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Long-term exposure to wildland fire smoke $PM_{2.5}$ and mortality in the contiguous United States

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Despite the substantial evidence on the health effects of short-term exposure to ambient fine particles ($PM_{2.5}$), including increasing studies focusing on those from wildland fire smoke, the impacts of long-term wildland fire smoke $PM_{2.5}$ exposure remain unclear. We investigated the association between long-term exposure to wildland fire smoke $PM_{2.5}$ and nonaccidental mortality and mortality from a wide range of specific causes in all 3,108 counties in the contiguous United States, 2007 to 2020. Controlling for nonsmoke $PM_{2.5}$, air temperature, and unmeasured spatial and temporal confounders, we found a nonlinear association between 12-mo moving average concentration of smoke $PM_{2.5}$ and monthly nonaccidental mortality rate. Relative to a month with the long-term smoke $PM_{2.5}$ exposure below 0.1 μg/m^3, nonaccidental mortality increased by 0.16 to 0.63 and 2.11 deaths per 100,000 people per month when the 12-mo moving average of $PM_{2.5}$ concentration was of 0.1 to 5 and 5+ μg/m^3, respectively. Cardiovascular, ischemic heart disease, digestive, endocrine, diabetes, mental, and chronic kidney disease mortality were all found to be associated with long-term wildland fire smoke $PM_{2.5}$ exposure. Smoke $PM_{2.5}$ contributed to approximately 11,415 nonaccidental deaths/y (95% CI: 6,754, 16,075) in the contiguous United States. Higher smoke $PM_{2.5}$-related increases in mortality rates were found for people aged 65 and above. Positive interaction effects with extreme heat were also observed. Our study identified the detrimental effects of long-term exposure to wildland fire smoke $PM_{2.5}$ on a wide range of mortality outcomes, underscoring the need for public health actions and communications that span the health risks of both short- and long-term exposure.

wildland fire | mortality | fine particulate matter | United States

Significance

Short-term exposure to smoke pollutants from wildland fires, particularly fine-particulate matter ($PM_{2.5}$), is associated with adverse health effects. Yet, the impacts of long-term exposure to wildland fire smoke $PM_{2.5}$ on health, specifically mortality, remain unclear. In the contiguous United States, data from 2007 to 2020 showed positive associations between long-term exposure to wildland smoke $PM_{2.5}$ and nonaccidental, cardiovascular, ischemic heart disease, digestive, endocrine, diabetes, mental, and chronic kidney disease mortality rates. Based on these results, wildland smoke $PM_{2.5}$ was estimated to contribute to 11,415 nonaccidental deaths/y in the United States (95% CI: 6,754, 16,075). These findings add to the growing evidence of detrimental effects of wildland fire smoke $PM_{2.5}$ on health and suggest more effective public health actions are needed.

Wildland fire is a growing public health concern in the United States. As a result of the warming climate (1), a long history of fire suppression (2), and an increase in human-caused fire ignitions (3), the country has witnessed a marked increase in the area affected by wildland fires over the past few decades, with the burned area roughly quadrupling (4). In recent years, wildland fire contributed to up to 25% of total fine particulate matter ($PM_{2.5}$) concentrations across the United States and up to half in some Western regions (4). Under climate change, the prevalence, frequency, and intensity of wildland fire activities are expected to increase in the future (5).

Wildland fire smoke is a complex mixture. Among the various air pollutants emitted by wildland fires, $PM_{2.5}$ is widely used as an indicator of exposure because it is a major component of smoke, can deeply penetrate the respiratory system, and has demonstrated links to public health (6). Previous studies on the health effects of wildland fire smoke mostly focused on the western United States, where the majority of large fires occurred (7–9). However, the pollutants from wildland fire smoke can travel long distances from the source, potentially affecting human health thousands of kilometers away outside the West (10).

Previous studies on the health effects of wildland fire exposure predominantly focused on the effects of short-term exposure, typically examining exposure periods within 1 or 2 wk. Most studies reported a positive relationship between short-term wildland fire smoke exposure and all-cause mortality (9, 11–13). A growing number of studies linked short-term exposure to wildland fire smoke to increased risks of respiratory mortality and presented mixed evidence regarding cardiovascular mortality (11–14). Recent studies have also documented worsened diabetic outcomes (15), higher mortality rates among patients with kidney failure (16), and impaired mental health (17, 18) associated with short-term wildland fire smoke exposure.

However, given that climate change has contributed to an increase in wildland fire season length, increasing the duration of exposure, the health impacts of long-term

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wildland fire smoke exposure should be a concern of growing importance (19–21). To date, little is known about the impacts of long-term exposure to wildland fire smoke on human health (19, 21). Most previous studies focused on mental health, reporting associations between long-term wildland fire exposure and mental outcomes, such as anger problems (22), posttraumatic stress disorder (23), depression (24), and anxiety (25). However, these studies could not distinguish between the effects of smoke and the overall impacts of wildland fires. A few studies suggested that exposure to wildland fires was associated with child mortality, COVID-19 mortality, cardiovascular disease mortality, and respiratory disease morbidity (21), but most of them did not measure the uncertainties of estimates. Given that short-term exposure to wildland fire smoke has been linked to a wide range of mortality outcomes, exploring whether long-term wildland fire smoke exposure is associated with these health effects is worthwhile.

Furthermore, the effects of wildland fire smoke $PM_{2.5}$ can be heterogeneous among population subgroups due to physiological, behavioral, and socioeconomic factors (26). Previous studies indicated that demographic factors such as sex, age, and race and ethnicity may modify the association between smoke $PM_{2.5}$ and health outcomes (11, 26, 27). However, existing research mostly focused on the effects of short-term wildland fire smoke exposure and generated mixed findings (9). To better prepare communities for smoke and tackle environmental justice issues, a deeper understanding of susceptibility to wildland fire exposure, particularly long-term exposure, among specific subgroups is needed to help inform targeted public health outreach efforts.

In the context of climate change, the co-occurrence of wildland fires and extreme heat events is expected to increase (28). In addition, both extreme heat and $PM_{2.5}$ were associated with impaired cardiopulmonary functions (29, 30). Therefore, extreme heat may interact with wildland fire smoke and further aggravate health effects. A previous study suggested synergistic effects between short-term extreme heat and wildland fire smoke exposures on daily cardiorespiratory hospitalizations in California (31). However, little is known about the potential interaction between extreme heat and long-term smoke $PM_{2.5}$ exposure nationwide.

Constrained by a lack of nationwide validated data on pollutant concentrations attributable to wildland fire smoke, many previous studies on the impact of wildland fire smoke on health outcomes have been focusing on episodes with high wildland fire smoke exposure (or smoke wave) using binary measures of smoke concentrations (32). Recently, a machine learning model was developed to estimate wildland fire smoke $PM_{2.5}$ concentrations for the contiguous United States, using a combination of meteorological factors, fire variables, aerosol measurements, and land use and elevation data (33). This high-resolution wildland fire smoke $PM_{2.5}$ dataset (10×10 km^2) enabled us to further examine the impact of wildland fire smoke, ranging from the more common, low-level smoke concentrations to the increasingly frequent extremely high concentrations, and to explore its potentially nonlinear effects on mortality.

