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Wildfire Smoke Exposure and Cardiovascular-related Effects Among the Medicare Population: A Case-crossover Study of the 2017 California Wildfire Season

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Abstract

Wildfire Smoke Exposure and Cardiovascular-related Effects Among the Medicare Population: A Case-crossover Study of the 2017 California Wildfire Season

By Andrew Rosenberg

Wildfire smoke is a significant source of exposure to elevated levels of fine particulate matter ($PM_{2.5}$), although the health effects of wildfire smoke have not been studied extensively. Previous epidemiological studies have reported inconsistent results for the cardiovascular-related health impacts associated with wildfire smoke exposure. A population-based analysis was conducted to estimate associations between incident cardio- and cerebrovascular events among the Medicare population and exposure to smoke density based on estimated concentrations of $PM_{2.5}$, comparing wildfire smoke days to non-smoke days in California during the 2017 wildfire season. A case-crossover design was applied using conditional logistic regression to compare ZIP code levels of smoke density (1 – light, 2 – moderate, and 3 – heavy) on case days and 3-4 control days, matched by day of the week and month, before and after the case day. Separate analyses were performed to examine exposure lag periods, 0-4 days before the case day. Subgroup analyses were performed by sex, race, ethnicity, age group (≤69, 70-74, 75-79, 80-84, 85-89, 90-94, ≥95), and Medicaid eligibility. No increased risk was observed for ischemic heart disease, congestive heart failure, COPD, acute myocardial infarction, or atrial fibrillation across all 0-4 lag days, after adjusting for temperature and relative humidity. A marginally significant increased risk of ischemic stroke was associated with the lagged effects of exposure to light density smoke at lag 1 (OR: 1.05, 95% CI: 1.01, 1.10), lag 3 (OR: 1.07, 95% CI: 1.02, 1.12), and lag 4 (OR: 1.07 (95% CI: 1.02, 1.12). For women, effect estimates for light smoke density were significantly higher at lag 1 (OR: 1.12, 95% CI: 1.05, 1.19 vs OR: 0.99, 95% CI: 0.92, 1.06). No significant differences were observed by age, race, ethnicity, or Medicaid eligibility at lag 0-4. These findings suggest evidence of a marginal increase in odds of ischemic stroke associated with previous-day, 3-day, and 4-day light density smoke exposure. Further research is needed to characterize better the extent to which cardiovascular and cerebrovascular effects are associated with wildfire smoke exposure among older adults and determine who among the population may be most susceptible to wildfire-related air pollution.

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Introduction

Wildfire smoke is a significant source of exposure to elevated levels of air pollution.[1-3] Extreme weather, such as increased seasonal temperatures and extended droughts, have intensified the frequency, severity, and duration of wildfire events over the last several decades, particularly in the Western U.S. [3-6] Despite the overall national decline in air pollution also witnessed in recent decades,[7] the increased prevalence of seasonal wildfire events is predicted to increase levels of fine particulate matter, particles with an aerodynamic diameter ≤2.5 μm ($PM_{2.5}$).[8-10] Concentrations of $PM_{2.5}$ are markedly elevated by wildfire smoke emissions,[11,12] exceeding levels well above the National Ambient Air Quality Standards (NAAQS) for criteria air pollutants regulated by the U.S. Environmental Protection Agency (EPA) under the Clean Air Act.[13] $PM_{2.5}$ is a known risk factor for respiratory and cardiovascular morbidity and mortality; thus, it is a particular pollutant of public health concern as populations become increasingly impacted by wildfire smoke exposure.[11,14-16]

While the health effects of acute exposure to ambient air pollution, including $PM_{2.5}$, NO_2, and O_3 have been widely reported,[17-22] the health effects associated with wildfire smoke have not been studied extensively. Among a few published toxicological studies, it is generally understood that wildfire-specific $PM_{2.5}$ may have a differential impact on human health than ambient air pollution from other sources due to its complex chemical composition.[23,24] Whereas previous epidemiological studies assessing the health impacts of wildfire smoke exposure have more consistently reported significant respiratory health effects,[25-27] the evidence for cardiovascular health impacts has been mixed.[5,26-32]

A recent critical review by Reid et al. (2016) concluded that the evidence of associations between wildfire smoke exposure and cardiovascular morbidity is inconsistent. However, recent studies suggest positive associations between wildfire smoke exposure and specific cardiovascular and cerebrovascular outcomes, such as out-of-hospital cardiac arrest (OHCA),[30,32] acute myocardial infarction (AMI),[29] congestive heart failure (CHF),[26,33] ischemic heart disease (IHD),[25] and ischemic stroke.[26,31] More recent evidence additionally suggests an increased risk of COPD mortality associated with wildfire smoke

exposure.[34] Previous studies have predominantly measured associations using health data from hospitalization and emergency department (ED) visits. To this author's knowledge, presently, no study has assessed the specific relationship between first occurring (e.g., first diagnosis) cardiovascular morbidity and wildfire smoke exposure. This study investigates associations between incident cardio- and cerebrovascular events among the Medicare population and exposure to smoke density, comparing wildfire smoke days to non-smoke days in California during the 2017 wildfire season. We leverage (1) remote sensing and ground-based air monitoring data to classify levels of smoke density based on estimated concentrations of $PM_{2.5}$ and characterize exposure at the ZIP code level, and (2) a large and representative study population of Medicare enrollees (aged 65 years and older). Thus, this study better clarifies the cardiovascular-related health risks of wildfire smoke exposure among older adults and evaluate whether specific populations are more susceptible to wildfire-related air pollution.

