target prevention efforts.

While the literature on the health effects of wildfire PM has grown in recent years, studies remain somewhat limited by data availability. One challenge in conducting epidemiological analyses of wildfire smoke related health effects is estimating exposure levels, because of the difficulty in differentiating PM originating from wildfire smoke from PM generated from other sources. Additionally, studies investigating sub-population vulnerabilities have been limited due to a paucity of spatially and temporally resolved respiratory and cardiovascular health data linked to relevant demographic information, such as sex, age, race, and wealth. As a result, few studies have focused on wildfire respiratory impacts in California, where high wildfire smoke exposure is increasingly a pressing concern for both urban and rural counties (Goss et al., 2020; Leibel et al., 2020; Mott et al., 2002; Reid, 2014; Reid et al., 2019; Shusterman et al., 1993).

Here, we leveraged unique exposure and hospitalization data to understand the impacts of wildfire specific PM<sub>2.5</sub> on respiratory and cardiovascular health in California, and to investigate potential sub-population vulnerability to wildfire emissions. We utilized daily modeled PM<sub>2.5</sub> concentrations derived specifically from wildfires from 2004 to 2009 across all California counties to analyze how these exposures influenced county-level rates of cause-specific respiratory and cardiovascular hospital visits. To investigate sub-population vulnerability, we stratified by age and race/ethnicity to elucidate potential wildfire specific PM<sub>2.5</sub> health effects among various subpopulations.

## 2. Methods

### 2.1. Wildfire Smoke Pollution Estimates

Daily wildfire smoke specific PM<sub>2.5</sub> exposure data was generated at 0.5° × 0.67° resolution using the Goddard Earth Observing System-Chem (GEOS-Chem; v9-01-03) chemical transport model framework. GEOS-Chem utilizes meteorological data from the Goddard Earth Observing System (GEOS-5) and daily wildfire emissions

from the Global Fire Emissions Database—which combines satellite observations of fire counts, area burned and fuel load to produce gridded maps of wildfire emissions—to estimate primary particle formation from wildfires. We used the aerosol-only version of GEOS-Chem, which includes emissions of all primary particulate matter and the gas-phase precursors to secondary particulate matter. Two simulations were generated—one representing total emissions (all-source  $PM_{2.5}$  including wildfires as well as non-fire sources such as transportation, industry, and power plants) and one excluding wildfire emissions (no-fire  $PM_{2.5}$ ). All-source  $PM_{2.5}$  was taken to be the sum of sulfate, nitrate, ammonium, organic carbon, and black carbon. The difference between the two simulations represents the contribution of wildfire-derived  $PM_{2.5}$ . Further information regarding the modeling structure can be found in Liu, Wilson, Mickley, Ebisu, et al. (2017) and Liu, Wilson, Mickley, Dominici, et al. (2017). County-level  $PM_{2.5}$  model estimates were calibrated with ground-level  $PM_{2.5}$  monitoring data by matching the quantile functions of the two datasets. This approach scales the distribution of modeled  $PM_{2.5}$  so that it resembles the distribution of the monitored data (Liu, Wilson, Mickley, Dominici, et al., 2017). We then obtained the calibrated wildfire-specific  $PM_{2.5}$  by multiplying the calibrated total modeled  $PM_{2.5}$  with the proportions of total modeled  $PM_{2.5}$  contributed by modeled wildfire-specific  $PM_{2.5}$  on each day.

## 2.2. Respiratory and Cardiovascular Disease Data

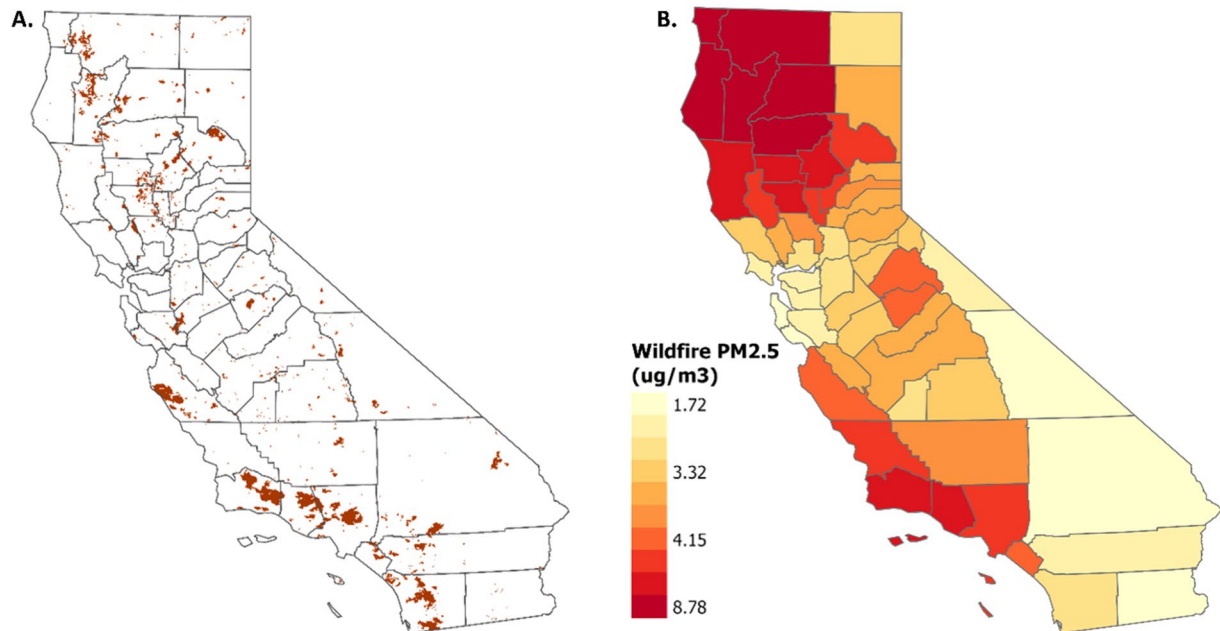
We obtained county-level daily records of unscheduled hospital visits across California spanning 6 years (2004–2009) from the Office of Statewide Health and Development. The data includes hospital visits for all respiratory diseases (ICD9-CM 460–519), and respiratory disease subgroups such as asthma (ICD9-CM 493), acute respiratory infections (ICD9-CM 460–466), chronic obstructive pulmonary disease (COPD; ICD9-CM 490–492, 494–496), all cardiovascular diseases (ICD9-CM 390–459), and cardiovascular disease subgroups, including heart failure (ICD9-CM 428), and ischemic heart disease (IHD; ICD9-CM 410–414). We extracted county-level daily hospital visits during the fire season (May 1–October 31) to match the temporal resolution of the wildfire emissions data. County-level hospital visit counts were also stratified by age group (0–5, 6–18, 19–64, and 65+ years) and race (Non-Hispanic white, Non-Hispanic Black, Non-Hispanic Asian, and Hispanic).