Utilizing the nationwide monthly wildland fire smoke $PM_{2.5}$ and mortality data from 2007 to 2020, this study aimed to a) estimate the potentially nonlinear associations of long-term smoke $PM_{2.5}$ exposure with county-level monthly nonaccidental and cause-specific mortality from a broad spectrum of diseases, b) calculate the attributable cause-specific mortality burden in each county, c) examine the associations in different sex, age, and racial and ethnic groups, and d) explore the interaction effect between smoke $PM_{2.5}$ and extreme heat on mortality.

Results

Description of Smoke $PM_{2.5}$ Exposure and Monthly Mortality in the Contiguous United States. For months from January 2007 to December 2020, we calculated the moving average of smoke $PM_{2.5}$ concentration of the current and previous 11 mo for each county to represent the average exposure to smoke $PM_{2.5}$ in the previous year. The average 12-mo moving average concentration of smoke $PM_{2.5}$ across all county-months during the study period was 0.4 $\mu g/m^3$, contributing to approximately 5% of all-source $PM_{2.5}$ (*SI Appendix*, Table S1).

From 2007 to 2020, all 3,108 counties in the contiguous United States experienced some amount of smoke $PM_{2.5}$, with the western, north central, and southeastern counties being exposed to higher long-term exposure (12-mo moving average concentration of smoke $PM_{2.5}$) than other regions (Fig. 1*A*). The temporal variability in this exposure was also higher in these regions compared with other regions (Fig. 1*B*). The overall temporal trend of the 12-mo moving average concentration of smoke $PM_{2.5}$ for all US contiguous counties is displayed in *SI Appendix*, Fig. S1.

To account for the potentially nonlinear health effects of smoke $PM_{2.5}$, we categorized the 12-mo moving average of smoke $PM_{2.5}$ concentrations into nine bins: 0 to 0.1 (reference), 0.1 to 0.2, 0.2 to 0.3, 0.3 to 0.4, 0.4 to 0.5, 0.5 to 0.7, 0.7 to 1, 1 to 5, and 5+ $\mu g/m^3$, corresponding to approximately 9.9%, 17.8%, 17.7%, 14.4%,

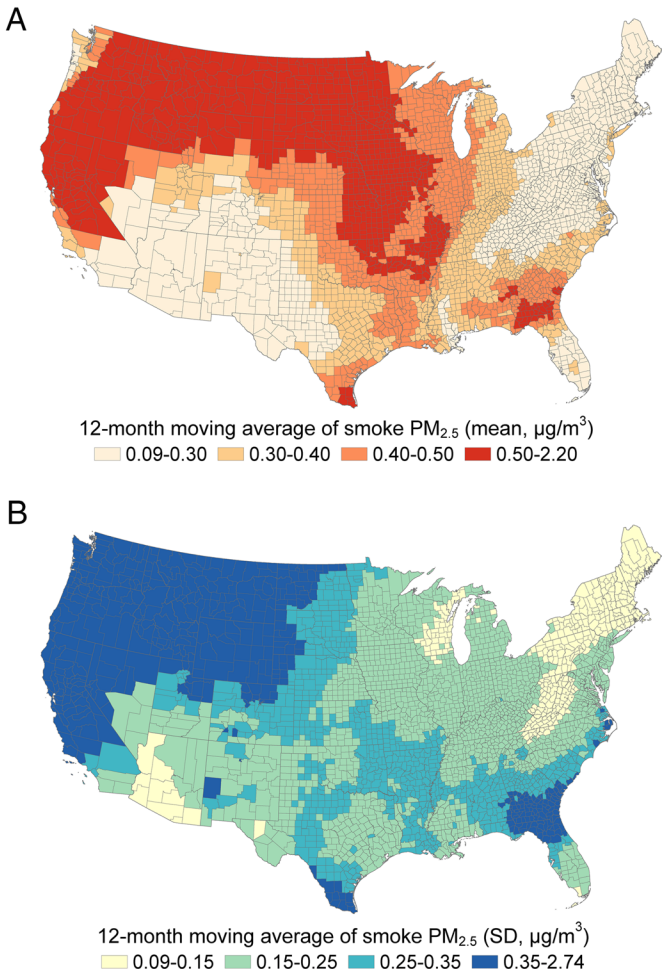

Fig. 1. Spatial distribution of 12-mo moving average of smoke $PM_{2.5}$ concentration in the contiguous United States, 2007 to 2020. (*A*) The distribution of the mean 12-mo moving average concentration of smoke $PM_{2.5}$ in the contiguous US counties ($\mu g/m^3$). (*B*) The distribution of the SD of the 12-mo moving average concentration of smoke $PM_{2.5}$ in the contiguous US counties ($\mu g/m^3$).

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11.1%, 14.9%, 9.1%, 5.0%, and 0.1% of county-months in the study period (*SI Appendix*, Fig. S2). Only 15 county-months were not exposed to any smoke $PM_{2.5}$ in the current and previous 11 mo.

A total of 33,902,722 nonaccidental deaths were included in this study, including 11,514,374 deaths from cardiovascular diseases, 3,584,654 from respiratory diseases, 1,624,915 from endocrine diseases, 939,531 from genitourinary diseases, 2,465,890 from nervous diseases, 1,823,243 from mental and behavioral disorders (hereafter referred to as "mental disorders"), and 1,406,184 from digestive diseases. From 2007 to 2020, the mean age-adjusted nonaccidental mortality rate was 61.9 (SD: 23.9) deaths per 100,000 people per month in all counties in the contiguous United States. The descriptive statistics of the age-adjusted mortality rate for each population subgroup and each specific cause are listed in *SI Appendix*, Table S1.

Association between Long-Term Smoke $PM_{2.5}$ Exposure and Cause-Specific Mortality Rate. Using a panel fixed effects model to control for air temperature, nonsmoke $PM_{2.5}$, time-invariant spatial confounders, county-invariant temporal confounders, and regional long-term and seasonal trends, we found a nonlinear association between 12-mo moving average of smoke $PM_{2.5}$ concentration and monthly nonaccidental mortality rate (Fig. 2). Compared to a month in the same county with the long-term smoke $PM_{2.5}$ exposure below 0.1 $\mu g/m^3$, nonaccidental mortality increased by 0.16 (95% CI: 0.06, 0.26), 0.40 (95% CI: 0.26, 0.54), 0.35 (95% CI: 0.21, 0.49), 0.34 (95% CI: 0.19, 0.50), 0.49 (95% CI: 0.33, 0.65), 0.63 (95% CI: 0.44, 0.83), 0.36 (95% CI: 0.11, 0.61), and 2.11 (95% CI: 1.24, 2.99) deaths per 100,000 people per month when the 12-mo moving average of smoke $PM_{2.5}$ concentration was in the range of 0.1 to 0.2, 0.2 to 0.3, 0.3 to 0.4, 0.4 to 0.5, 0.5 to 0.7, 0.7 to 1, 1 to 5, and 5+ $\mu g/m^3$, respectively (Fig. 2).