Methods

Study Population and Health Data

Health data were obtained from the Centers for Medicare and Medicaid Services (CMS) and include all California-based Medicare beneficiaries aged 65 years or older, from January 1, 2017 to December 31, 2017. Data were extracted for all Medicare beneficiaries who had a first-occurring cardiovascular-related disease, defined as any health event causing cardiac or circulatory system dysfunction during the wildfire season between April 1, 2017 and December 31, 2017. This study period matches the duration of events that occurred during the 2017 wildfire season. For each beneficiary, information on the date of first diagnosis, age, sex, race, ethnicity, ZIP code of residence, and Medicaid eligibility (a proxy for socioeconomic status (SES), representing individuals eligible for both Medicare and Medicaid, was extracted. In addition, each beneficiary had an associated de-identified beneficiary ID. First-occurring diagnoses for cardiovascular endpoints include ischemic heart disease (IHD), congestive heart failure (CHF), acute myocardial infarction (AMI), and atrial fibrillation (AF). The cerebrovascular endpoint of interest was ischemic stroke. Chronic obstructive pulmonary disease (COPD) was included in the

analysis as a cardiopulmonary endpoint. For each health outcome, the ZIP code of residence and the date of the first diagnosis defined the location and exposure time of the case.

Exposure Data

Air pollution data, including daily average $PM_{2.5}$ concentrations ($\mu g/m^3$) and smoke plume density, were estimated at 3-km spatial resolution for all of California during the study period (April – December) in 2017. These data were obtained from a larger dataset, which comprises a data fusion product that integrates several exposure modeling techniques and data sources to quantify spatiotemporal estimates of $PM_{2.5}$ and smoke concentrations. Details of each data source and methodology have been previously published.[35-37] In brief, daily $PM_{2.5}$ measures were estimated on a gridded spatial surface using an established geostatistical surfacing algorithm developed by Al-Hamdan et al. (2009). The algorithm integrates satellite measurements of aerosol optical depth (AOD) from the Moderate Resolution Imaging Spectrometer (MODIS) instrument aboard the National Aeronautics and Space Administration (NASA) Aqua satellite and ground-level $PM_{2.5}$ monitoring data from the EPA air quality system (AQS) using multiple regression models, B-Spline smoothing, and inverse distance weighted (IDW) surface-fitting approaches to estimate daily $PM_{2.5}$ on a 3-km gridded surface across the United States.[35]

All covered 3 km^2 grid cells were linked to smoke plume density estimates obtained from the National Oceanic and Atmospheric Administrations' (NOAA) Office of Satellite and Product Operations (OSPO)'s Hazard Mapping System's Smoke Product (HMS). HMS utilizes satellite fire detection algorithms, and visible imagery collected multiple times per day during daylight hours from Polar Operational Environmental Satellites (POES) and Geostationary Operational Environmental Satellites (GOES) to provide daily measures of the geographic extent, period of time, and estimated concentration of visible smoke plumes.[36] To further characterize smoke-associated $PM_{2.5}$ levels, satellite measures are assessed by analysts and a categorical estimate of smoke density is assigned to each grid cell within a geographic area where a smoke plume is detected.[38] Smoke plume density values range from 0-3,

corresponding to either no observed smoke plume (0), or light (1), moderate (2), and heavy (3) smoke density categories, which are associated with smoke-attributable $PM_{2.5}$ concentrations ranging from 0-10 $\mu g/m^3$; 10.5–21.5 $\mu g/m^3$; ≥22 $\mu g/m^3$, respectively.[36,39]

Meteorological Data

In order to adjust for potential confounding, meteorological covariates, including daily 1-km resolution air temperature and relative humidity, were included in the statistical analysis. Data were acquired from a larger dataset previously published by Bi et al., 2020, and subsetted to align with the study period.[40] Bi and colleagues (2020) interpolated meteorological parameters from the North American Regional Reanalysis data (NARR) at 32 km^2 gridded resolution and from the North American Land Data Assimilation System (NLDAS) at 0.125° resolution to produce daily estimates in 1-km^2 grid cells.

Exposure Assessment

Grid-level exposure and meteorological data were linked to the health data by ZIP code and the date on which the first diagnosis occurred to characterize population exposure to wildfire smoke. Daily values were assigned to each Medicare beneficiary's residential ZIP code by linking each ZIP code centroid to the nearest 3-km grid cell for wildfire smoke density values (0-3) and 1-km grid cell for temperature and relative humidity to produce daily estimates for each ZIP code in California, between April 1, 2017 to December 31, 2017. A smoke-day is defined as a day with a smoke density value > 0 at a given ZIP code centroid, where a categorical value for smoke plume density corresponds to 1 – light, 2 – moderate, and 3 – heavy. Health events in ZIP code locations that did not match with exposure data were excluded.

Statistical Analysis

A case-crossover design was employed using conditional logistic regression to estimate associations between wildfire smoke exposure and cardiovascular-related health outcomes. Using this approach, time-invariant confounding factors, such as individual-level characteristics or risk factors, are controlled by design.[41] By matching individual cases to themselves at referent or control times, each case serves as their own control.[42] As such, the analysis makes within-subject comparisons while controlling for temporal trends in the exposure based on the referent selection.[43] In this analysis, a case day is defined as the date of first diagnosis for each health outcome. The level of smoke exposure on each case day, corresponding to the ZIP code of residence, was compared to the level of smoke exposure on control days, before and after the day on which the event occurred. Each case day was matched by the day of the week, within the same month, yielding 3 or 4 referent control days per case.

By fitting conditional logistic regression models, smoke exposure was compared on case days and control days using odds ratios (ORs) to estimate the association between first diagnoses for each cardiovascular-related event on smoke days (levels of smoke exposure: 1-3) relative to non-smoke days (no exposure). The outcome measures include ischemic heart disease (IHD), congestive heart failure (CHF), acute myocardial infarction (AMI), and atrial fibrillation (AF), ischemic stroke, and chronic obstructive pulmonary disease (COPD). The primary exposure measure was specified as a categorical variable for daily smoke level, corresponding to 1 – light, 2 – moderate, and 3 – heavy smoke density. In addition, continuous daily air temperature and relative humidity were included in all models to adjust for potential temporal trends in the exposure.