## 2.3. Temperature and Population Data

To address potential confounding or effect modification by temperature, we obtained temperature measurements from all meteorological stations across California from the National Centers for Environmental Information to include as a variable in our analyses. Measurements from stations within the same county were averaged to generate mean 24-hr (daily) county-level temperature from 2004 to 2009. County level population data was obtained from the 2010 Census Bureau survey.

## 2.4. Smoke Event Definition

In our analyses, we aimed to understand the impact of extremely high wildfire smoke on respiratory and cardiovascular health. The continuous wildfire  $PM_{2.5}$  estimates were extremely skewed with 81% of the monthly observations below  $5 \mu\text{g}/\text{m}^3$  (Figure S1 in Supporting Information S1), and therefore did not provide sufficient statistical power to detect associations between wildfire  $PM_{2.5}$  and the health outcomes. As a result, we adapted an existing exposure metric to develop a dichotomous exposure variable termed “smoke event day” to isolate periods of extreme wildfire  $PM_{2.5}$  (Liu, Wilson, Mickley, Dominici, et al., 2017). To define smoke event days, we first summed the wildfire-derived  $PM_{2.5}$  on each day with the wildfire-derived  $PM_{2.5}$  on the preceding day to generate a variable representing cumulative 0–1 day lagged wildfire  $PM_{2.5}$ . We utilized this aggregate measure of current and preceding day fire  $PM_{2.5}$  to best capture short-term exposure to wildfire emissions using multiple thresholds. Preliminary analyses indicated that the associations between hospital visits and wildfire  $PM_{2.5}$  were highest when wildfire  $PM_{2.5}$  was either unlagged or lagged 1 day. Next, we generated wildfire  $PM_{2.5}$  thresholds using percentiles of all cumulative 0–1 lag day wildfire  $PM_{2.5}$  measurements. Days were categorized as smoke event days when the cumulative 0–1 lag day wildfire  $PM_{2.5}$  for that day exceeded the wildfire  $PM_{2.5}$  threshold. Thresholds were set using the 94th, 96th, 98th, and 99th percentiles of all county-level cumulative 0–1 lag day wildfire  $PM_{2.5}$  estimates from 2004 to 2009. Hence, we generated four different smoke event day exposure variables based on the different wildfire  $PM_{2.5}$  thresholds. Preliminary results showed the strongest associations between smoke event days and health outcomes when the threshold was set at the 98th percentile, so the 98th percentile results



**Figure 1. California wildfire activity during study period.** Panel (a) indicates locations of satellite-derived burned area (red) shown across California from 2004 to 2009 from the MODIS MCD64A1 Collection 6 monthly burned area product. Panel (b) depicts average daily PM<sub>2.5</sub> emitted by wildfires ( $\mu\text{g}/\text{m}^3$ ) in California counties from May-October 2004 to 2009.

are presented as the main definition of a smoke event day. However, we also include results using the 94th, 96th, and 99th percentiles of cumulative 0–1 lag day wildfire PM<sub>2.5</sub> as sensitivity analyses.

