Wildfire smoke $PM_{2.5}$ and mortality in the contiguous United States

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Abstract

Despite the growing evidence on the health effects of wildfire smoke in the western U.S., the nationwide mortality risk and burden attributable to wildfire smoke fine particles ($PM_{2.5}$) remain unclear. This study aims to investigate the association between wildfire smoke $PM_{2.5}$ and mortality from all causes, cardiovascular diseases, respiratory diseases, and mental disorders, and calculate the corresponding attributable mortality burden in all 3,108 counties in the contiguous U.S., 2006–2016. Monthly county-level mortality counts were collected from National Center for Health Statistics. Wildfire smoke $PM_{2.5}$ concentration was derived from a 10×10 km^2 resolution spatiotemporal model. Controlling for non-smoke $PM_{2.5}$, air temperature, and unmeasured spatial and temporal confounders, we found that a 1 $\mu g/m^3$ increase in smoke $PM_{2.5}$ was significantly associated with an increase of 0.14% (95% confidence interval [CI]: 0.11%, 0.17%) in all-cause mortality, 0.13% (95% CI: 0.08%, 0.18%) in cardiovascular mortality, 0.16% (95% CI: 0.07%, 0.25%) in respiratory mortality, and 1.08% (95% CI: 0.93%, 1.23%) in mental disorder mortality. Smoke $PM_{2.5}$ contributed to approximately 1,141 all-cause deaths/year (95% CI: 893, 1,388) in the contiguous U.S., of which over three-fourths were from cardiovascular, respiratory, and mental causes. We found a higher vulnerability among males than females, people aged 0 to 64 years than those ≥ 65 years, and racial/ethnic minorities than non-Hispanic White people. Mild droughts were found to enhance the association between smoke $PM_{2.5}$ and mortality. Our results indicate that wildfire smoke $PM_{2.5}$ harms both physical and mental health, which suggests the need for more effective wildfire mitigation strategies and public health responses in the U.S.

Significance Statement

Wildfires activities have significantly increased in the United States in recent decades. Smoke pollutants emitted by wildfires, particularly $PM_{2.5}$, can bring adverse health effects. However, the nationwide wildfire smoke $PM_{2.5}$-related mortality risk and burden remain unclear. Utilizing wildfire smoke $PM_{2.5}$ and mortality data in the contiguous U.S. from 2006 to 2016, we found significant associations between smoke $PM_{2.5}$ and increased mortality risks from all causes, cardiovascular diseases, respiratory diseases, and mental disorders. Each year, smoke $PM_{2.5}$ contributed to an estimated over one thousand deaths in the U.S., indicating a great number of indirect deaths brought by wildfires that official tolls could not capture. This study demonstrates the detrimental effects of wildfire smoke $PM_{2.5}$ on both physical and mental health and calls for more effective wildfire prevention and mitigation policies in the U.S.

Main Text

Introduction

Wildfire is a growing public health concern in the United States. The country has witnessed a marked increase in the area affected by wildfires over the past few decades, with the burned area roughly quadrupling (1). In recent years, wildfire contributed to up to 25% of fine particulate matter ($PM_{2.5}$) across the U.S., and up to half in some Western regions (1). Driven by the warming climate, the prevalence, frequency, and intensity of wildfire activities are expected to increase in the future (2). Among the various air pollutants emitted by wildfires, $PM_{2.5}$ has received great attention due to its ability to deeply penetrate the respiratory system and demonstrated links to public health (3). In addition, because of different chemical composition and smaller particle size, studies suggested that the toxicity of wildfire smoke $PM_{2.5}$ could be different from urban background $PM_{2.5}$, potentially more lethal (4, 5). Previous studies on the health effects of wildfire smoke mostly focused on the western U.S., where the majority of large fires occurred (5-7). However, the pollutants from wildfire smoke can travel long distances from the source, potentially affecting human health thousands of kilometers away outside the West (8).

In recent years, studies consistently reported a positive relationship between wildfire smoke exposure and all-cause mortality (7, 9, 10). Among specific causes of mortality, respiratory and cardiovascular diseases received most attention, with growing studies linking human exposure to wildfire smoke with increased risks of respiratory and cardiovascular mortality (9-11). However, in addition to the physical health harms, mental health can also be potentially threatened by wildfire smoke. Some studies have linked wildfires to mental outcomes, such as anxiety, depression, poor sleep quality, and posttraumatic stress disorder (7, 12, 13), but the relationship between wildfire smoke and mental disorder mortality was rarely analyzed in previous studies.

Furthermore, the effects of wildfire smoke $PM_{2.5}$ can be heterogenous among population subgroups due to physiological, behavioral, and socioeconomic factors (14). Previous studies indicated that demographic factors such as sex, age and race/ethnicity may modify the association between smoke $PM_{2.5}$ and health outcomes (9, 14, 15). However, existing research generated contradictory findings and is insufficient to identify specific subpopulations that are more susceptible to wildfire smoke exposure (7). For example, a study in Australia reported that people ≥ 65 years old had higher bushfire smoke-related rates of respiratory hospitalizations compared to their younger counterparts (16), but another study in North Carolina found that the association between peat bog wildfire smoke and emergency department visits for chronic obstructive pulmonary disease, pneumonia, and acute bronchitis were higher among people < 65 years old than those older (17). Greater understanding of susceptibility to wildfire exposure among specific subgroups is needed to help inform wildfire mitigation policies and address environmental justice issues.