In the primary analysis, exposure was defined as the level of smoke exposure on the day of the event (lag 0). Separate analyses were performed to examine individual exposure lag periods, 1-4 days before the day on which the health event occurred (lag 1-4), adjusted for corresponding lags in temperature and relative humidity. Subgroup analyses were performed by sex, race, or ethnicity (Unknown, White, Black, Other, Asian, Hispanic, Native American), age group (≤69, 70-74, 75-79, 80-84, 85-89, 90-94, ≥95), and

Medicaid eligibility to assess for effect modification. Separate models were fitted for each subgroup to evaluate differences in estimated ORs between categories.

All computations for this study were run on the Rollins High-Performance Computing (HPC) Cluster at Emory University. All statistical analyses were conducted using R software, version 4.0.2. The Emory Institution Review Board approved this research under the Environmental Exposures and Health Impacts Study (IRB ID: STUDY00000316). A waiver of informed consent was granted.

Results

Descriptive characteristics of the study population are presented in Table 1. A total of 5 cases were excluded due to non-matching between exposure data and the location of the event. One day of weather data was interpolated by averaging the values on the day prior and the day after for each ZIP code due to missingness. A total of 247,571 incident cardiovascular-related health events occurred among the Medicare population during the study period (April 1 – December 31, 2017) in California. Of these, 30,464 were ischemic stroke, 71,920 ischemic heart disease, 56,324 congestive heart failure, 44,132 chronic obstructive pulmonary disease, 11,629 acute myocardial infarction, and 33,102 atrial fibrillations. The mean age was 76.12 years (73.42 – 78.89), and 50% were between the ages of 65-74. Approximately 50% were female (45.8% - 53.3%), 70% were White (70.1% - 77.2%), and 32% were Medicaid eligible (27.3% - 35.5%).

The exposure data represent full spatiotemporal coverage over the study period. Daily average $PM_{2.5}$ concentrations ($\mu g/m^3$) and meteorological data are presented in Table 2. Overall, the average (±SD) daily $PM_{2.5}$ concentration among ZIP codes where Medicare beneficiaries resided was 11.48 ± 5.46 $\mu g/m^3$ [Median: 10.70 $\mu g/m^3$; IQR: 529.40 $\mu g/m^3$]. The average (±SD) air temperature was 74.06 ± 12.49 °F, and average (±SD) relative humidity was 46.53% ± 22.40% (Table 2). There was considerable variability in $PM_{2.5}$ values over the study period. Elevated levels of $PM_{2.5}$ peaked in December 2017 with a maximum concentration of 529.4 $\mu g/m^3$ in Ojai, CA, which tracks with the time point of the Thomas Fire in Ventura

and Santa Barbara Counties.[44] Of the total cardiovascular-related events that occurred during the wildfire season, 87.57% occurred on non-smoke days, and 10.5%, 1.51%, and 0.42% occurred on light, moderate, and heavy smoke days, respectively. Moderate and heavy smoke days occurred most frequently between July and December (Fig. 1). Figure 1 presents the association between Daily $PM_{2.5}$ concentrations and smoke density during the wildfire season (April 1 – December 31, 2017). Comparing across categories of smoke density, daily mean $PM_{2.5}$ on non-smoke days was 11.17 $\mu g/m^3$ (0 - 196.9 $\mu g/m^3$), followed by daily averages of 12.62 $\mu g/m^3$ (0 – 139.4 $\mu g/m^3$), 17.23 $\mu g/m^3$ (1.4 – 185.6 $\mu g/m^3$), and 27.65 $\mu g/m^3$ (1.3 – 529.4 $\mu g/m^3$) on light, moderate, and heavy smoke days, respectively (Fig. 2).

For each cardiovascular health outcome assessed, the estimated odds (ORs) associated with exposure to increased levels of wildfire smoke density were largely null (Table 3). No increased risk was observed for ischemic heart disease, congestive heart failure, COPD, acute myocardial infarction, or atrial fibrillation. These results were generally consistent across the lagged effect estimates (1-4 days). Ischemic stroke was associated with light wildfire smoke density at lag 1 (OR: 1.05, 95% CI: 1.01, 1.10), lag 3 (OR: 1.07, 95% CI: 1.02, 1.12), and lag 4 (OR: 1.07 (95% CI: 1.02, 1.12), though effect estimates were null at lag 0 (OR: 1.02, 95% CI: 0.97, 1.07) and lag 2 (OR: 1.03, 95% CI: 0.99,1.08). No corresponding associations were observed for exposure to moderate and heavy smoke density.

In subgroup analyses, the estimated risk of ischemic stroke differed by sex. For women compared to men, effect estimates for light smoke density were significantly higher at lag 1 (OR: 1.12, 95% CI: 1.05, 1.19 vs OR: 0.99, 95% CI: 0.92, 1.06) and marginally higher at lag 2 (OR: 1.06, 95% CI: 0.99, 1.13 vs OR: 1.01, 95% CI: 0.94, 1.08) and lag 4 (OR: 1.08, 95% CI: 1.01, 1.15 vs OR: 1.06, 95% CI: 0.99, 1.14). However, significant positive effect estimates were observed among men at lag 3 (OR: 1.09, 95% CI: 1.02, 1.17 vs OR: 1.05, 95% CI: 0.99, 1.12). Comparisons at increased levels of smoke density were largely null, although at lag 4, we observed notably larger effect estimates among women for heavy smoke density (OR: 1.30, 95% CI: 0.98, 1.70 vs. OR: 1.07, 0.79, 1.44). No significant differences were observed by age, race, ethnicity, or Medicaid eligibility at lag 0-4. Higher uncertainty was indicated by wider confidence intervals, which may be attributed to the overall lower number of health events across these subgroups. Among the

≥65 age groups, at lag 1, positive associations for light smoke density were largest among cases 90-94 years old (OR: 1.09, 95% CI: 0.93, 1.30). Among race and ethnic groups, effect estimates for light smoke density were the largest among Hispanics (OR: 1.20, 95% CI: 0.99,1.44). Larger effect estimates were not observed by Medicaid eligibility (OR: 0.93, 95% CI: 0.93, 1.10 vs OR: 1.08, 95% CI: 1.02, 1.14). Figure 3. presents the effect estimates for ischemic stroke stratified by sex.