We also observed positive associations between 12-mo moving average of smoke $PM_{2.5}$ concentrations and monthly mortality rates from cardiovascular diseases, ischemic heart diseases, digestive diseases, endocrine diseases, diabetes, mental disorders, and chronic kidney diseases (Fig. 2). Compared to a month with the long-term smoke $PM_{2.5}$ exposure below 0.1 $\mu g/m^3$, cardiovascular mortality rates increased when the 12-mo moving average of smoke $PM_{2.5}$ concentration was from 0.5 to 1 $\mu g/m^3$ and above 5 $\mu g/m^3$, and ischemic heart disease mortality rates increased when the concentration was from 0.1 to 5 $\mu g/m^3$. A nearly linear association was observed for mortality rates from endocrine diseases, including diabetes: The central estimates were generally higher as the concentration bin increased. Digestive mortality was found sensitive to the 12-mo moving average of smoke $PM_{2.5}$ when the concentration was 0.5 to 0.7 and 5+ $\mu g/m^3$. Mortality from mental disorders (such as dementia, schizophrenia, and posttraumatic stress disorder) increased in all concentration bins compared to a month with the 12-mo moving average concentration below 0.1 $\mu g/m^3$. In addition, mortality from chronic kidney diseases was found sensitive to long-term smoke $PM_{2.5}$ exposure when the12-mo moving average concentration was 0.3 to 0.4 and 0.5 to 1 $\mu g/m^3$.

We also examined the associations between 12-mo moving average of smoke $PM_{2.5}$ concentrations and monthly mortality rates from other specific causes, including stroke, myocardial infarction, hypertensive diseases, hypertensive heart diseases, respiratory diseases, chronic obstructive pulmonary disease (COPD), nervous diseases, Alzheimer's disease and related dementias (ADRD), and genitourinary diseases (*SI Appendix*, Fig. S3). Although some of them were also found to be sensitive to long-term smoke $PM_{2.5}$ exposure, such as mortality from stroke, myocardial infarction, respiratory diseases, and ADRD, these specific causes were not presented in the main figures or included in further analysis because their estimates were either insignificant after the Bonferroni correction for multiple comparisons or inconsistent in direction across smoke $PM_{2.5}$ concentration bins. Negative effect estimates were found for hypertensive heart disease, COPD, and nervous disease mortality in some concentration bins, but none of them remain statistically significant after Bonferroni correction. The detailed estimates for all examined specific causes are listed in *SI Appendix*, Table S2.

Cause-Specific Mortality Burden Attributable to Long-Term Smoke $PM_{2.5}$ Exposure. Assuming the homogeneity within each smoke $PM_{2.5}$ bin and the causality of the estimated smoke $PM_{2.5}$-mortality relationships, we further quantified the mortality burden attributable to long-term smoke $PM_{2.5}$ exposure. As nonsmoke $PM_{2.5}$ was adjusted for in the model, the estimated smoke $PM_{2.5}$-attributable mortality burden is in addition to the well-recognized burden from nonsmoke $PM_{2.5}$. On average, approximately 11,415 nonaccidental deaths (95% CI: 6,754, 16,075) were attributable to smoke $PM_{2.5}$ in the contiguous United States per year. The spatial distribution of this attributable burden was generally consistent with the distribution of smoke $PM_{2.5}$ concentration (Fig. 3*A*). The estimated attributable nonaccidental mortality burden for each year is displayed in *SI Appendix*, Fig. S4.

For mortality from other specific causes, each year, long-term smoke $PM_{2.5}$ exposure contributed approximately 4,512 deaths (95% CI: 1,922, 7,102) from cardiovascular diseases, including 3,753 (95% CI: 1,915, 5,592) ischemic heart disease deaths, 1,142 deaths (95% CI: 285, 1,999) from endocrine diseases, including 858 (95% CI: 149, 1,566) diabetes deaths, 2,083 deaths (95% CI: 1,143, 3,022) from mental disorders, 537 deaths from digestive diseases (95% CI: −200, 1,273), and 320 deaths (95% CI: −72, 713) from chronic kidney diseases. Among the total long-term smoke $PM_{2.5}$-attributable nonaccidental deaths, approximately 72.5% were from cardiovascular diseases, mental disorders, endocrine diseases, and digestive diseases (Fig. 3*B* and *SI Appendix*, Table S3).

Association between Long-Term Smoke $PM_{2.5}$ and Monthly Mortality Rate by Subgroup. We examined the association between 12-mo moving average of smoke $PM_{2.5}$ concentrations and monthly nonaccidental mortality rates across different sex, age, and race and ethnicity groups (Table 1). No significant difference in effect estimates was observed between males and females. Compared with people aged 0 to 64, greater increases in mortality rates were observed among people who aged 65 and above across all smoke $PM_{2.5}$ concentration bins. Among different racial and ethnic groups, compared with non-Hispanic White people, significantly higher associations were observed for non-Hispanic Black and Hispanic people when smoke $PM_{2.5}$ concentration was from 1 to 5 $\mu g/m^3$. After considering multiple comparisons, the difference between racial and ethnic minorities and non-Hispanic White people became insignificant, but the significant differences between age groups remained.

Subgroup analyses were also performed for major categories of mortality that showed consistent and significant sensitivity to long-term exposure to smoke $PM_{2.5}$: cardiovascular, endocrine, digestive, and mental mortality (*SI Appendix*, Table S4). In general, no significant difference between sex or race and ethnicity groups was detected for these four outcomes after considering multiple comparisons. Consistent with the findings for nonaccidental mortality, greater smoke $PM_{2.5}$-related increases in mortality rates from cardiovascular diseases and mental disorders were observed among people who aged 65 and above.