Besides demographic factors, drought, which often co-occurs with wildfires, may also serve as an effect modifier. Drought is a complex phenomenon resulting from precipitation deficiency, high temperature, low relative humidity, and other meteorological and hydrological factors (18). Studies have shown stronger mortality effects of air pollution at higher air temperatures and lower humidity levels (19-21), but little is known about whether drought, the manifestation of the complicated interactions among multiple environmental factors, can enhance the association between wildfire smoke $PM_{2.5}$ and mortality.

Constrained by a lack of nationwide validated data on pollutant concentrations attributable to wildfire smoke, many previous studies on the impact of wildfire smoke on health outcomes have been focusing on episodes with high wildfire smoke exposure (or smoke wave) using binary measures of smoke concentrations (22). Recently, a machine learning model was developed to estimate daily wildfire smoke $PM_{2.5}$ concentrations for the contiguous U.S., using a combination of meteorological factors, fire variables, aerosol measurements, and land use and elevation data (23). This new, high-resolution wildfire smoke $PM_{2.5}$ dataset (10×10 km^2) enabled us to further examine the impact of wildfire smoke over a full range – from the more common, low-level smoke concentrations to the increasingly frequent extremely high concentrations.

Utilizing the nationwide wildfire smoke $PM_{2.5}$ and mortality data, this study aimed to (a) estimate the associations of smoke $PM_{2.5}$ exposure with county-level all-cause mortality and mortality of cardiovascular and respiratory diseases and mental disorders, (b) calculate the attributable cause-specific mortality burden from 2006 to 2016, and (c) examine whether the smoke $PM_{2.5}$ related mortality risk varies among people of different sex, age, and racial/ethnicity groups and different levels of drought.

Results

Description of wildfire smoke $PM_{2.5}$ and mortality in the contiguous U.S.

From 2006 to 2016, all 3,108 counties in the contiguous U.S. had experienced some amount of wildfire smoke $PM_{2.5}$, with the western, north central, and southeastern counties being exposed to higher monthly average concentrations than other regions (**Fig. 1A**). Although wildfire smoke $PM_{2.5}$ concentrations were generally higher in summer months than in winter months, the average concentration remained above zero for the majority of the study period (**Fig. S1**). The average concentration of smoke $PM_{2.5}$ across all county-months was 0.39 μg/m^3, but the highest smoke $PM_{2.5}$ concentration could exceed 70 μg/m^3 (e.g., 70.95 μg/m^3 levels observed in September 2012 in Lemhi County, Idaho). A total of 27,812,837 deaths were included in this study, including 8,826,110 deaths from cardiovascular diseases, 2,713,137 deaths from respiratory diseases, and 1,364,807 deaths from mental and behavioral disorders (hereafter referred to as "mental disorders"; **Table S1**).

Wildfire smoke $PM_{2.5}$ related cause-specific mortality risk and mortality burden

The association between smoke $PM_{2.5}$ and all-cause mortality was found to be near-linear in the linearity test (**Fig. S2**), so we used a linear term to model this relationship in the main model. Using a two-way fixed effects (TWFE) model to control for air temperature, non-smoke $PM_{2.5}$, and unmeasured spatial and temporal confounders, we found that a 1 μg/m^3 increase in smoke $PM_{2.5}$ concentration was significantly associated with a 0.14% (95% confidence interval [CI]: 0.11%, 0.17%) increase in all-cause mortality (**Fig. 2A**). On average, approximately 1,141 all-cause deaths (95% CI: 893, 1,388) were attributable to smoke $PM_{2.5}$ in the contiguous U.S. per year. The spatial distribution of this attributable burden was generally consistent with the distribution of smoke $PM_{2.5}$ concentration (**Fig. 1B**).

As shown in **Fig. 2A**, for cause-specific mortality, a 1 μg/m^3 increase in smoke $PM_{2.5}$ was significantly associated with an increase of 0.13% (95% CI: 0.08%, 0.18%) in cardiovascular disease mortality, 0.16% (95% CI: 0.07%, 0.25%) in respiratory disease mortality, and 1.08%

(95% CI: 0.93%, 1.23%) in mental disorder mortality. Each year, smoke $PM_{2.5}$ contributed approximately 333 deaths from cardiovascular diseases (95% CI: 207, 459), 118 deaths from respiratory diseases (95% CI: 48, 187), and 417 deaths from mental disorders (95% CI: 360, 473). Among the total wildfire smoke $PM_{2.5}$-attributable deaths, approximately 76.07% were from these three specific causes (**Fig. 2B**).