Discussion

This study investigated associations between incident cardio- and cerebrovascular health events and acute exposure to wildfire smoke among the Medicare population, comparing levels of smoke density on wildfire smoke days to non-smoke days in California during the 2017 wildfire season. Using spatiotemporal data that leverages remote sensing and ground-based air monitoring network data to classify levels of smoke density based on estimated concentrations of $PM_{2.5}$ at the ZIP code level and a large and representative study population of Medicare enrollees (aged 65 years and older), this investigation found no evidence of increased risk for first-occurring cardiovascular health events across all exposure time points (lag days 0-4), after adjusting for temperature and relative humidity. A marginally significant increased risk of ischemic stroke was associated with the lagged effects of exposure to light density smoke, which corresponds to NOAA HMS smoke plume densities associated with smoke-attributable $PM_{2.5}$ concentrations ranging from 0-10 $\mu g/m^3$.[39]

Given the large variability in the distribution of $PM_{2.5}$ concentrations observed across categories, particularly between none and light smoke densities (Fig. 1) over the study period, further validation is warranted to assess whether this misalignment is a result of a weak correlation between HMS smoke data and ground-level $PM_{2.5}$ concentrations, particularly at lower densities. This finding is consistent with the results of a similar study reported by Fadadu et al. (2020). There is concern that exceptionally high $PM_{2.5}$ values characterized within a smoke density level of 0 in the HMS Smoke data may underestimate smoke-related $PM_{2.5}$ captured by satellite imagery. Therefore, the use of multiple exposure assessment methods

may provide more precise estimates. In subgroup analyses, this study observed larger estimated odds of ischemic stroke among women relative to men. However, there was no evidence of a clear, increasingly positive trend in effects. While the positive association may suggest differential outcomes by sex to light and heavy density smoke exposure during this period in California, more research on possible sex differences in susceptibility is needed to further substantiate this.

The link between short-term ambient $PM_{2.5}$ exposure and cardiovascular-related health outcomes, including ischemic heart disease, myocardial infarction, congestive heart failure, and out-of-hospital cardiac arrest, is well-established.[19,20,45] However, the current evidence regarding the cardiovascular effects of wildfire smoke exposure is limited and remains inconclusive. Several previous studies have reported null results for cardiovascular-related health effects,[5,14,15,26,46-49] although a few recent studies have found increased cardiovascular-related risks.[18,29-32] Specifically, significant effects have been reported for ischemic heart disease;[25,28] out-of-hospital cardiac arrest;[29,30,32] acute myocardial infarction;[29] and congestive heart failure.[33] Two other comparable studies have investigated effects for cerebrovascular health outcomes using similar methods and found significant associations with wildfire-specific $PM_{2.5}$. [26,31]

The positive associations observed between wildfire smoke exposure and ischemic stroke in this study are most comparable to the effects reported in a recent study by Wettstein et al. (2018), which evaluated the effects of wildfire smoke density and cardiovascular and cerebrovascular endpoints in eight air basins in California during the wildfire season in 2015. Overall, their study found significant positive associations between wildfire smoke density and both cardiovascular and cerebrovascular endpoints among the total adult population. Comparatively, Wettstein et al. (2018) observed a larger relative risk of ischemic stroke at increasing levels of smoke density among older adults (≥65 years old), finding a significantly positive association with moderate smoke density at lag day 3 (RR: 1.25, 95% CI: 1.04, 1.50). This difference may be due, in part, to the larger proportion of days with moderate to heavy smoke densities reported during the study period, given that their study found similar, although null, positive associations with light density smoke as the present analysis at lag 0 (RR: 1.07, 95% CI: 0.96, 1.20); lag 1 (RR: 1.08, 95% CI: 0.96, 1.21); lag 2 (RR: 1.12, 95% CI: 1.00, 1.25); and lag 4 (1.11, 95% CI: 1.00, 1.24). In contrast

to the present analysis, Wettstein et al. (2018) linked emergency department (ED) visit data to ZIP code-level HMS smoke density to estimate effects using a quasi-Poisson regression model. Given the smaller sample size and limited geographic extent, their study may be less statistically powered, yielding less precise effect estimates for cerebrovascular health events, as indicated by the overall wider confidence intervals reported.

The evidence of cerebrovascular impacts related to all-source ambient $PM_{2.5}$ exposure also remains inconsistent. Few observational studies have demonstrated associations between ambient $PM_{2.5}$ exposure and onset of ischemic stroke,[50-52] while others have reported null or negative results.[53,54] For example, a study by Wellenius et al. (2012) found an increased risk of stroke onset (OR: 1.34, (95% CI: 1.13, 1.58) was associated with exposure to $PM_{2.5}$ concentrations within a range of 15-40 $\mu g/m^3$ at lag 0-1, in Boston. However, their study found no increased risk when exposures preceded stoke onset beyond one day.[51] However, in a systematic review and meta-analysis, Shah et al. (2015) reported an association between $PM_{2.5}$ and stroke (RR: 1.011, 95% CI: 1.011, 1.012) per 10 $\mu g/m^3$ increase in $PM_{2.5}$ on both the day on which the event occurred and at lag 2.[22] While focused specifically on ambient $PM_{2.5}$, these findings elucidate inconsistencies in the magnitude of effects currently reported in the literature.