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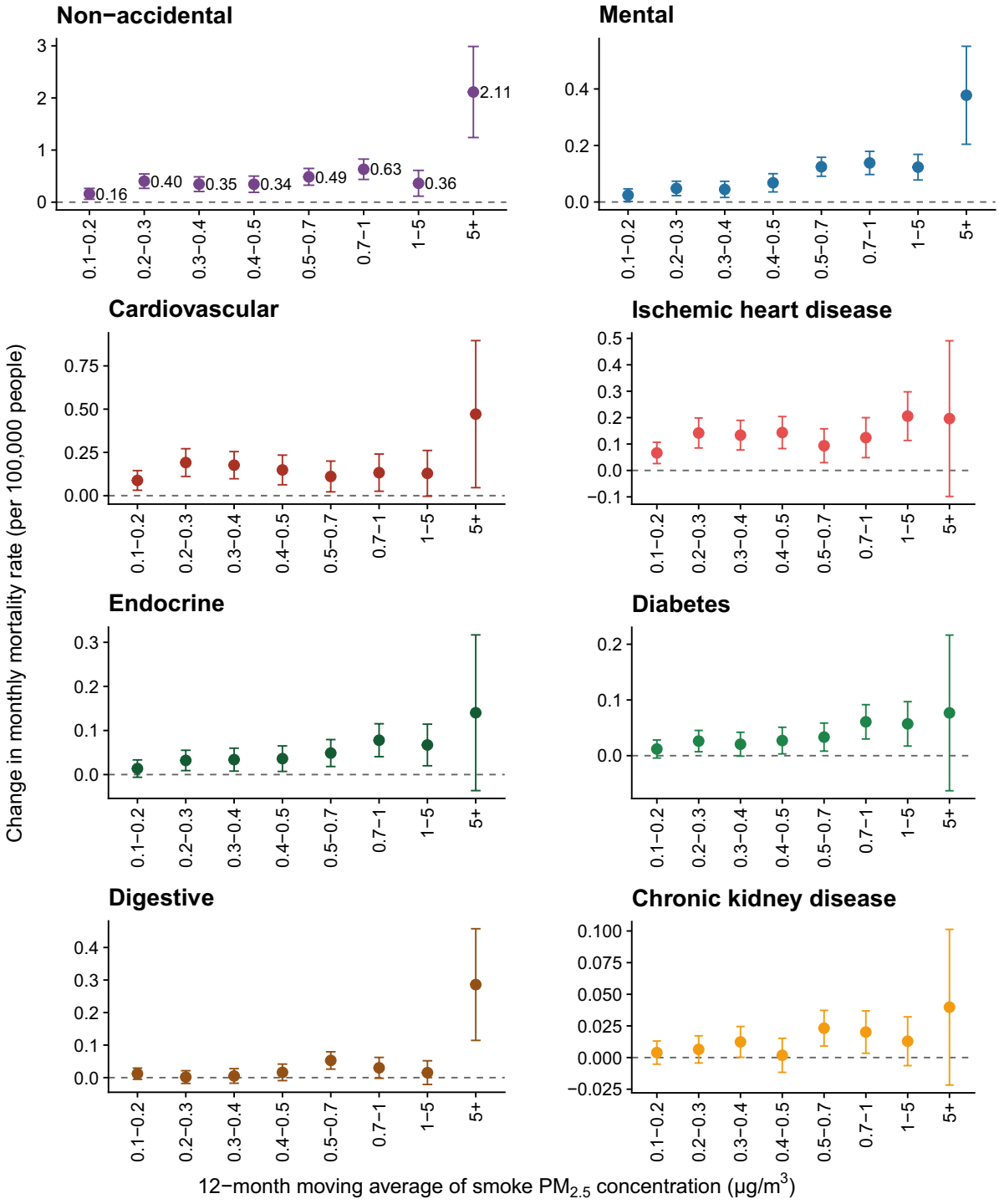

Fig. 2. Association between 12-mo moving average concentration of smoke $PM_{2.5}$ and monthly mortality rate. This figure displays the estimated changes in monthly cause-specific mortality rate (per 100,000 people) associated with each bin of 12-mo moving average of smoke $PM_{2.5}$ concentration, relative to a month in the same county with the long-term smoke $PM_{2.5}$ exposure below 0.1 μg/m^3. The error bars indicate 95% CI.

Interaction between Long-Term Smoke $PM_{2.5}$ and Extreme Heat Days. Extreme heat commonly co-occurred with wildland fire smoke $PM_{2.5}$ in the contiguous United States. Here, we examined the interaction effects of long-term smoke $PM_{2.5}$ and current-month extreme heat days. For each county, we defined extreme heat days as days with daily mean air temperature higher than the county's 90th percentile warm season air temperature (May to September, 2007 to 2020). From 2007 to 2020, a total of 657,402 extreme heat days were identified in the counties studied, spanning 126,237 county-months. We calculated the number of extreme heat days in each county for each month to represent monthly extreme heat exposure. Based on the spatial distribution of the 12-mo moving average of smoke $PM_{2.5}$ concentrations and the current-month number of extreme heat days (Fig. 4*A*), the North Central, South, Southeast, and West regions experienced higher coexposure to smoke $PM_{2.5}$ and extreme heat than other regions.

By including an interaction term for the current-month number of extreme heat days and 12-mo moving average of smoke $PM_{2.5}$ concentration bins in our model, we found a significantly positive interaction between extreme heat and smoke $PM_{2.5}$ at levels ranging from 0.1 to 5 μg/m^3 (Fig. 4*B*). The interaction results in general remained robust when we used alternative temperature thresholds

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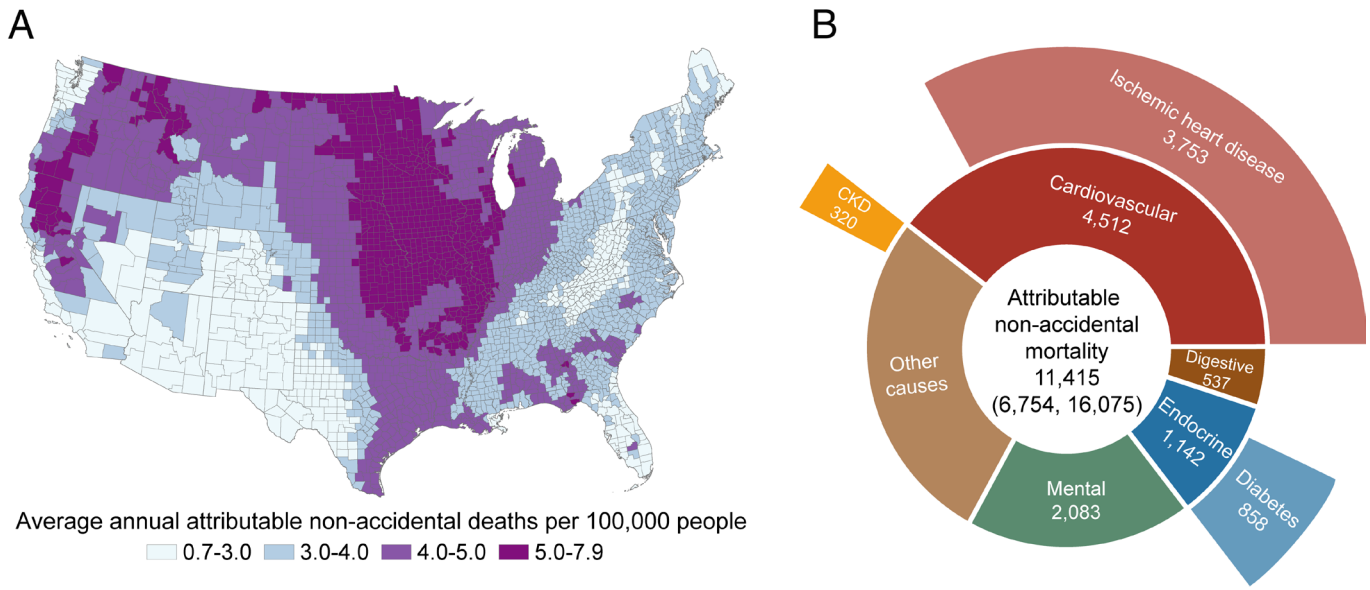

Fig. 3. Average annual nonaccidental mortality burden attributable to long-term smoke $PM_{2.5}$ exposure. (*A*) The spatial distribution of average annual nonaccidental deaths (per 100,000 people) attributable to long-term smoke $PM_{2.5}$ exposure (12-mo moving average). (*B*) Estimated average annual cause-specific deaths attributable to long-term smoke $PM_{2.5}$ exposure.

in the definition of extreme heat days (85th or 95th percentile of local warm-season temperature distribution). Among mortality of specific causes, positive interactions were found for cardiovascular and mental disorder mortality (*SI Appendix*, Fig. S5).