Wildfire smoke $PM_{2.5}$ related all-cause mortality risk in different subgroups

The association between smoke $PM_{2.5}$ and all-cause mortality varies across different sex, age, and race/ethnicity groups (**Fig. 3**). The estimated percent change in all-cause mortality per 1 $\mu g/m^3$ increase in smoke $PM_{2.5}$ was significantly higher in males (0.18%; 95% CI: 0.15%, 0.22%) compared to females (0.10%; 95% CI: 0.06%, 0.14%; *p* value of difference: 0.002). Compared to people aged 65 years and above (0.17%; 95% CI: 0.14%, 0.21%), people aged 0 to 64 years (0.31%; 95% CI: 0.26%, 0.36%) had significantly higher smoke $PM_{2.5}$ related all-cause mortality risk (*p* value of difference: <0.001). In addition, the between-group difference was particularly evident across race/ethnicity, with non-Hispanic Black people (0.78%; 95% CI: 0.72%, 0.84%) and Hispanic people (0.69%; 95% CI: 0.64%, 0.74%) significantly more vulnerable than non-Hispanic White people (0.12%; 95% CI: 0.08%, 0.16%; *p* values of difference: < 0.001).

Effect modification by drought

From 2006 to 2016, 23.28% of the county-months had mild droughts and 8.68% had severe droughts, with western and southern counties being exposed most. **Fig. 4A & B** display the overlaps of the distribution of mild and severe droughts and wildfire smoke $PM_{2.5}$ in contiguous U.S. counties, indicating the prevalent co-occurrence of these two conditions. Specifically, the western and southern counties experienced the most months with both mild drought and smoke $PM_{2.5}$, while severe drought co-occurred with smoke $PM_{2.5}$ mostly in southern U.S. counties in Texas, Louisiana, and Florida.

We observed a significant effect modification by drought for the association between smoke $PM_{2.5}$ and all-cause mortality (**Fig. 4C**). Compared to county-months with no drought (0.10%; 95% CI: 0.07%, 0.14%), the estimated percent change in all-cause mortality per 1 μg/m^3 increase in smoke $PM_{2.5}$ became significantly higher during mild droughts (0.50%; 95% CI: 0.42%, 0.57%; *p* value of difference: < 0.001). No significant association was observed when there were severe droughts.

Sensitivity analyses

Sensitivity analyses showed that our results generally remained robust when additionally adjusting for dew point temperature and nitrogen dioxide (NO_2) and ozone (O_3), not adjusting for non-smoke $PM_{2.5}$, using alternative numbers of degree of freedom for air temperature, and restricting the analysis to counties that have high smoke $PM_{2.5}$ exposure (≥ 20 μg/m^3). The association between smoke $PM_{2.5}$ and all-cause mortality tend to be the highest during the current month and decreasing over the later one and two months.

Discussion

To the best of our knowledge, this is the first study evaluating the wildfire smoke $PM_{2.5}$ related cause-specific mortality risk and attributable mortality burden for all ages in the whole contiguous U.S. Using 11-year full spatial and temporal coverage data, we found that wildfire smoke $PM_{2.5}$ exposure was significantly associated with increased mortality risks of all causes, cardiovascular diseases, respiratory diseases, and mental disorders. Each year, smoke $PM_{2.5}$ contributed to an estimated more than one thousand all-cause deaths in the contiguous U.S., of which over three-fourths were from cardiovascular, respiratory, and mental causes. In addition, males, people aged 0 to 64, racial/ethnic minorities, and those living in mild drought conditions appeared to be more sensitive to smoke $PM_{2.5}$ exposure.

Most previous studies have explored the relationship between wildfire and health outcomes by comparing periods with no fire and periods during or after fire events, or comparing regions affected by wildfire smoke and unaffected regions (22), which generated effect estimates that are difficult to directly compare to our estimates. Only a few studies have isolated wildfire-specific $PM_{2.5}$ from other sources, and used a continuous variable for smoke $PM_{2.5}$ concentrations instead of a binary variable to estimate the health effects of smoke $PM_{2.5}$ (9, 10). Our findings on the associations between smoke $PM_{2.5}$ and all-cause, cardiovascular, and respiratory mortality are consistent with these studies in terms of both magnitude and direction of the estimates. For example, using a two-stage time-series analysis, a recent multi-country study based on 749 cities reported that a 1 $\mu g/m^3$ increase in wildfire-related $PM_{2.5}$ associated with an increase of 0.19%, 0.17%, and 0.19% in all-cause, cardiovascular, and respiratory mortality, respectively (10). Despite the different statistical methods and data sources used in our study and this global study, the estimated effect estimates were roughly similar.

In addition to cardiovascular and respiratory mortality, we found a strong association between smoke $PM_{2.5}$ and mortality from mental disorders. In a scoping review, the authors proposed a multi-level conceptual framework for understanding the pathways connecting wildfire smoke with mental health and well-being, which includes the interaction among individual, social and community networks, living and working conditions, and ecological levels (12). However, empirical evidence on this topic is still limited. More high-quality studies assessing smoke exposure independently of other wildfire-related experiences and exploring the specific sub-categories of mental disorders are needed to further explain the observed high smoke $PM_{2.5}$ related mortality risk from mental disorders.