In addition to epidemiological studies, toxicological and experimental studies have provided broader insight into the underlying pathophysiological mechanism of association between particulate pollution exposure and cardiovascular-related health effects.[11,19,55] Three specific mechanisms characterize these biological responses. Generally, it is thought that exposure to fine particulate matter may induce oxidative stress and systemic inflammation by penetrating deep into the alveolar-capillary cells of the lungs.[11] Translocation across alveolar tissue may cause physiological responses such as endothelial cell dysfunction and alterations of blood proteins, lipid peroxidation, platelet activation, and thrombosis, which may impact blood vessels, increase the potential for blood clotting, and trigger cardiac stress.[11,51] Second, disturbances of the autonomic nervous system may induce inflammatory responses that diffuse into systemic circulation, leading to increased heart rate blood pressure.[53] Additionally, inflammation may cause abnormal platelet activation of the hemostatic system leading to hypercoagulation of the blood, potentially

triggering thrombosis.[56] These mechanisms form the basis of the association between adverse cardiovascular diseases and short-term exposure to elevated levels of ambient $PM_{2.5.}$

While it is plausible that vascular dysfunction, increased blood pressure, vasoconstriction, and thrombosis may be compounded by the effects of $PM_{2.5}$ from other sources,[19,22,56] less is understood about the pathophysiological mechanism underlying stroke, and specifically, of the pathways relative to the distinct subtypes of ischemic stroke and wildfire-specific $PM_{2.5}$. Further research is needed to characterize better the specific mechanisms underlying cardio- and cerebrovascular morbidity resulting from acute exposures to $PM_{2.5}$. Moreover, improved exposure assessment methods are needed to distinguish wildfire-specific $PM_{2.5}$ from all-sources particulate matter. Future studies would benefit from the use of multipollutant models, given that the distinct chemical composition of wildfire smoke is materially different from that of $PM_{2.5}$ from other sources.[14,57]

Several limitations of this study should be noted. The focus on one particular wildfire season in California limits the generalizability of the results. The analysis may not have been sufficiently powered to estimate cardiovascular-related effects at increased densities of smoke exposure accurately. With regard to the health data, the use of first-occurring cardiovascular and cerebrovascular health endpoints, as indicated by the date of first diagnosis in the Medicare data, did not provide information regarding baseline health characteristics, such as pre-existing comorbidities, which may be important indicators for measuring the increased risk of incident cardiovascular health outcomes associated with acute exposure to wildfire smoke. Similarly, Medicaid eligibility may be too crude of an indicator of SES, leading to unmeasured confounding. Further, the ascertainment of cases by diagnostic date may have led to outcome misclassification. As with any exposure assessment at an ecologic scale, the potential for exposure misclassification is of particular concern. Despite adjustment for meteorological factors, there remains a potential for residual confounding bias. Estimating daily concentrations at ZIP code-scale may not correlate well with individual-level exposure. Furthermore, the methods of exposure classification may have underestimated the spatial variability within ZIP codes, and further, the use of daily estimates may not characterize the dispersion of wildfire emissions accurately. Lastly, while satellite-based measurements

may improve the accuracy of exposure estimates by addressing the limitations of ground-based monitors, cloud cover and limited night-time coverage remain a limiting factor. Validated methods are needed to distinguish and better quantify source-specific wildfire $PM_{2.5}$. Improved spatiotemporal assessments of wildfire smoke pollution will strengthen hazard mapping tools and better inform wildfire risk management policy to protect public health.

Conclusion

This study examined associations between wildfire smoke exposure and incident cardio- and cerebrovascular events among the Medicare population. Using a large, geographically representative sample to compare levels of smoke density on wildfire smoke days to non-smoke days in California during the 2017 wildfire season, overall, this investigation did not identify an association between wildfire smoke exposure and increased cardiovascular morbidity. The findings suggest evidence of a marginal increase in odds of ischemic stroke associated with previous-day, 3-day, and 4-day light density smoke exposure. While the subgroup analyses should be considered cautiously, the findings suggest that women were more susceptible to ischemic stroke resulting from previous-day light density smoke exposure during this period in California. However, further investigation is warranted. Further research is needed to better characterize the extent to which cardiovascular and cerebrovascular effects are associated with wildfire smoke exposure among older adults and better determine who among the population may be most susceptible to wildfire-related air pollution. Improved methods for characterizing the health impacts of wildfire smoke exposure will better inform policy decisions surrounding wildfire smoke mitigation and other public health action to reduce threats to public health.

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Tables and Figures

Table 1. Descriptive Characteristics of the Medicare Population by Health Outcome Between April 1 to December 31, 2017.