Sensitivity Analyses, Placebo Tests, and Stratification by Distance to Fire. Our results generally remained robust across various sensitivity analyses: when including different combinations of fixed effects, when additionally adjusting for dew point temperature, when excluding adjust for nonsmoke $PM_{2.5}$ or current-month air temperature, when adjusting for 12-mo moving average of air temperature instead of current-month temperature, and when using alternative degrees of freedoms in the natural cubic spline of air temperature in the model (*SI Appendix*, Fig. S6). The estimated nonlinear pattern also remained consistent when we used a quasi-Poisson model and used finer bins or a natural cubic spline for smoke $PM_{2.5}$ in the model (*SI Appendix*, Figs. S7–S9). The results of the spatial and temporal randomization tests indicated that the estimates in our study were unlikely driven by spatial or temporal dependence due to model misspecification (*SI Appendix*, Fig. S10). When the exposure period to smoke $PM_{2.5}$ was extended from 12 mo to 24 and 36 mo, the model coefficients decreased and eventually becoming null at a 36-mo exposure window in most bins (*SI Appendix*, Fig. S11).

In a stratified analysis by distance to fire, we observed that the association between long-term smoke $PM_{2.5}$ exposure and nonaccidental mortality was significantly higher in counties far away from the fire point (≥150 km) in the current and past 11 mo compared with those close to an active fire (<150 km) when the 12-mo moving average of smoke $PM_{2.5}$ concentrations was from 0.2 to 0.4 μg/m^3 and from 1 to 5 μg/m^3 (*SI Appendix*, Fig. S12). However, when the smoke $PM_{2.5}$ concentrations were above 5 μg/m^3, the estimate was only significantly positive in counties close to fire. This result suggests that being close to a fire was unlikely to be a main driver of the estimated results in our study.

Discussion

This study comprehensively examines the associations between long-term exposure to wildland fire smoke $PM_{2.5}$ and mortality from a wide range of specific causes for all ages in the whole contiguous United States. We found that average exposure to wildland fire smoke $PM_{2.5}$ in the past 1 y was associated with increases in nonaccidental, cardiovascular, ischemic heart disease, digestive, endocrine, diabetes, mental, and chronic kidney disease mortality. In addition to the well-documented mortality burden from nonsmoke $PM_{2.5}$, in total, we estimated that smoke $PM_{2.5}$ contributed to over 10,000 nonaccidental deaths in the contiguous United States each year. Higher smoke $PM_{2.5}$-related increases in mortality rates were found for people aged 65 and above. In addition, positive interaction effects between 12-mo moving average of smoke $PM_{2.5}$ concentrations and current-month number of extreme heat days on nonaccidental, cardiovascular, and mental disorder mortality were observed.

The impacts of long-term wildland fire smoke exposures on mortality are understudied in existing literature. However, our results are in general consistent with a few previous findings that long-term exposure to wildland fire smoke is associated with increased premature mortality (21). For example, a study in Brazil observed a significant association between long-term exposure to forest fire $PM_{2.5}$ (measured by percentage hours of $PM_{2.5}$ concentrations > 25 μg/m^3 divided by the total number of estimated hours of $PM_{2.5}$ in 2005) and increases in cardiovascular disease mortality rates in older adults (≥65 y) (34). Controlling for non-fire-sourced $PM_{2.5}$, a case–control study in low-income and middle-income countries reported that each 1 μg/m^3 increment of monthly mean fire-sourced $PM_{2.5}$ concentration was associated with a 2.31% increased risk of child mortality, but this estimate became statistically insignificant after extending the exposure time window from 1 mo to 12 mo (35). However, given the differences in study population and location, exposures (e.g., the intensity, frequency, and duration of wildfire smoke), study design, and outcome measures, estimates are not directly comparable across studies. More studies investigating the long-term impacts of wildland fire smoke exposure on mortality from a comprehensive spectrum of specific causes and conditions are needed in the future.

Although the health impacts of wildland fire smoke $PM_{2.5}$ could be different from urban background $PM_{2.5}$ due to differences in chemical composition and particle size, and the episodic nature of smoke (7, 36), the biological mechanisms are likely to align with those documented for all-source (i.e., total mass) $PM_{2.5}$. $PM_{2.5}$ can travel into the respiratory tract and bloodstream and trigger oxidative

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Table 1. Associations between 12-mo moving average of smoke $PM_{2.5}$ concentration bins and monthly nonaccidental mortality rate (per 100,000 people) in population subgroups

Subgroup	Smoke $PM_{2.5}$ concentration bin ($\mu g/m^3$)	Associated change in monthly mortality rate (95% CI)	*P* value*
By sex			
Male	0.1 to 0.2	0.11 (−0.05, 0.26)	Reference
	0.2 to 0.3	0.41 (0.22, 0.61)	Reference
	0.3 to 0.4	0.32 (0.11, 0.53)	Reference
	0.4 to 0.5	0.41 (0.18, 0.65)	Reference
	0.5 to 0.7	0.49 (0.25, 0.74)	Reference
	0.7 to 1	0.74 (0.45, 1.04)	Reference
	1 to 5	0.38 (0.02, 0.74)	Reference
	5+	2.25 (1.09, 3.41)	Reference
Female	0.1 to 0.2	0.19 (0.08, 0.31)	0.386
	0.2 to 0.3	0.38 (0.24, 0.53)	0.795
	0.3 to 0.4	0.35 (0.20, 0.50)	0.788
	0.4 to 0.5	0.27 (0.09, 0.44)	0.311
	0.5 to 0.7	0.45 (0.27, 0.63)	0.784
	0.7 to 1	0.51 (0.29, 0.72)	0.203
	1 to 5	0.28 (0.03, 0.54)	0.652
	5+	1.90 (0.91, 2.90)	0.657
By age			
0 to 64	0.1 to 0.2	0.05 (−0.01, 0.10)	Reference
	0.2 to 0.3	0.10 (0.04, 0.17)	Reference
	0.3 to 0.4	0.13 (0.06, 0.20)	Reference
	0.4 to 0.5	0.10 (0.02, 0.18)	Reference
	0.5 to 0.7	0.22 (0.14, 0.31)	Reference
	0.7 to 1	0.30 (0.20, 0.40)	Reference
	1 to 5	0.07 (−0.05, 0.19)	Reference
	5+	0.55 (0.05, 1.05)	Reference
65+	0.1 to 0.2	0.67 (0.00, 1.35)	0.069
	0.2 to 0.3	2.20 (1.27, 3.13)	< 0.001
	0.3 to 0.4	1.33 (0.41, 2.26)	0.011
	0.4 to 0.5	0.77 (−0.25, 1.80)	0.198
	0.5 to 0.7	1.18 (0.13, 2.24)	0.076
	0.7 to 1	2.34 (1.06, 3.61)	0.002
	1 to 5	1.36 (−0.23, 2.96)	0.112
	5+	7.08 (2.22, 11.93)	0.009
By race and ethnicity			
Non-hispanic white	0.1 to 0.2	0.11 (−0.00, 0.22)	Reference
	0.2 to 0.3	0.27 (0.14, 0.39)	Reference
	0.3 to 0.4	0.23 (0.09, 0.38)	Reference
	0.4 to 0.5	0.27 (0.11, 0.42)	Reference
	0.5 to 0.7	0.36 (0.19, 0.53)	Reference
	0.7 to 1	0.50 (0.30, 0.70)	Reference
	1 to 5	0.01 (−0.23, 0.24)	Reference
	5+	1.36 (0.51, 2.21)	Reference
Non-hispanic black	0.1 to 0.2	0.20 (−0.15, 0.54)	0.631
	0.2 to 0.3	0.49 (0.06, 0.92)	0.327
	0.3 to 0.4	0.45 (−0.01, 0.91)	0.377
	0.4 to 0.5	0.29 (−0.22, 0.81)	0.922
	0.5 to 0.7	0.74 (0.20, 1.28)	0.190
	0.7 to 1	0.72 (0.05, 1.40)	0.536
	1 to 5	0.93 (0.11, 1.75)	0.035
	5+	3.91 (−0.31, 8.13)	0.245