We reported a higher vulnerability to smoke $PM_{2.5}$ among males than females, people aged 0 to 64 than older adults, and non-Hispanic Black and Hispanic people than non-Hispanic White people. Previous wildfire studies on the most vulnerable subpopulations have been inconclusive (7, 14). The observed high risks among males and younger population may be related to occupational and behavioral factors. For example, wildland firefighters, mostly non-elderly males, are at increased risk of lung cancer and cardiovascular disease mortality regardless of career durations or fire days per year (24). Compared to females and older adults, males and younger people also tend to spend more time outdoors, resulting in higher exposure to wildfire smoke (25, 26). Consistent with our finding, racial/ethnic minorities were found to be vulnerable subgroups in several previous studies (14, 15), which could be explained by pre-existing health conditions and limited access to high-quality healthcare due to structural racism in the U.S. (27, 28).

A higher association between smoke $PM_{2.5}$ and mortality was found in counties and months with mild drought compared to those with no drought. We did not observe a statistically significant association during severe droughts, possibly due to the relatively small sample size for this category. This effect modification can be potentially explained by both increased risk of exposure and higher human susceptibility brought by droughts. First, droughts can produce conditions that are favorable to dust storms, which increase the distribution and concentration of particulate matter in the air (13). In addition, drought has been linked to a variety of adverse health outcomes, such as cardiovascular disease, respiratory diseases, and psychosocial stress (29-31), leading to higher susceptibility to smoke pollutants. This effect modification by drought may be of great importance to public health benefits because both drought and wildfire smoke are projected to increase in many regions in the coming century (32, 33).

Our study found that about 1,141 deaths per year were contributed by wildfire smoke $PM_{2.5}$ in the contiguous U.S., which is over 100 times higher than the recorded wildfire deaths in the U.S. Billion-dollar Weather and Climate Disasters report by the National Oceanic and Atmospheric Administration's National Centers for Environmental Information (10 deaths/year) (34). This indicates a great number of indirect deaths brought by wildfires that could not be captured by official tolls. In addition, the U.S. Billion-dollar Weather and Climate Disasters report estimated that wildfire events cost about 3.1 billion dollars per year in the U.S. (34), but this estimate does not take into account health care related losses or values associated with loss of life (35). A recent study reported that the economic value of the health impacts of wildfires could be in the tens to hundreds of billions of U.S. dollars, but the exposure-response function for the $PM_{2.5}$-mortality relationship they used was for all-source $PM_{2.5}$, not wildfire-specific $PM_{2.5}$ (36). Our study suggests a tremendous wildfire smoke-related mortality burden, and our effect estimates for the relationship between wildfire $PM_{2.5}$ and mortality could be applied in future estimations of the wildfire costs.

Some limitations of this study should be noted. First, the wildfire smoke $PM_{2.5}$ concentrations were modelled and subject to uncertainty. Because direct measurements of the smoke contribution to $PM_{2.5}$ pollution are not available, the smoke $PM_{2.5}$ prediction was based on $PM_{2.5}$ anomalies at monitoring stations, which may be an imprecise estimate of the concentrations from smoke (23). A more accurate exposure assessment of wildfire smoke $PM_{2.5}$, especially different chemical components of smoke $PM_{2.5}$, is needed in the future. Second, we assumed that the non-smoke $PM_{2.5}$ was the difference between the all-source $PM_{2.5}$ and the smoke $PM_{2.5}$ concentrations, but they were generated using different methods and may introduce measurement error. Third, lacking detailed location information, this county-level ecological study is susceptible to ecological fallacy. We were also unable to analyze the influence of wildfire evacuation in this study. In addition, although our model specification can account for unmeasured confounders that vary only across time or space, the association between smoke $PM_{2.5}$ and mortality may be confounded by unmeasured time-varying individual county effects, such as other wildfire-related pollutants including carbon monoxide. Furthermore, the monthly resolution of mortality data is not fine enough for us to capture more acute effects of wildfire smoke within a few days, especially on respiratory outcomes. Finally, there is no standard way to define and categorize drought. Our findings on the effect modification by drought may be influenced by different drought definitions and categorizations.

In conclusion, our study estimated the detrimental effects of wildfire smoke $PM_{2.5}$ on both physical and mental health in the U.S. With wildfire intensity and frequency anticipated to increase in the future driven by climate change (2), more effective wildfire preparedness and mitigation strategies are urgently needed. Public health responses that protect people against wildfire smoke pollution is crucial both in and outside the areas where the wildfires occur.

Materials and Methods

Mortality and population data

We obtained mortality data for all 3,108 counties or county equivalents in the contiguous U.S. from 2006 to 2016 from the National Center for Health Statistics. The mortality dataset includes the year and month of death, the cause of death (International Statistical Classification of Diseases and Related Health Problems, 10^{th} Revision [ICD-10] codes), and the sex, age, race, and ethnicity of each deceased person. Based on the findings from previous studies (7, 14, 22), this study focused on all-cause mortality (ICD-10 code: A00-Z99) and mortality from three major specific causes: cardiovascular diseases (I00-I99), respiratory diseases (J00-J99), and mental and behavioral disorders (F00-F99). For each county, we summarized the monthly mortality counts for each cause (all-cause, cardiovascular, respiratory, and mental), sex (male and female), age group (0 to 64, 65 and above), and race/ethnicity (non-Hispanic White, non-Hispanic Black, and Hispanic).