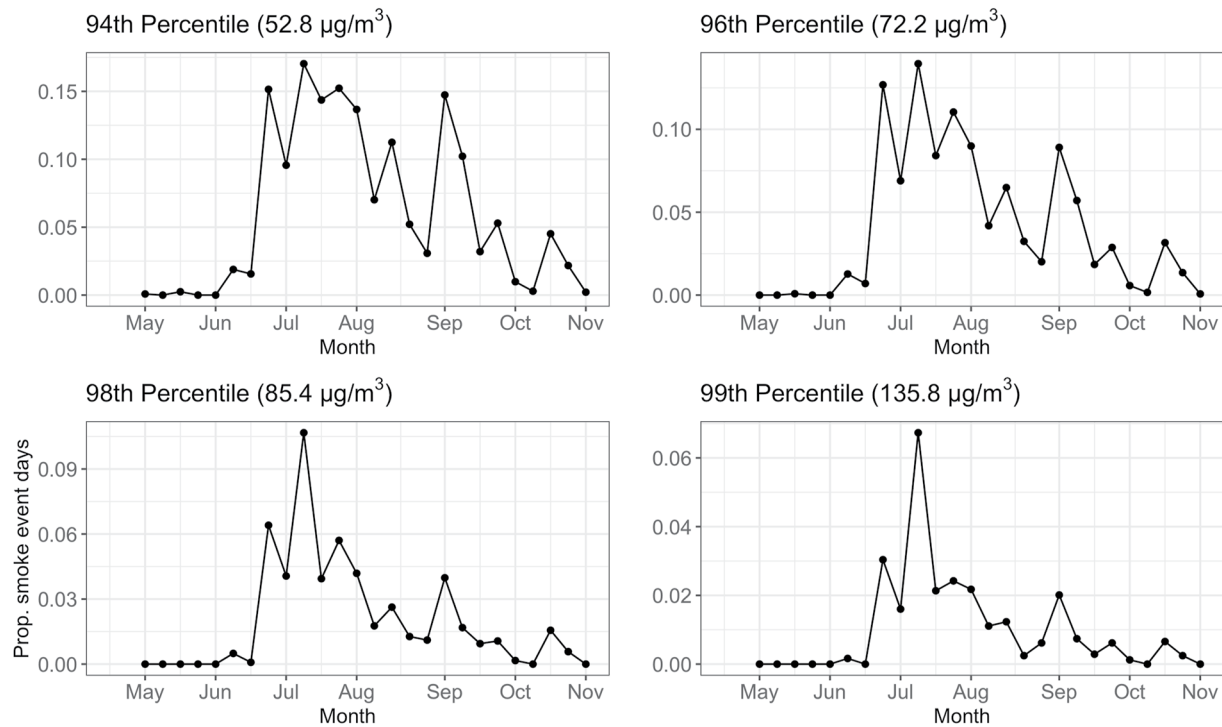
### 2.5. Statistical Analyses

We used negative binomial regression models to compare daily hospital visit rates on smoke event days and non-smoke event days. Separate regression models were used to predict the effects of smoke event days on hospital visits for each health outcome considered. All models included county fixed effects, an indicator variable for day of week, county-level measurements of daily average temperature, county-level estimates of non-wildfire PM<sub>2.5</sub>, and a county-level offset for population. Additionally, we controlled for seasonal and long-term trends using indicator variables for month and year. Individual regression models were run for each health outcome using smoke event days as defined by the different wildfire PM<sub>2.5</sub> thresholds (based on the 94th, 96th, 98th, and 99th percentiles of cumulative 0–1 lag day PM<sub>2.5</sub> measurements). Stratification analyses were performed for all age and race/ethnicity categories using the same model structures. Additionally, we tested an interaction term between smoke event days and average daily temperature for each health outcome to investigate whether temperature modified the effect of wildfire emissions on health.

We also investigated lagged associations between wildfire PM<sub>2.5</sub> and hospital visits using single lag negative binomial regressions. In contrast to the main regression models, exposure in these models was defined as a “single wildfire day.” A single wildfire day was defined as a day when the wildfire PM<sub>2.5</sub> was above the designated percentiles of single day wildfire PM<sub>2.5</sub> (i.e., wildfire emissions were not summed between current and preceding day in this analysis to test effects of specific lag days). Regression models were run with single wildfire days lagged from 0 to 10 days to understand the lagged effects of wildfire emissions on hospital visits for each health outcome.

## 3. Results

We observed wide spatial and interannual variability in wildfire specific PM<sub>2.5</sub> estimates across California counties from 2004 to 2009 (Figure 1). The highest daily average wildfire specific PM<sub>2.5</sub> estimates were seen in Trinity, Humboldt, and Siskiyou counties. Within the fire season (May-October), we also observed seasonal patterns



**Figure 2.** Seasonal trends in wildfire emissions across the summer seasons (May–October, 2004–2009). Proportion of days per week that are smoke event days, that is, sum of the current and preceding day wildfire PM<sub>2.5</sub> above the 94th percentile, 96th percentile, 98th percentile, and 99th percentile, of 2-day wildfire PM<sub>2.5</sub>.

in wildfire specific PM<sub>2.5</sub> across all counties, with the highest average exposures occurring in July (Figure 2). Table 1 shows the average PM<sub>2.5</sub> levels on smoke event days and non-smoke event days. When using the 98th percentile of wildfire specific PM<sub>2.5</sub> (85.4 µg/m<sup>3</sup>) as the cutoff for smoke event days the average difference in PM<sub>2.5</sub> between smoke event and non-smoke event days was 42.62 µg/m<sup>3</sup>. Health outcomes also showed varying spatial patterns across the state (Figure S2 in Supporting Information S1) and some seasonal patterns (Figures S3 and S4 in Supporting Information S1). On average, the lowest disease rates during the fire season occurred in

**Table 1**  
Average Wildfire PM<sub>2.5</sub> Concentrations on Smoke Event Days and Non-Smoke Event Days Across All Counties in California Using Different Percentile Thresholds From 2004 to 2009

Percentile threshold	Type	Number of days	Wildfire PM <sub>2.5</sub> (µg/m <sup>3</sup> )
Cumulative 0–1 day, 94% (52.8 µg/m <sup>3</sup> )	Smoke event days	3,822	33.3
	Non-smoke event days	59,862	2.15
	Difference	–	31.15
Cumulative 0–1 day, 96% (72.2 µg/m <sup>3</sup> )	Smoke event days	2,548	38.3
	Non-smoke event days	61,136	2.59
	Difference	–	35.71
Cumulative 0–1 day, 98% (85.4 µg/m <sup>3</sup> )	Smoke event days	1,274	45.8
	Non-smoke event days	62,410	3.17
	Difference	–	42.63
Cumulative 0–1 day, 99% (135.7 µg/m <sup>3</sup> )	Smoke event days	637	52.4
	Non-smoke event days	63,047	3.53
	Difference	–	48.87

*Note.* Percentile thresholds (94th, 96th, 98th, and 99th) represent the percentile of all cumulative (0–1 day) wildfire PM<sub>2.5</sub> concentrations. A smoke event day occurred when the sum of the current and preceding day wildfire PM<sub>2.5</sub> was above the 98th percentile of cumulative 2-day wildfire PM<sub>2.5</sub>.



**Table 2**  
*Average Annual Hospital Visits (Per 100,000 People) Across All Counties in California, 2004–2009*

	All respiratory	Asthma	Acute respiratory infections	COPD <sup>a</sup>	All cardiovascular	IHD <sup>b</sup>	Heart failure
Total #	17,111	1,757	738	2,903	29,217	8,577	5,146
<b>Age</b>							
0–5	1,451 (8.4)	359 (20.4)	398 (53.9)	8 (0.2)	66 (0.2)	0 (0.0)	8 (0.1)
6–18	572 (0.3)	190 (10.8)	47 (6.3)	6 (0.2)	112 (0.3)	1 (0.0)	4 (0.1)
19–64	5,858 (34.3)	818 (46.5)	166 (22.4)	997 (34.3)	10,439 (35.7)	3,729 (43.5)	1,333 (25.9)
65+	9,231 (53.9)	389 (22.1)	127 (17.2)	1,891 (65.1)	18,601 (63.6)	4,847 (56.5)	3,800 (73.8)
<b>Race</b>							
White	12,690 (74.2)	1,022 (58.1)	404 (54.7)	2,458 (84.6)	22,129 (75.7)	6,552 (76.4)	3,826 (74.3)
Black	721 (4.2)	180 (10.2)	28 (3.8)	98 (3.3)	1,281 (4.3)	273 (3.2)	315 (6.1)
Asian	602 (3.5)	89 (5.0)	29 (3.8)	65 (2.2)	1,129 (3.8)	339 (3.9)	185 (3.6)
Hispanic	2,441 (14.2)	375 (21.3)	237 (32.1)	210 (7.2)	3,420 (11.7)	935 (10.9)	657 (12.7)

<sup>a</sup>COPD: chronic obstructive pulmonary disease. <sup>b</sup>IHD: ischemic heart disease.