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Table 1. (Continued)

Subgroup	Smoke $PM_{2.5}$ concentration bin ($\mu g/m^3$)	Associated change in monthly mortality rate (95% CI)	*P* value*
Hispanic	0.1 to 0.2	0.26 (−0.01, 0.52)	0.304
	0.2 to 0.3	0.60 (0.27, 0.93)	0.062
	0.3 to 0.4	0.39 (0.03, 0.75)	0.431
	0.4 to 0.5	0.36 (−0.06, 0.77)	0.682
	0.5 to 0.7	0.38 (−0.05, 0.81)	0.945
	0.7 to 1	0.35 (−0.20, 0.90)	0.617
	1 to 5	0.96 (0.33, 1.59)	0.005
	5+	2.12 (−0.42, 4.66)	0.578

*The *P* value indicates the statistical significance of between-group difference, with males, people aged 0 to 64, and non-Hispanic White people as the reference group. We added an interaction term of the subgroup variable and smoke $PM_{2.5}$ variable into the main model and reported the *P* value of this interaction term.

stress and inflammation, leading to impaired lung and vascular function (37). $PM_{2.5}$ may deposit in the kidney, contributing to the development of kidney diseases (38). $PM_{2.5}$ can also enter the gastrointestinal tract, causing imbalances in the intestinal microecology (39). In addition, $PM_{2.5}$ exposure has been associated with insulin resistance, which may progress to diabetes and other endocrine diseases (40). Furthermore, the oxidative stress, systemic and neuroinflammation, and hypothalamic–pituitary–adrenal axis dysregulation triggered by $PM_{2.5}$ have been linked to psychological diseases (41). The aggravation of physical health conditions could also worsen mental health (42). A multilevel conceptual framework has also been proposed for understanding the pathways connecting wildland fire smoke with mental health and well-being, which involves loss of nature, reduced access to livelihoods, reduced outdoor activities, and many other social and behavioral factors (17). More research is needed in the future to better understand the underlying mechanisms of the health impacts of wildland fire smoke.

In our study, higher effect estimates were found for older adults compared with people aged 0 to 64, which is consistent with the literature of all-source $PM_{2.5}$. The greater increases in mortality rates associated with smoke $PM_{2.5}$ among older adults reflect both higher baseline mortality rates and higher susceptibility to air pollution in the older population as found in previous studies due to decreased physiological, metabolic, and compensatory processes and a higher prevalence of comorbidities (43). In addition, we found higher effect estimates in counties far away from the fire point compared with those close to an active fire when the 12-mo moving average of smoke $PM_{2.5}$ concentrations was below 5 $\mu g/m^3$. This finding suggests a substantial public health burden from smoke, given that the population residing near the fires is likely much smaller compared to the larger number of people affected downwind due to smoke transport.

Furthermore, we observed a positive interaction effect between long-term exposure to wildland fire smoke $PM_{2.5}$ and current-month extreme heat. To date, although research has highlighted the synergistic health impacts of heat and air pollution (44), only a limited number of studies have specifically examined the interaction with $PM_{2.5}$ from wildland fire smoke. A recent study in California found evidence of synergistic effects between extreme heat and wildland fire smoke (31); however, since this study focused on short-term smoke $PM_{2.5}$ exposure, its results are not directly comparable to those of our study. The positive interaction between wildland fire smoke $PM_{2.5}$ and extreme heat indicates an increasing mortality burden for US populations in the future given that the coexposure to both hazards is expected to increase under the changing climate (28). Further studies on the compounding effects of wildland fires and other climate-related events, such as heatwaves and droughts, are warranted.

Our study estimated that over 10,000 nonaccidental deaths per year resulted from wildland fire smoke $PM_{2.5}$ in the contiguous United States, which is over 1,000 times higher than the recorded wildfire deaths in the US Billion-dollar Weather and Climate Disasters report by the National Oceanic and Atmospheric Administration's National Centers for Environmental Information (10 deaths/y due to the fire itself) (45). This indicates a great number of deaths brought by wildland fires that could not be captured by official tolls. According to the Global Burden of Disease Study, ambient $PM_{2.5}$ pollution contributed to an average of approximately 67,800 deaths annually in the contiguous United States from 2007 to 2020 (46, 47). Using this number as a reference, our results indicate that smoke $PM_{2.5}$-related deaths account for about 16.8% of the deaths associated with all-source $PM_{2.5}$. In addition, the US Billion-dollar Weather and Climate Disasters report estimated that wildfire events cost about 3.1 billion dollars per year in the United States (45), but this estimate does not take into account the health care–related losses or values associated with loss of life due to the fire itself or smoke (48). A recent study reported that the economic value of the health impacts of wildland fire smoke could be in the tens to hundreds of billions of US dollars, but the exposure-response function for the $PM_{2.5}$-mortality relationship they used was for all-source $PM_{2.5}$, not wildland fire-specific $PM_{2.5}$ (49). Our study suggests a tremendous wildland fire smoke-related mortality burden, and our effect estimates for the relationship between wildland fire $PM_{2.5}$ and mortality could be applied in future estimates of the costs of wildland fires to more fully account for the fire and smoke impacts.