County-level population data was collected from the Surveillance, Epidemiology, and End Results Program, National Cancer Institute (37). The total population and population estimate by sex, age, race, and Hispanic origin were extracted for each county, 2006–2016. Using anonymized monthly county-level mortality data, this study was determined as a Not Human Subject research by the Yale Institutional Review Boards (protocol ID: 2000026808).

Wildfire smoke $PM_{2.5}$ and other air pollutants

Ambient wildfire smoke $PM_{2.5}$ estimates for the contiguous U.S. was provided by a recent study by Childs et al. (23). In brief, station-based ground smoke $PM_{2.5}$ was defined as anomalies above the median on days in which wildfire smoke was overhead, then a model was trained to predict the station-based smoke $PM_{2.5}$ using meteorological factors, fire variables, aerosol measurements, and land use and elevation data. Finally, the trained model was applied to produce daily estimates of smoke $PM_{2.5}$ over the contiguous U.S. at a resolution of 10×10 km^2 (23). This model performed well over the entire range of observed smoke $PM_{2.5}$, without saturation at very high daily $PM_{2.5}$ levels (23). We additionally validated this model against a recently published wildfire-specific $PM_{2.5}$ model in California, which applied a novel ensemble-based statistical approach to isolate wildfire-specific $PM_{2.5}$ from other sources of emissions (38). This external validation showed a great consistency between the monthly county-level predictions from these two models in California, 2006–2016, with an R-squared (R^2) value of 0.92 and a root-mean-square error (RMSE) of 0.57 μg/m^3 (**Fig. S3**).

Data of daily NO_2, O_3, and total all-source $PM_{2.5}$ concentrations at 1×1 km^2 resolution were obtained from the NASA Socioeconomic Data and Applications Center (39-44). Non-smoke $PM_{2.5}$ concentrations were calculated by subtracting the smoke $PM_{2.5}$ from the all-source $PM_{2.5}$ concentrations. For negative values produced by this subtraction (0.4% of the total observations), the non-smoke $PM_{2.5}$ concentrations were recoded as 0. The daily smoke $PM_{2.5}$, non-smoke $PM_{2.5}$, NO_2, and O_3 concentrations were aggregated into monthly county-level average using population-weighted averaging to match with the mortality data. The cartographic boundary for counties in the contiguous U.S. was downloaded from the U.S. Census Bureau's TIGER/Line geodatabase (45).

Meteorological factors and drought

Monthly mean air temperature and mean dew point temperature data at 4×4 km^2 were obtained from the PRISM Climate Group (46). Similar to the air pollution data, we generated monthly averages for these two variables for each county.

Drought was measured by standardized precipitation evapotranspiration index (SPEI), a recently developed index considering both precipitation and temperature variables (47). Compared with other drought indices, SPEI has the advantages of being multi-scalar, reflecting the responses of different systems based on several water deficit accumulation periods, and being sensitive to changes in evaporation demand caused by temperature (48). This index has been increasingly applied in epidemiological studies in recent years to determine the onset, duration and magnitude of drought conditions (49, 50).

We extracted SPEI data at one-month timescale with a 0.5 degrees spatial resolution for each county from the Global SPEI database (51). Based on the severity of drought, we classified each month of each county into no drought (SPEI ≥ -0.4), mild drought (-1.2 ≤ SPEI ≤ -0.5), and severe drought (SPEI ≤ -1.3) (50, 52).

Statistical analysis

We applied a TWFE model with a quasi-Poisson regression to estimate the association between wildfire smoke $PM_{2.5}$ exposure and mortality. TWFE model has been increasingly applied in environmental epidemiology in recent years (53, 54). By introducing the indicators for each county and each month, TWFE model can potentially control for all spatial confounders that only vary across counties (e.g., urbanicity) and all temporal confounders that only vary by time (e.g., seasonality), either measured or unmeasured (55). In our study, the main TWFE model can be expressed as

$$\ln[E(Y_{i,t})] = \mu + \alpha_i + \theta_t + \beta_1 SmokePM_{2.5_{i,t}} + \beta_2 NonSmokePM_{2.5_{i,t}} + ns(Temperature_{i,t}, df = 5) + \varepsilon_{i,t} + offset[\ln(Population_{i,t})],$$

where $Y_{i,t}$ represents the number of all-cause or cause-specific deaths in county i, month t. $SmokePM_{2.5_{i,t}}$ and $NonSmokePM_{2.5_{i,t}}$ are the mean smoke $PM_{2.5}$ and non-smoke $PM_{2.5}$ concentrations in county i, month t. α_i refers to time-invariant county effects and θ_t refers to time-varying effects that are common in all counties. Air temperature was controlled by a flexible natural cubic spline with five degrees of freedom (df). $\ln(Population_{i,t})$ is an offset term which represents the natural log of the population in county i, month t. μ is the intercept term and $\varepsilon_{i,t}$ is the error term. We weighted models using the population size in each county to improve the precision of our estimates (56). The TWFE model requires no unmeasured confounders that display different temporal variations across counties (i.e., time-varying individual county effects) (55). Here, we assumed that non-smoke $PM_{2.5}$ and air temperature are the only candidates of such confounders.