August for all health outcomes. Table 2 presents the breakdown of all hospital visits for each health outcome by age and race classification.

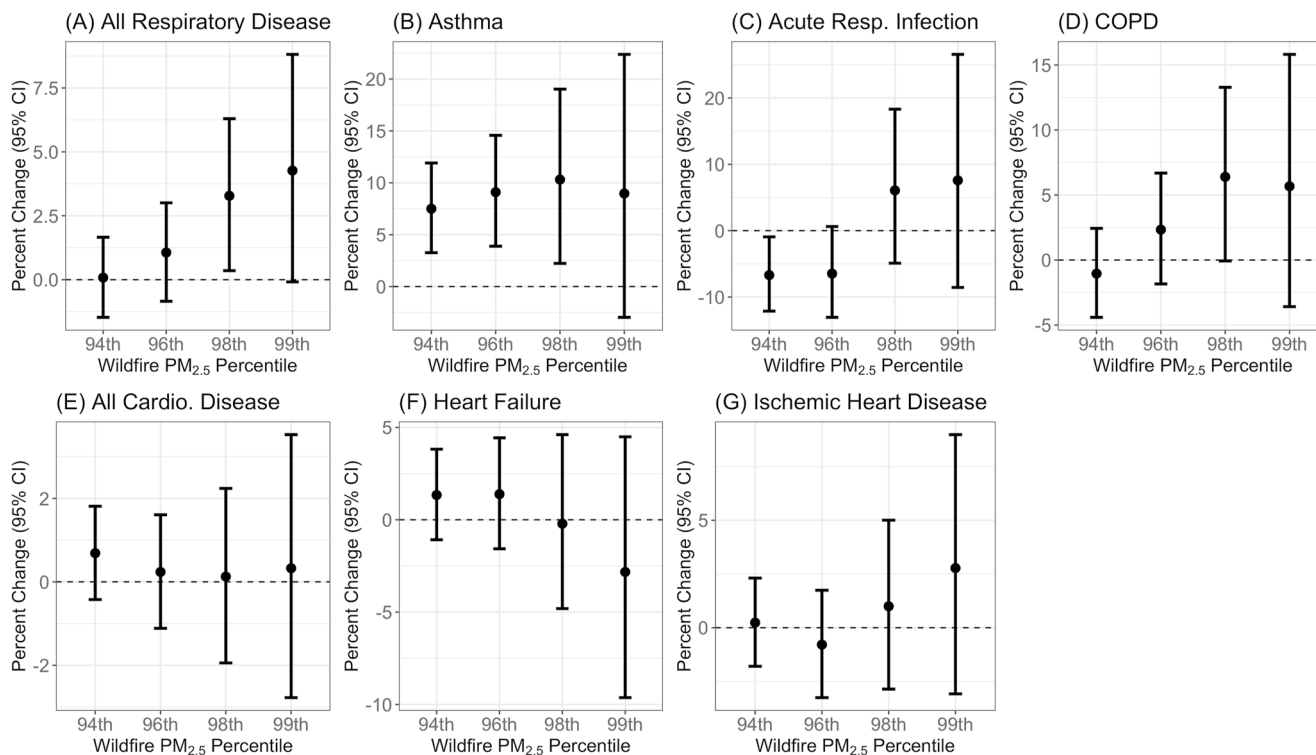
### 3.1. Associations Between Smoke Event Days and Respiratory Health Outcomes

The main analyses showed that smoke event days (defined based on cumulative wildfire PM<sub>2.5</sub> exposure from lag days 0–1) were positively associated with hospital visits for all respiratory diseases and asthma (Figure 3). Using the 98th percentile cutoff for smoke event days, we estimated a 3.3% (95% CI: [0.4%–6.3%]) increase in hospital visits for all respiratory diseases on smoke event days compared to non-smoke event days. We observed a larger association for asthma, with a 10.3% (95% CI: [2.3%, 19.0%]) increase in hospital visits on smoke event days compared to non-smoke event days. Results for COPD were marginally non-significant, with an estimated 6.4% (95% CI: [–0.1%, 13.3%]) increase in hospital visits on smoke event days compared to non-smoke event days. Results for acute respiratory infections were non-significant.

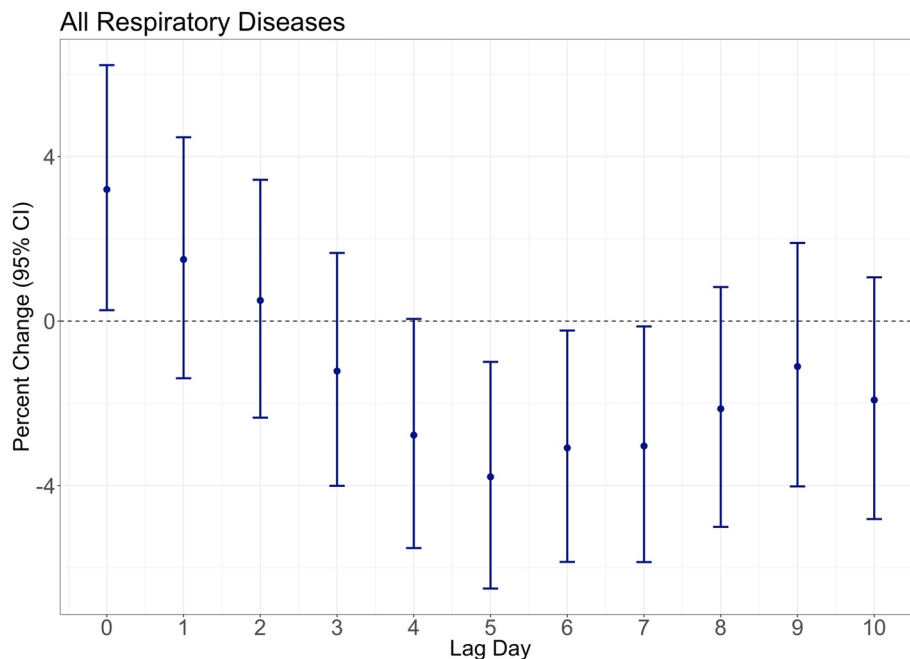
The lagged analyses, in which single wildfire days were defined based on current day wildfire-derived PM<sub>2.5</sub>, showed acute (0 lag day) positive effects of single wildfire days on hospital visits for all respiratory diseases, asthma, and COPD (Figure 4, Table S1 in Supporting Information S1). In contrast, we estimated significant decreases in hospital visits for all respiratory diseases 5–7 days after a single wildfire day compared to a non-wildfire day (Figure 4). We observed a similar decline in hospital visits for acute respiratory infections at lags days 5–13 (Table S1 in Supporting Information S1).