The findings of our study have several key implications. First, wildland fire smoke is a national concern in the United States. Its health effects extend beyond the western regions where wildland fires mostly occur, impacting the entire country. Second, the health impacts of wildland fire smoke are not limited to those in response to short-term (daily) exposures. Long-term exposure to smoke $PM_{2.5}$ contributed to substantial mortality burden in the United States and will become increasingly important in the future due to the prolonged wildland fire seasons under climate change. Third, the health impacts of wildland fire smoke cover a wide spectrum of causes of death ranging from cardiovascular and endocrine diseases to mental disorders and digestive diseases. Furthermore, in addition to the well-recognized detrimental effects of extremely high concentrations of smoke $PM_{2.5}$, even relatively low levels can be harmful. Finally, the relationship between wildland fire smoke and mortality appears to be nonlinear, underscoring the necessity for further research into the modifying factors of this association and highlighting the importance of utilizing concentration-specific exposure-response functions in future health impact assessments.

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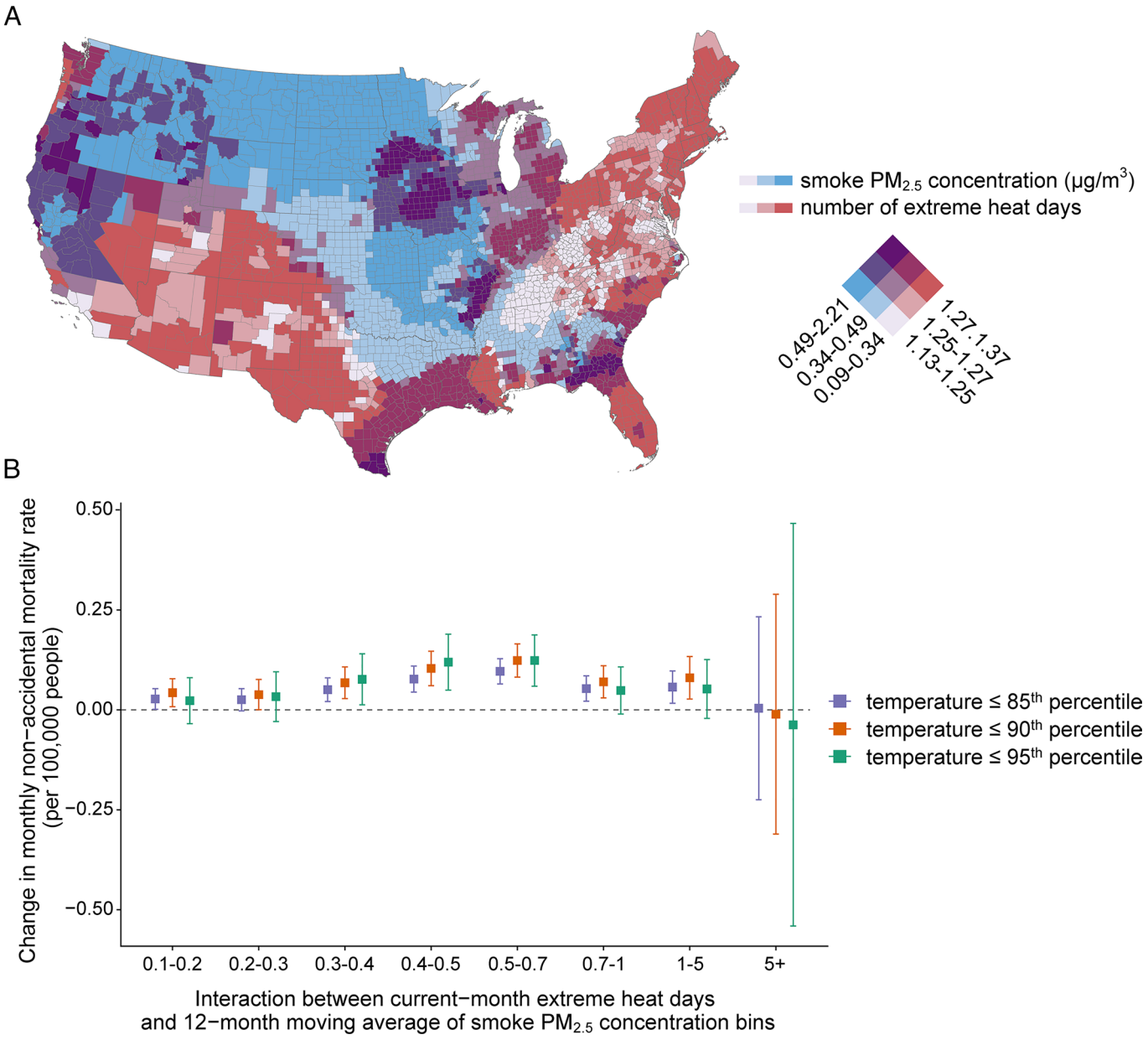

Fig. 4. Interaction effects between extreme heat and smoke $PM_{2.5}$ on nonaccidental mortality rate. (*A*) This bivariate choropleth map shows the spatial distribution of the 12-mo moving average of smoke $PM_{2.5}$ concentrations and the average number of current-month extreme heat days in each county, 2007 to 2020. Darker blue indicates higher average smoke $PM_{2.5}$ concentrations; darker red indicates more average extreme heat days; and darker purple indicates higher values of both variables. (*B*) The interaction effects between the number of current-month extreme heat days (a continuous variable) and 12-mo moving average of smoke $PM_{2.5}$ concentration bins (a categorial variable). The error bars indicate 95% CI. Extreme heat days were defined as days with daily mean air temperature higher than the county's 90th (main analysis), 85th, or 95th (sensitivity analyses) percentile warm season air temperature (May to September, 2007 to 2020).

Some limitations of this study should be noted. First, the wildland fire smoke $PM_{2.5}$ concentrations were modeled 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 of smoke (33). $PM_{2.5}$ from prescribed fire smoke is underrepresented in the model output; therefore, the exposure data we used do not fully capture the total smoke exposure people experience from wildland fires (i.e., both wildfire and prescribed fire). Additionally, wildland fire smoke has a unique spatiotemporal pattern, and measuring long-term smoke $PM_{2.5}$ exposure using average concentrations may overlook its episodic nature. Average smoke $PM_{2.5}$ concentrations primarily reflect intensity but do not adequately capture the frequency and duration aspects of long-term smoke $PM_{2.5}$ exposure (50). Future studies using different exposure metrics that better reflect various aspects of long-term smoke $PM_{2.5}$ exposure are warranted. Furthermore, 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 errors.