Based on the estimated coefficient of $SmokePM_{2.5_{i,t}}$ (β_1) for each cause, we calculated the number of deaths attributable to smoke $PM_{2.5}$ (AN) using the attributable fraction (AF) method. Specifically, AF was defined as follows: $AF = 1 - e^{-\beta_1 SmokePM_{2.5_{i,t}}}$. AF was then multiplied by the monthly cause-specific number of deaths to estimate the smoke $PM_{2.5}$ attributable deaths in each county in each month.

In subgroup analyses, we further estimated the association between smoke $PM_{2.5}$ and all-cause mortality by sex, age, and race/ethnicity. We also conducted stratified analysis by drought severity (no drought, mild drought, and severe drought) to investigate its potential modification effect. We tested the statistical difference in effect estimates between different subgroups and drought levels by calculating the z score as $(\hat{Q}_1 - \hat{Q}_2)/\sqrt{(S\hat{E}_1)^2 + (S\hat{E}_2)^2}$, where $\hat{Q}_1$and $\hat{Q}_2$ are the estimates, and $S\hat{E}_1$and $S\hat{E}_2$ are their respective standard errors (57).

Several sensitivity analyses were performed to test the robustness of our results: (a) we additionally adjusted for NO_2, O_3, or dew point temperature in the model; (b) we removed non-smoke $PM_{2.5}$ from the model; (c) an alternative four or six dfs was used in the natural cubic spline of air temperature; (d) we tested the delayed effects of smoke $PM_{2.5}$ in the previous one or two months; and (e) we restricted the analysis to counties that had at least one day with smoke $PM_{2.5}$ higher than 20 μg/m^3. To test the linearity of the relationship between smoke $PM_{2.5}$ and mortality, we replaced the linear term of smoke $PM_{2.5}$ by a natural cubic spline with three dfs in the model and visualized the estimated curve.