Stratification analyses revealed differential effects on all respiratory hospitalizations by age group, with no effect seen in ages 0–5 years and positive effects seen among ages 6–18 years, 19–64 years, and older than 65 years. Positive effects of smoke event days on asthma hospitalizations were observed for all age groups (Figure 5). We found the largest positive effect of smoke event days on asthma hospitalizations among those aged 0–5 years (10.8%, 95% CI: [6.7%, 15.2%]), and also among those aged 6–18 years (8.1%, 95% CI: [0.8%, 24.5%]), 19–64 years (8.4%, 95% CI: [3.5%, 13.8%]), and older than 65 years (4.4%, 95% CI: [0.8%, 8.4%]). Additionally, acute respiratory infections showed differential associations when stratifying on age, with a positive association observed among those aged 0–5 years (Figure 5, Figure S7 in Supporting Information S1). For COPD hospital visits, we observed the largest positive association with smoke event days among those older than 65 (Figure 5).

When stratifying by race/ethnicity, increased hospitalizations for all respiratory hospital visits were exhibited in non-Hispanic white (47%, 95% CI: [24%, 74%]) and Hispanic individuals (43%, 95% CI: [25%, 64%]) on a smoke event day compared to a non-smoke event day. The largest association between smoke event days and hospital visits for acute respiratory infections was observed among Hispanic individuals (Figure 6, Figure S8 in Supporting Information S1). Positive associations between smoke event days and visits for COPD were only observed

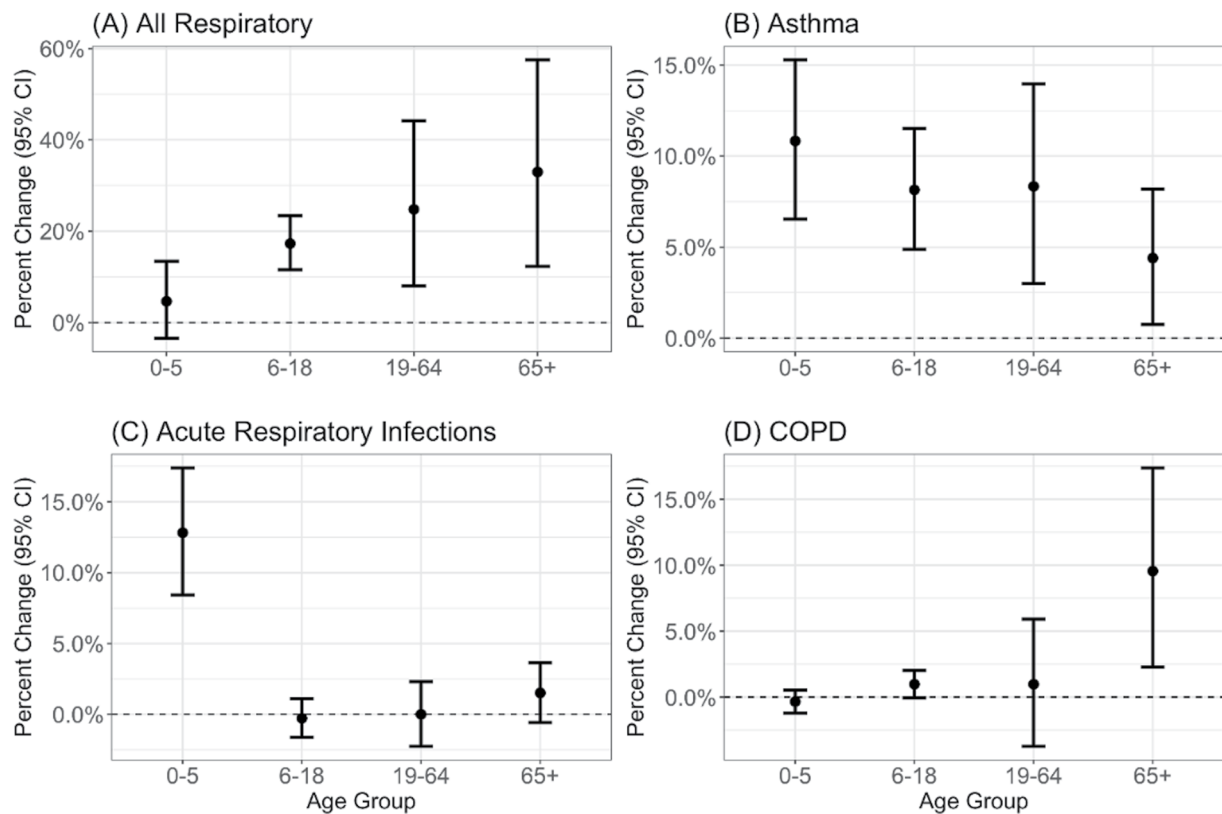


**Figure 3.** Effect of wildfire emissions on all health outcomes. Estimates and 95% confidence intervals on the y-axis represent the percent change in the number of hospital visits associated with a smoke event day compared to a non-smoke event day. A smoke event day occurred when the sum of the current and preceding day wildfire PM<sub>2.5</sub> was above the percentile (x-axis) of cumulative 2-day wildfire PM<sub>2.5</sub>.



**Figure 4.** Association of single wildfire days lagged 0–10 days with hospital visits for all respiratory diseases. Estimates and 95% confidence intervals (y-axis) represent the percent change in the number of hospital visits associated with a wildfire day compared to a non-wildfire day lagged 0–10 days (x-axis). A single wildfire day occurred when the current day wildfire PM<sub>2.5</sub> was above the 98th percentile of daily wildfire PM<sub>2.5</sub>.