Variables	All CVD	Ischemic Stroke	Ischemic Heart Disease	Congestive Heart Failure	COPD	Acute Myocardial Infarction	Atrial Fibrillation
Case, n	247,571	30,464	71,920	56,324	44,132	11,629	33,102
Age (years), mean (SD)	76.12 (8.69)	78.01 (8.65)	73.42 (7.79)	77.27 (8.79)	75.65 (8.60)	78.89 (8.94)	77.98 (8.86)
Age Group (5-year) (%)							
65-69	72,019 (29.1)	6,264 (20.6)	29,140 (40.5)	13,589 (24.1)	13,696 (31.0)	2,182 (18.8)	7,148 (21.6)
70-74	51,720 (20.9)	5,814 (19.1)	17,048 (23.7)	11,188 (19.9)	9,476 (21.5)	2,113 (18.2)	6,081 (18.4)
75-79	41,570 (16.8)	5,614 (18.4)	10,841 (15.1)	9,833 (17.5)	7,319 (16.6)	2,004 (17.2)	5,959 (18.0)
80-84	33,219 (13.4)	5,065 (16.6)	6,763 (9.4)	8,512 (15.1)	5,601 (12.7)	1,929 (16.6)	5,349 (16.2)
85-89	26,626 (10.8)	4,217 (13.8)	4,603 (6.4)	7,099 (12.6)	4,351 (9.9)	1,742 (15.0)	4,614 (13.9)
90-94	15,992 (6.5)	2,531 (8.3)	2,519 (3.5)	4,384 (7.8)	2,613 (5.9)	1,134 (9.8)	2,811 (8.5)
95+	6,425 (2.6)	959 (3.1)	1,006 (1.4)	1,719 (3.1)	1,076 (2.4)	525 (4.5)	1,140 (3.4)
Female (%)	125,207 (50.6)	16,251 (53.3)	35,018 (48.7)	29,019 (51.5)	23,357 (52.9)	5,321 (45.8)	16,241 (49.1)
Race (%)							
White	177,652 (71.8)	21,345 (70.1)	50,405 (70.1)	39,969 (71.0)	31,812 (72.1)	8,575 (73.7)	25,546 (77.2)
Black	12,945 (5.2)	1,843 (6.0)	3,606 (5.0)	3,208 (5.7)	2,519 (5.7)	630 (5.4)	1,139 (3.4)
Asian	22,977 (9.3)	3,062 (10.1)	6,717 (9.3)	5,283 (9.4)	4,270 (9.7)	1,033 (8.9)	2,612 (7.9)
Hispanic	12,437 (5.0)	1,706 (5.6)	3,701 (5.1)	3,039 (5.4)	2,090 (4.7)	540 (4.6)	1,361 (4.1)
Native American	992 (0.4)	127 (0.4)	277 (0.4)	233 (0.4)	198 (0.4)	65 (0.6)	92 (0.3)
Other	12,778 (5.2)	1,676 (5.5)	4,087 (5.7)	2,959 (5.3)	2,014 (4.6)	594 (5.1)	1,448 (4.4)
Unknown	7,790 (3.1)	705 (2.3)	3,127 (4.3)	1,633 (2.9)	1,229 (2.8)	192 (1.7)	904 (2.7)
Medicaid Eligibility (%)	80,810 (32.6)	10,300 (33.8)	22,538 (31.3)	19,229 (34.1)	16,121 (36.5)	3,574 (30.7)	9,048 (27.3)

Values are counts for case, number (%) for categorical variables, mean (standard deviation) for continuous variables.
CVD – Cardiovascular disease; COPD – Chronic obstructive pulmonary disease.

Table 2. Summary Statistics for Daily Average $PM_{2.5}$ and Meteorological Data by ZIP Code, During the California Wildfire Season, 2017.

			Percentile			
Variable	**Mean (SD)**	**Maximum**	**25%**	**50%**	**75%**	**IQR**
$PM_{2.5}$ ($\mu g/m^3$), mean (SD)	11.48 (5.46)	529.40	9.60	10.70	12.5	529.40
Temperature (°F), mean (SD)	74.06 (12.49)	116.71	65.11	72.63	82.36	95.42
Relative Humidity (%), mean (SD)	46.53 (22.40)	97.10	28.38	45.15	62.01	96.10

Daily modeled $PM_{2.5}$ estimates were linked to 2,251 ZIP code centroids corresponding to the residential address of each Medicare beneficiary. IQR, interquartile range.

Table 3. Odd Ratios for Cardiovascular-related Events on Smoke Days Relative to Non-Smoke Days at Lag 0 – 4 Days, by Health Outcome and Smoke Density.

Health Outcome	Lag (Days)	Lag 0	Lag 1	Lag 2	Lag 3	Lag 4
	Smoke Density	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
Ischemic Stroke	Light	1.02 (0.97, 1.07)	1.05 (1.01, 1.10) *	1.03 (0.99,1.08)	1.07 (1.02, 1.12) *	1.07 (1.02, 1.12) *
	Moderate	0.89 (0.80, 1.00)	0.98 (0.87, 1.09)	0.92 (0.82,1.02)	1.00 (0.89, 1.11)	0.99 (0.88, 1.10)
	Heavy	0.91 (0.75, 1.11)	0.89 (0.73, 1.09)	0.98 (0.79, 1.21)	0.94 (0.75, 1.18)	1.18 (0.97, 1.44)
Ischemic Heart Disease	Light	0.99 (0.96, 1.02)	1.00 (0.97, 1.03)	0.98 (0.95, 1.01)	0.99 (0.96,1.02)	1.00 (0.97, 1.03)
	Moderate	0.88 (0.82, 0.95)	0.93 (0.87, 1.00)	0.99 (0.93, 1.06)	0.96 (0.90, 1.03)	0.97 (0.90, 1.04)
	Heavy	0.86 (0.75, 0.98)	0.92 (0.81, 1.05)	0.82 (0.71, 0.94)	0.93 (0.80, 1.07)	0.97 (0.85, 1.12)
Congestive Heart Failure	Light	0.99 (0.96, 1.02)	1.01 (0.97, 1.04)	1.00 (0.97, 1.04)	0.98 (0.95, 1.01)	1.00 (0.96, 1.03)
	Moderate	0.88 (0.82, 0.95)	1.02 (0.94, 1.11)	0.97 (0.90, 1.06)	0.90 (0.83, 0.98)	0.96 (0.89, 1.05)
	Heavy	0.86 (0.75, 0.98)	1.00 (0.86, 1.15)	0.96 (0.82, 1.11)	0.82 (0.69, 0.97)	1.04 (0.89, 1.22)
COPD	Light	1.01 (0.97, 1.05)	1.02 (0.98, 1.06)	1.01 (0.97, 1.05)	1.03 (0.99, 1.07)	1.03 (0.99, 1.07)
	Moderate	0.94 (0.85, 1.03)	0.92 (0.84, 1.02)	1.01 (0.93, 1.11)	0.87 (0.79, 0.96)	1.00 (0.91, 1.10)
	Heavy	0.91 (0.77, 1.08)	1.04 (0.88, 1.22)	0.87 (0.73, 1.04)	0.88 (0.73, 1.07)	0.94 (0.79, 1.12)
Acute Myocardial Infarction	Light	0.97 (0.89, 1.04)	1.02 (0.95, 1.10)	1.01 (0.94, 1.09)	0.99 (0.91, 1.06)	0.98 (0.91, 1.06)
	Moderate	1.06 (0.89, 1.25)	0.98 (0.82, 1.17)	0.83 (0.69, 1.00)	0.91 (0.76, 1.08)	0.90 (0.75, 1.07)
	Heavy	1.11 (0.80, 1.54)	1.18 (0.88, 1.58)	1.33 (0.99, 1.78)	1.01 (0.74, 1.39)	1.19 (0.87, 1.63)
Atrial Fibrillation	Light	1.01 (0.97, 1.06)	1.01 (0.96, 1.05)	1.02 (0.98, 1.07)	0.99 (0.94, 1.03)	1.00 (0.95, 1.04)
	Moderate	0.92 (0.82, 1.02)	0.97 (0.87, 1.07)	0.92 (0.83, 1.02)	0.92 (0.83, 1.02)	1.03 (0.93, 1.13)
	Heavy	0.88 (0.73, 1.07)	0.78 (0.64, 0.95)	1.07 (0.88, 1.29)	1.05 (0.86, 1.28)	0.82 (0.67, 1.02)