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Figures

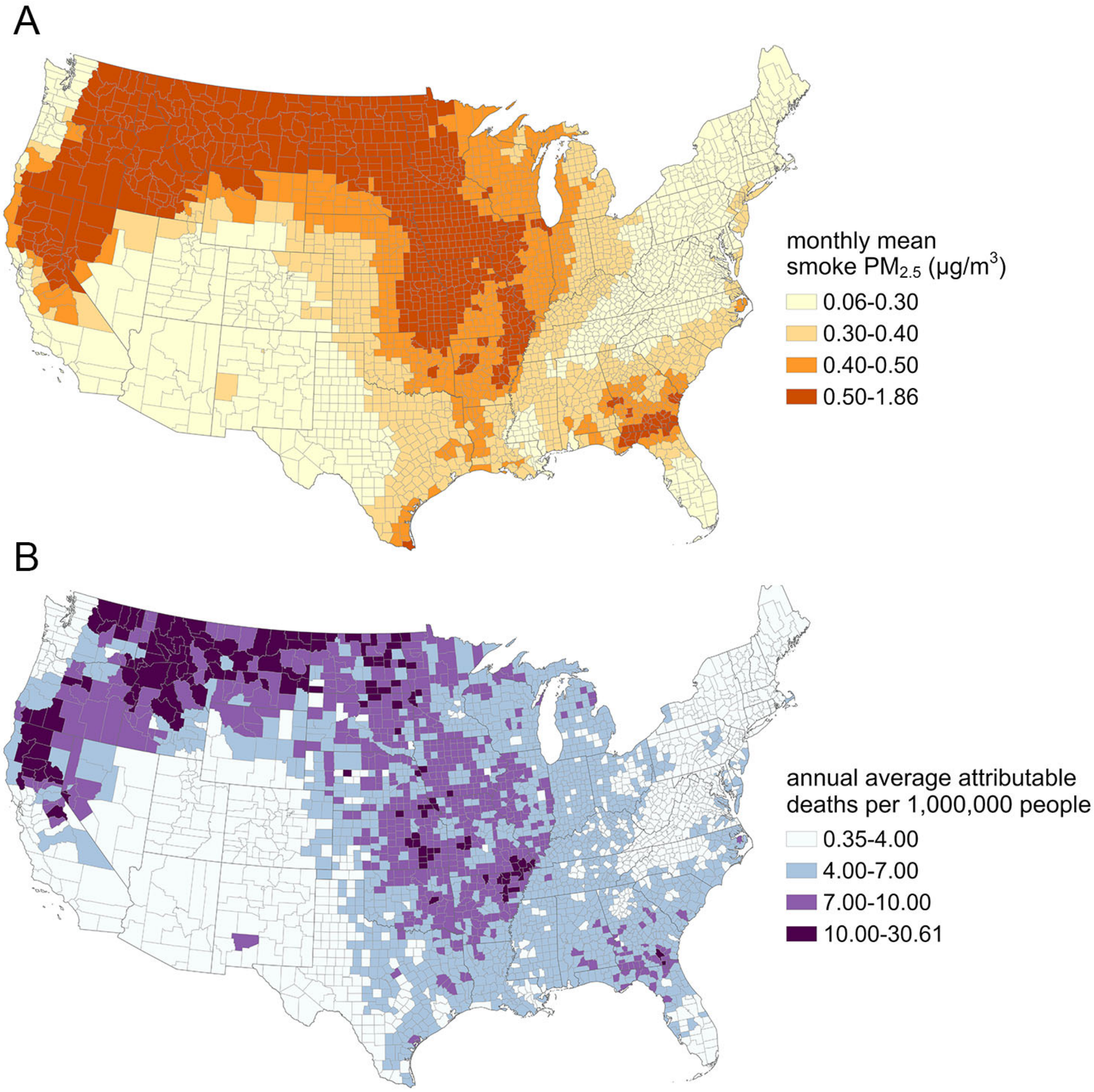

Fig. 1. Map of monthly county-level mean wildfire smoke $PM_{2.5}$ concentration and annual average attributable all-cause mortality burden in the contiguous U.S., 2006–2016. A: The distribution of monthly mean smoke $PM_{2.5}$ in contiguous U.S. counties ($\mu g/m^3$). **B**: The distribution of annual average all-cause mortality burden attributable to wildfire smoke $PM_{2.5}$ in contiguous U.S. counties (deaths per 1,000,000 people).

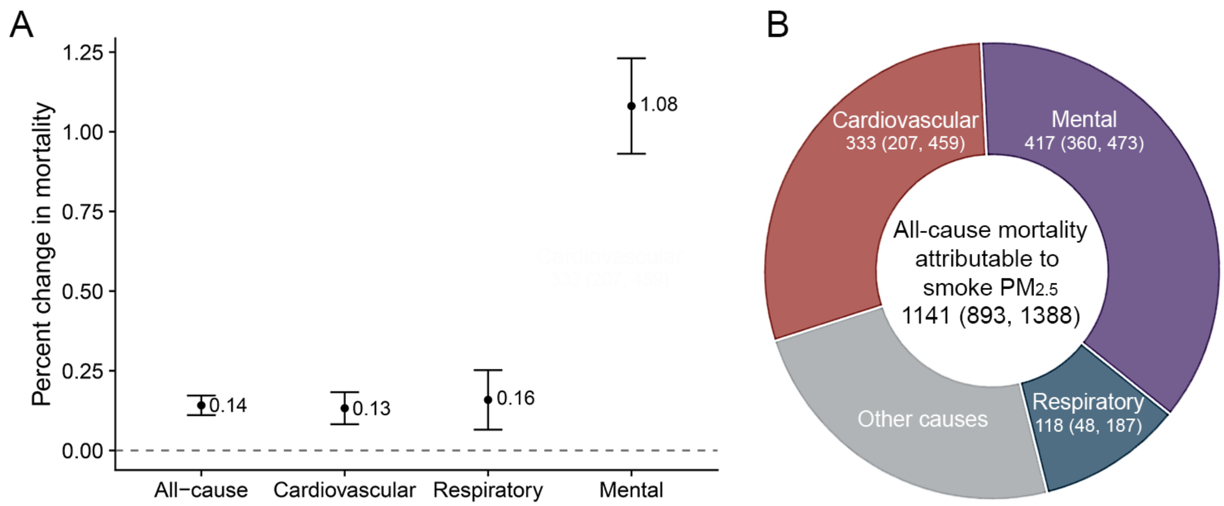

Fig. 2. Association between wildfire smoke $PM_{2.5}$ and cause-specific mortality risk and annual average attributable cause-specific mortality burden. A: estimated percentage changes in monthly mortality per 1 μg/m^3 increase in smoke $PM_{2.5}$ concentration, for all-cause mortality, cardiovascular disease mortality, respiratory disease mortality, and mental disorder mortality. The error bars indicate 95% confidence intervals. **B**: estimated annual average mortality burden attributable to smoke $PM_{2.5}$, for all causes, cardiovascular diseases, respiratory diseases, and mental and behavioral disorders. The numbers in parentheses are 95% confidence intervals.