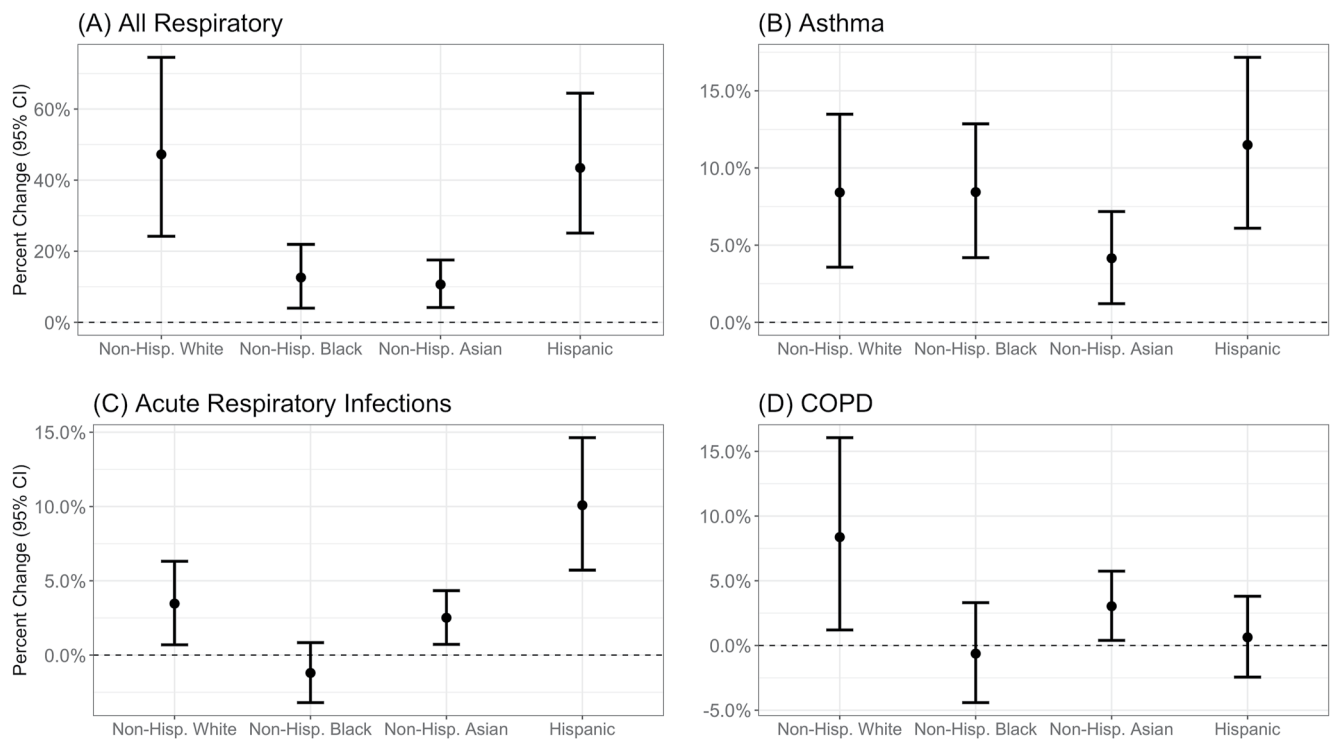
**Figure 5.** Results from age stratification analyses for (a) all respiratory outcomes, (b) asthma, (c) acute respiratory infections, and (d) chronic obstructive pulmonary disease (COPD). Estimates and 95% confidence intervals (y-axis) represent the percent change in the number of hospital visits associated with a smoke event day compared to a non-smoke event day for all age groups (x-axis). A smoke event day occurred when the sum of the current and preceding day wildfire  $PM_{2.5}$  was above the 98th percentile of cumulative 2-day wildfire  $PM_{2.5}$ .

among non-Hispanic white individuals (Figure 6, Figure S10 in Supporting Information S1). No other consistent differences between age or race strata were observed (Figures S4–S11 in Supporting Information S1).

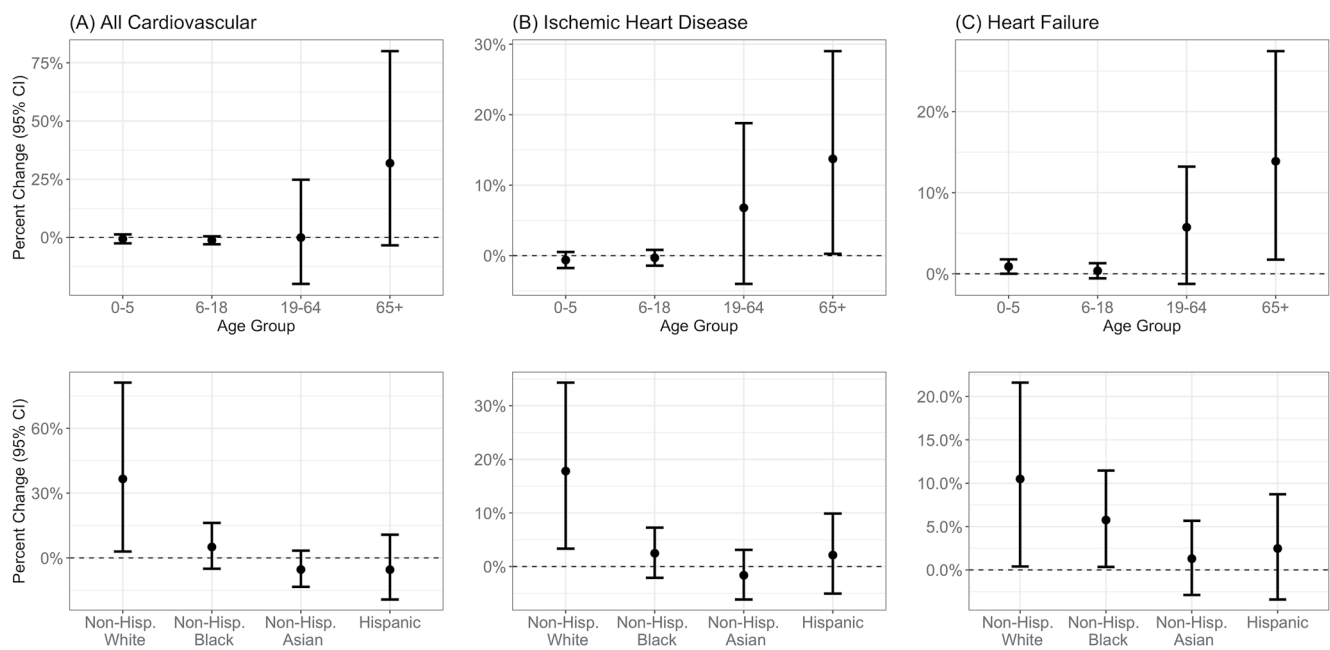
### 3.2. Associations Between Smoke Event Days and Cardiovascular Health Outcomes