[a]Models adjusted for temperature and relative humidity. OR, odds ratio; 95% CI, Confidence interval

* Statistically significant odds ratios

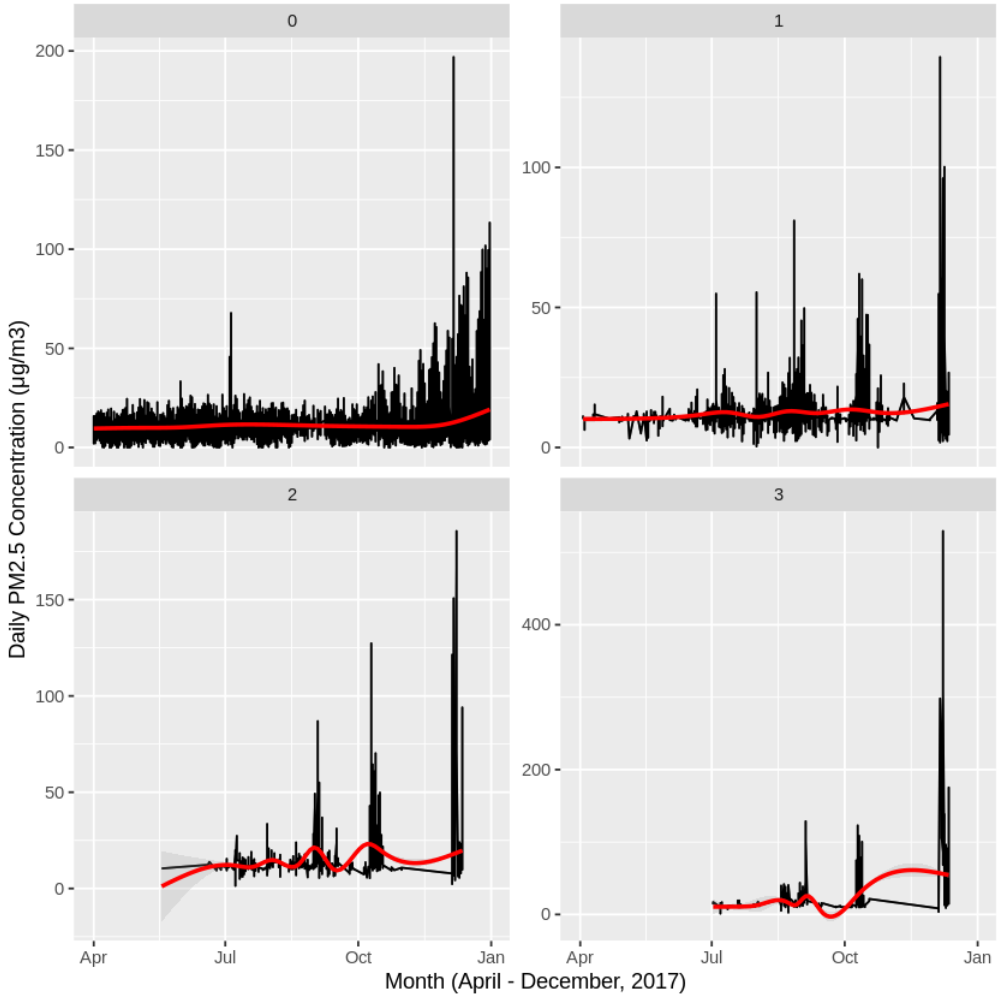

Figure 1. Daily $PM_{2.5}$ concentrations and smoke density (0-3) at ZIP code-scale by day and month during the wildfire season (April 1 – December 31, 2017). The red line depicts smoothed conditional mean $PM_{2.5}$ levels.