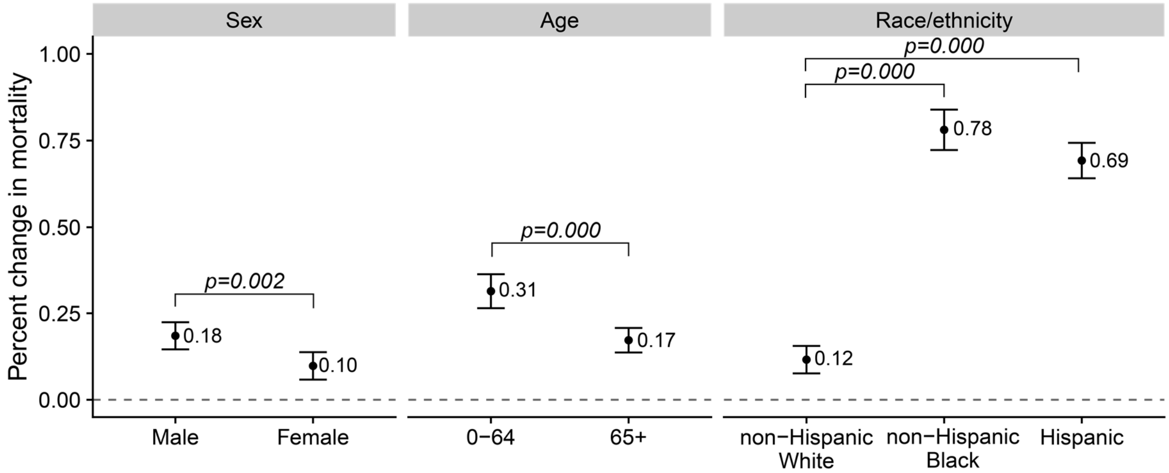

Fig. 3. Percent change in all-cause mortality associated with a 1 μg/m^3 increase in smoke $PM_{2.5}$ for each subgroup. This figure shows the estimated associations between each 1-μg/m^3 increase in smoke $PM_{2.5}$ concentration and all-cause mortality risks for different sex, age, and race/ethnicity groups. Based on the z score calculated using the coefficients and standard errors for different subgroup, we tested the statistical difference in effect estimates among different sex, age, and race/ethnicity groups, using males, people aged 0 to 64 years, and non-Hispanic White people as the reference group.

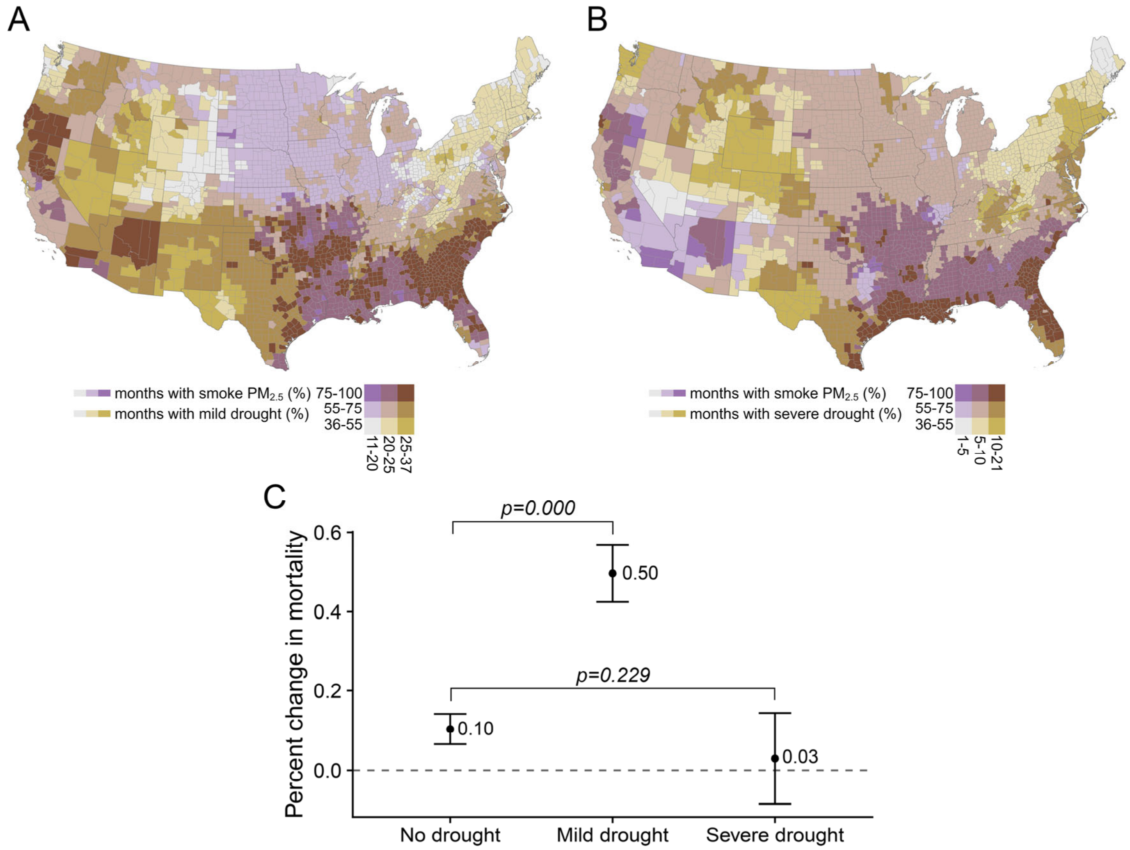

Fig. 4. Distribution of smoke $PM_{2.5}$ and drought and effect modification by drought. A, B: This bivariate choropleth map shows the percentage of months with non-zero smoke $PM_{2.5}$ concentrations and the percentage of months with mild (A) or severe (B) drought in each contiguous U.S. county, from 2006 to 2016. **C**: The estimated percent changes in all-cause mortality per 1 μg/m^3 increase in smoke $PM_{2.5}$ concentration when there was no drought (86.03% county-months), mild drought (23.28% county-months), or severe drought (8.68% county-months). Based on the z score calculated using the coefficients and standard errors for different levels of drought, we tested the statistical difference in effect estimates between different drought levels, using no drought as the reference.