Notably, we did not observe significant associations between smoke event days and any cardiovascular health outcomes (Figure 3) when analyzing for the entire population. However, we did observe a significant positive interaction between average temperature and smoke event days in our models predicting hospital visits for all cardiovascular diseases when defining smoke event days using the 94th and 96th percentiles (the interaction was not significant when using the 98th or 99th percentile) (Table S2 in Supporting Information S1). We estimated a 1.0% (95% CI: [0.1%, 1.5%]) increase in cardiovascular disease hospital visits associated with every 5°C increase on smoke event days (defined using the 94th percentile of wildfire-derived  $PM_{2.5}$ ).

Age stratification analysis revealed significant increases in IHD and heart failure hospital visits among adults older than 65 (Figure 7). Furthermore, when stratifying by race/ethnicity, we observed a positive association between smoke event days and all cardiovascular disease among non-Hispanic whites (1.7%, 95% CI: [0.4%, 2.9%]) based on the 98th percentile cutoff, as shown in Figure 7. Significant positive associations were also observed among non-Hispanic white individuals for IHD hospital visits and in both non-Hispanic white and non-Hispanic Black subgroups for heart failure hospital visits (Figure 7). We did not see any significant lagged effects for cardiovascular health outcomes or any other consistent difference between race/ethnicity and age group strata (Figures S12–S17 and Table S2 in Supporting Information S1).



**Figure 6.** Associations between smoke event days and hospital visits for respiratory outcomes stratified by race group. Different definitions of a smoke event day are shown on the x-axis. A smoke event day occurred when the sum of the current and preceding day wildfire  $PM_{2.5}$  was above the 98th percentile of cumulative 2-day wildfire  $PM_{2.5}$ . The y-axes show estimated percent change in hospital visits for outcome associated with a smoke event day compared to a non-smoke event day.



**Figure 7.** Results from stratification analyses for (a) all cardiovascular disease, (b) ischemic heart disease, and (c) heart failure. Estimates and 95% confidence intervals (y-axis) represent the percent change in the number of hospital visits for each outcome associated with a smoke event day compared to a non-smoke event day for all age and race strata (x-axis). A smoke event day occurred when the sum of the current and preceding day wildfire  $PM_{2.5}$  was above the 98th percentile of cumulative 2-day wildfire  $PM_{2.5}$ .

#### 4. Discussion

Wildfire intensity, frequency and duration are increasing rapidly in California and across the western United States, and our results indicate that wildfire smoke pollution has significant detrimental health impacts across the state. We found that smoke event days (i.e., days when the cumulative 0–1 wildfire specific  $PM_{2.5}$  concentration was above the 98th percentile) were significantly associated with increased hospital visits for all respiratory diseases and asthma, as well as varied risk effect estimates when stratifying on age and race/ethnicity. We also found a significant interaction between smoke event days and ambient temperature for all cardiovascular disease hospital visits, suggesting that days with both high wildfire  $PM_{2.5}$  concentrations and hot temperatures may pose greater risk for cardiovascular disease.

Our study contributes to a growing literature showing negative impacts of wildfire smoke on respiratory health outcomes (Liu et al., 2015; Reid et al., 2016), and our results indicate that young children and older adults are particularly vulnerable to these health impacts. While our stratified analyses revealed positive associations between smoke event days and hospital visits for all respiratory disease among all age groups except children between 0 and 5, we estimated the strongest association among individuals older than 65 years. Smoke event days were similarly associated with increased hospital visits for asthma among all age groups, but the highest estimated effects were among children 0–5 and 6–18 years. This agrees with other findings, such as a study by Hutchinson et al. that estimated a significant increase in children's ED visits for asthma associated with exposure to wildfire smoke (risk ratio of 2.36 (95% CI: 1.27–4.39) among children aged 0–4 years and 1.25 (95% CI: 1.05–1.48) among children aged 5–17 years) (Hutchinson et al., 2018). It is important to understand the vulnerability of specific subgroups, such as young children and older adults, to inform planning and response measures before, during, and following wildfire events. For example, it may be important to direct safety messaging surrounding staying indoors during high smoke conditions toward parents of young children and older adult subpopulations.

When stratifying on race, we estimated significant increases in all respiratory diseases, asthma, COPD, and acute respiratory infections on smoke event days across all racial groups, but the largest effects were often among Hispanic individuals, who may be at increased risk from greater smoke exposures due to the combined effects of occupation and lower-income status. For example, a research group at Berkeley found that, in the state of California, there is a large outdoor agricultural workforce estimated to be approximately 80% low-income earners and 93% Latinx, putting this particular subgroup at risk for additional wildfire smoke exposure (Thomason & Bernhardt, 2020). These results could point to specific vulnerabilities in this race sub-population, but further information is needed. Future analyses should continue to investigate vulnerable subpopulations, especially other understudied and potentially susceptible subpopulations, such as low-income groups, pregnant women, and individuals with pre-existing medical conditions to target high-risk groups and help prevent wildfire smoke related adverse health outcomes.