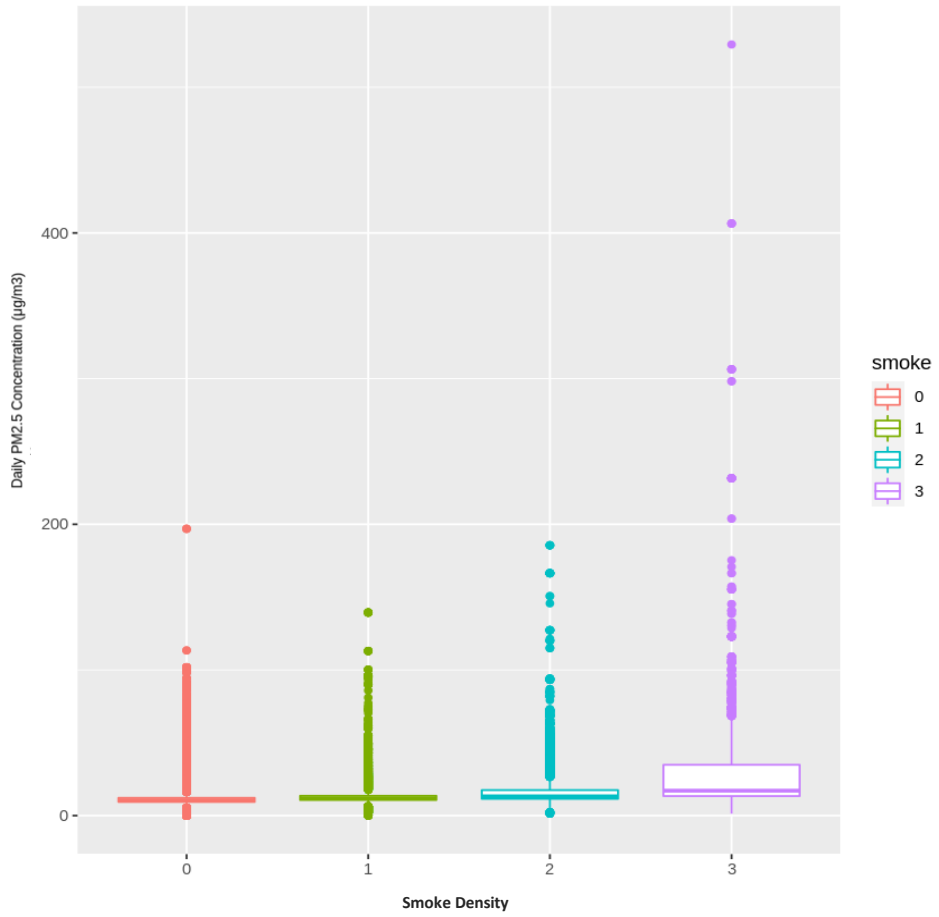

Figure 2. Box plot comparing daily $PM_{2.5}$ concentrations and smoke plume density categories (0-3) at ZIP code-scale for each day during the wildfire season (April 1 – December 31, 2017).

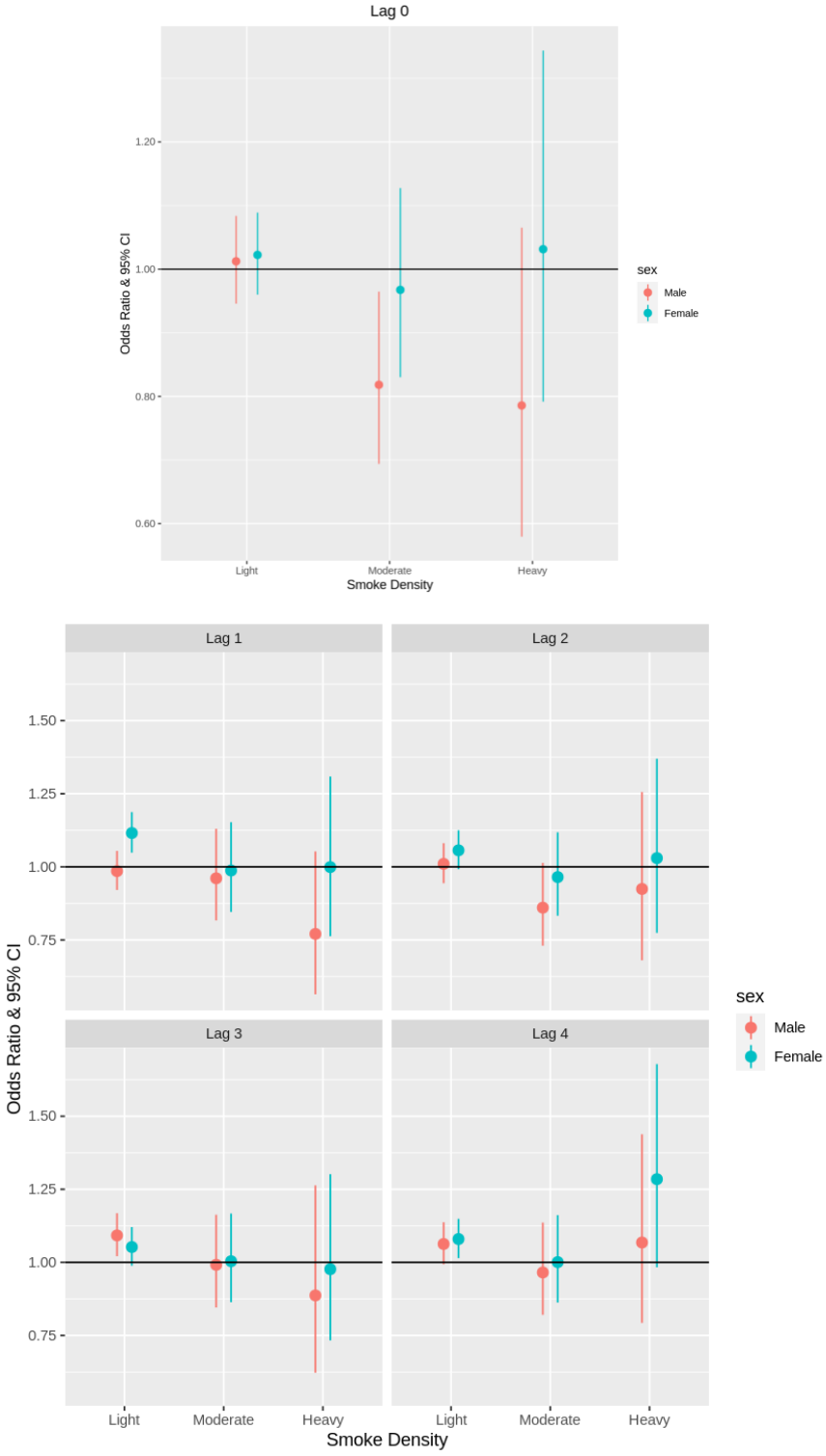

Figure 3. Odd ratios for ischemic stroke on smoke days relative to non-smoke days at lag 0 – 4 days during the wildfire season (April 1 – December 31, 2017), stratified by smoke density and by sex.