In this study, we did not find significant associations between short-term or lagged wildfire  $PM_{2.5}$  concentrations and hospital visits for any cardiovascular outcome in the full study population. Still, we observed that hospital visits for all cardiovascular outcomes, IHD, and health failure were significantly increased among non-Hispanic white individuals on smoke event days, which could be due to the large portion of the study sample identified as white ( $N = 980,360$ , 59%), resulting in greater statistical power to detect an effect in this subpopulation. We additionally found significant increases in hospital visits for all cardiovascular diseases, heart failure, and IHD among individuals older than 65 on smoke event days. While there is robust literature showing that exposure to ambient  $PM_{2.5}$  negatively impacts cardiovascular health (Cohen et al., 2017; Murray et al., 2020), evidence from epidemiological studies has been mixed when assessing associations between wildfire smoke and cardiovascular disease. Some previous studies have found positive associations between cardiovascular disease outcomes and wildfire smoke exposure (Jones et al., 2020; Malig et al., 2021), but other studies have found no association between wildfire smoke pollution and cardiovascular health outcomes (Alman et al., 2016; Stowell et al., 2019). Given the robust literature and multiple potential biological mechanisms of  $PM_{2.5}$  exposure impacting cardiovascular disease (Adetona et al., 2016), it is not clear why the epidemiological literature for wildfire smoke exposure has been mixed. To date, several studies suggest inflammation and oxidative stress caused by  $PM_{2.5}$  exposure may be responsible for the negative impacts of air pollution on the cardiovascular system (Xiao et al., 2003). Potential endogenous generation of reactive oxygen species (ROS) may be responsible for a majority of these negative effects, with some studies suggesting a similarity to the toxicity of other combustion products such as diesel fuel, and ROS increases are clearly linked to oxidative stress, causing induction of certain enzymes and subsequent

airway inflammation. Finally, there is evidence that the organic constituents of wildfire particulate matter may be the primary drivers of the resulting airway inflammation (Bolling et al., 2009). Wildfire PM<sub>2.5</sub> may affect the cardiovascular system through other mechanisms, such as the crossing of ultrafine PM from airways to the circulations system and pulmonary inflammation spillover to the vasculature of the body, both of which can be involved in additional oxidative stress (Brook et al., 2010).

In addition, our results suggest that there may be a synergistic effect of wildfire PM<sub>2.5</sub> and hotter temperatures on cardiovascular disease, given that wildfires typically have occurred during the warm season and hotter temperatures have also become more frequent and intense in recent years due to climate change. Epidemiologic studies have shown potential mechanisms for increased temperature to impact cardiovascular disease through thermoregulatory and endocrine-related mechanisms (Cheng et al., 2019; Stewart et al., 2017). Although there is only limited literature studying the synergistic effects of wildfire-PM<sub>2.5</sub> and temperature directly, there is growing literature assessing the association of ambient PM<sub>2.5</sub> and temperature on cardiovascular disease. And yet, because wildfires often occur during heat waves, the synergistic health effects of increased wildfire-derived PM<sub>2.5</sub> and temperatures are of particular concern (Shaposhnikov et al., 2014). Furthermore, the magnitude and duration of both heat waves and wildfires are likely to increase due to climate change (Abatzoglou & Williams, 2016; Argueso et al., 2016; Di Virgilio et al., 2019; Goss et al., 2020; Lyon et al., 2019; Mitchell et al., 2016). Future work should continue to investigate the combined impacts of exposure to extreme high temperatures and wildfire smoke on cardiovascular disease.

The findings presented in this study should be contextualized within its limitations. This study focuses on the wildfire seasons between 2004 and 2009 in California. However, wildfire activity has increased in recent years, suggesting that exposures to wildfire smoke have likely been higher and of longer duration in recent years (Liu et al., 2016). Utilizing more recent data could enable a better characterization of the current burden of disease due to exposure on smoke event days. Furthermore, as is common in air pollution epidemiological studies, certain assumptions regarding the activities of the study population must be made. For instance, in our analyses, the health data used from California was supplied at the county level. Counties, especially in the West, can often cover very large geographical areas and are at a coarse spatial resolution for exposure data. However, monitors are typically placed in areas with greater population density in each county, likely capturing urban or semi-urban areas. Despite these limitations and potential exposure misclassification particularly in larger counties, this study estimates the effects of both cumulative and lagged smoke PM<sub>2.5</sub> exposure in California over multiple years. Given gaps in knowledge surrounding the effects of smoke exposure, especially cumulative effects, this investigation provided valuable information regarding non-acute (day of) non-lag distributed wildfire exposures.

The results of this analysis point to substantial increases in adverse respiratory and cardiovascular health outcomes due to multiple consecutive exposures to wildfire smoke PM<sub>2.5</sub>, with potentially differential risk to different subpopulations. As evidenced over the past decade, wildfires are increasing in frequency and intensity in California—a trend which shows no indication of significant change. Moving forward, it is evident that adaptation and prevention strategies must be put into place to protect the most vulnerable from exposure to wildfire smoke. These strategies should include improved statewide guidelines regarding actions to take during wildfire events, evacuation plans, school closures, proper protective equipment (i.e., masks), and when to remain indoors.

### Conflict of Interest

The authors declare no conflicts of interest relevant to this study.

### Data Availability Statement

The R code used to complete this analysis is available at <https://dataverse.harvard.edu/dataverse/akheaneywildfire/>. Emergency department data supporting this research are not accessible to the public or research community. To request California epidemiological data, researchers may contact the California Department of Healthcare Access and Information at <https://hcai.ca.gov/> and access fees may apply (*California Healthcare Access and Information*, <https://hcai.ca.gov/> [Data Set]). Exposure data used to identify smoke events were derived using the Goddard Earth Observing System-Chem (GEOS-Chem) platform and Global Fire Emissions Database (GFED-3) wildfire product. The processed data set has been used in previous publications (Liu, Wilson, Mickley, Dominici, et al., 2017).

To gain access to the complete wildfire particulate matter data set, interested parties will need to contact authors of the manuscript mentioned above. However, input data are publicly available with no associated fees or permissions required. GEOS-Chem data and platform are available at: <https://geos-chem.seas.harvard.edu/> and GFED data is available at: <https://www.globalfiredata.org/data.html> (*GEOS-Chem*, <https://geos-chem.seas.harvard.edu/> [Data Set]; *GFED Data*, <https://www.globalfiredata.org/data.html> [Data Set]). Air monitoring data for calibration was acquired from US EPA and is also publicly available at: [https://aqs.epa.gov/aqsweb/airdata/download\\_files.html](https://aqs.epa.gov/aqsweb/airdata/download_files.html) (*USEPA Pre-Generated Data Files*, [https://aqs.epa.gov/aqsweb/airdata/download\\_files.html](https://aqs.epa.gov/aqsweb/airdata/download_files.html) [Data Set]). Meteorological data was acquired from NCEI/NOAA and is available at: <https://data.noaa.gov/onestop/> (*NOAA Data Search Platform*, <https://data.noaa.gov/onestop/collections?q=weather> [Data Set]).

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