Second, lacking detailed location information, this county-level ecological study is susceptible to ecological fallacy. We were unable to capture the within-county heterogeneity of smoke $PM_{2.5}$ exposure among different subgroups or analyze the influence of wildfire evacuation in this study. Besides, the estimates of smoke $PM_{2.5}$ in our study may partially capture the health effects of other pollutants within the smoke mixture. Due to the absence of publicly available, full-spatial coverage data updated to 2020, we were unable to adjust for other wildland fire-related air pollutants, such

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as nitrogen dioxide, ozone, carbon monoxide, and polycyclic aromatic hydrocarbons. In addition, we used the smoke $PM_{2.5}$ concentration range of 0 to 0.1 $\mu g/m^3$ as the reference due to the limited number of county-months with 0 $\mu g/m^3$ long-term exposure. This choice of reference could result in an underestimation of both the smoke $PM_{2.5}$-related mortality changes and the attributable mortality burden. Furthermore, although we examined mortality from a wide range of plausible specific causes, we did not cover all possible causes of death (e.g., infectious diseases and cancer were excluded). Future studies are warranted to explore the association between wildland fire smoke and these diseases. Finally, the calculation of attributable mortality burden was based on the assumptions of homogeneity and causality of the estimated smoke $PM_{2.5}$-mortality relationships (see details in *Materials and Methods*). Violation of these assumptions may bias the results.

In conclusion, our study identified the detrimental effects of long-term wildland fire smoke $PM_{2.5}$ exposure on a wide range of mortality outcomes in the United States. With wildland fire intensity and frequency anticipated to increase in the future driven by climate change (5), more effective public health actions and communications that span the health risks of short- and long-term exposure are urgently needed both in and outside the areas where the wildland fires occur.

Materials and Methods

Mortality and Population Data. We obtained mortality data for all 3,108 counties or county equivalents in the contiguous United States from 2007 to 2020 from the National Center for Health Statistics (51). The mortality dataset includes the year and month of death, the primary cause of death (International Statistical Classification of Diseases and Related Health Problems, 10th Revision [ICD-10] codes), and the sex, age, race, and ethnicity of each deceased person. This study covered nonaccidental mortality (ICD-10 code: A00–R99) and cause-specific mortality from major categories: cardiovascular diseases (I00–I99), respiratory diseases (J00–J99), endocrine diseases (E00–E90), genitourinary diseases (N00–N99), nervous diseases (G00–G99), mental and behavioral disorders (F00–F99), and digestive diseases (K00–K93). Deaths from more specific causes, including ischemic heart disease (I20–I25), myocardial infarction (I20–I23), stroke (I60–I69), hypertensive disease (I10–I15), hypertensive heart disease (I11), COPD (J41–J44), diabetes (E10–E14), chronic kidney disease (N18), and ADRD (F00–F03, G30) were also examined in this study.

County-level population data were collected from the Surveillance, Epidemiology, and End Results Program, National Cancer Institute (52). The total population and population estimate by sex, age, race, and Hispanic origin were extracted for each county, 2007 to 2020. We calculated the monthly county-level cause-specific mortality rates for different sex (male and female), age (0 to 64, 65, and above), and race and ethnicity (non-Hispanic White, non-Hispanic Black, and Hispanic) groups. All mortality rates, except those specific to age groups, were age adjusted by direct standardization using the 2000 US Census population as the standard population. 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).

Wildland Fire Smoke $PM_{2.5}$ and Nonsmoke $PM_{2.5}$. Ambient wildland fire smoke $PM_{2.5}$ estimates for the contiguous United States were provided by a recent study by Childs et al. (33). In brief, smoke days were identified as days when smoke was overhead based on satellite imagery, and station-based ground smoke $PM_{2.5}$ on those days was calculated as anomalies above the median on nonsmoke days. 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 United States at a resolution of 10 × 10 km^2 (33). This model performed well over the entire range of observed smoke $PM_{2.5}$ ($R^2 = 0.67$), but the model performance was lower on days with station-based smoke $PM_{2.5}$ concentrations above 50 $\mu g/m^3$ compared to days with concentrations below 50 $\mu g/m^3$ (33). We additionally validated this model against a recently published wildland fire-specific $PM_{2.5}$ model in California, which applied an ensemble-based statistical approach to isolate wildland fire-specific $PM_{2.5}$ from other sources of emissions (53). This external validation showed a great consistency between the monthly county-level predictions from these two models in California, 2006 to 2020, with an R-squared (R^2) value of 0.92 and a rms error of 1.14 $\mu g/m^3$ (*SI Appendix*, Fig. S13). The daily smoke $PM_{2.5}$ concentrations were aggregated into monthly county-level average using population-weighted averaging to match with the mortality data. For months from January 2007 to December 2020, we calculated the 12-mo moving average of smoke $PM_{2.5}$ concentration for each county to represent the average exposure to smoke $PM_{2.5}$ in the previous year. To account for the potentially nonlinear effects, we divided the 12-mo moving average smoke $PM_{2.5}$ concentrations into 9 bins: 0 to 0.1 (reference), 0.1 to 0.2, 0.2 to 0.3, 0.3 to 0.4, 0.4 to 0.5, 0.5 to 0.7, 0.7 to 1, 1 to 5, and 5+ $\mu g/m^3$. The distribution of samples across the bins is shown in *SI Appendix*, Fig. S2.

Data of daily total all-source $PM_{2.5}$ concentrations at 1 × 1 km^2 resolution were obtained from the USHighAirPollutants dataset (54). These daily surface $PM_{2.5}$ concentration data were derived via a deep learning model that integrated big data from satellites, models, and surface observations (54). Similar to smoke $PM_{2.5}$, we averaged the daily all-source $PM_{2.5}$ concentrations into monthly county-level data. Nonsmoke $PM_{2.5}$ concentrations were then calculated by subtracting the smoke $PM_{2.5}$ from the all-source $PM_{2.5}$ concentrations. For negative values produced by this subtraction (0.07% of the total observations), the nonsmoke $PM_{2.5}$ concentrations were recoded as 0. We calculated the moving average nonsmoke $PM_{2.5}$ concentrations of the current and previous 11 mo for months from January 2007 to December 2020. The cartographic boundary for counties in the contiguous United States was downloaded from the US Census Bureau's TIGER/Line geodatabase (55).

Meteorological Factors. Daily mean air temperature and mean dew point temperature data at 4 × 4 km^2 were obtained from the Parameter-elevation Regressions on Independent Slopes Model Climate Group (56). Similar to the air pollution data, we generated monthly averages for these two variables for each county.

We also utilized the daily mean air temperature data from the PRISM Climate Group to detect extreme heat days (56). In each county, extreme heat was defined as days with daily mean air temperature higher than the county's 90th percentile warm season air temperature (May to September, 2007 to 2020). The monthly number of extreme heat days in each county were calculated. In sensitivity analysis, temperature thresholds of 85th and 95th percentiles were used as alternative definitions of extreme heat.

Distance to Fire. Daily active fire location data from 2006 to 2020 were obtained from the Hazard Mapping System. This system combines near real-time satellite observations into a common framework in which trained satellite analysts perform quality control of automated fire detections (57). For each county, we calculated the distance from its population centroid to the nearest active fire point each day and aggregated the daily data to monthly level using the median value. Then, we calculated the 12-mo moving average of this distance for each county to represent the average distance to active fires in the previous year. We classified the distance to fire into two categories: close (<150 km) and far (≥150 km).

Statistical Analysis. To estimate the association between long-term exposure to wildland fire smoke $PM_{2.5}$ and monthly mortality rates, we applied a panel fixed effects model which exploits local temporal variation in both exposure and outcome. Panel fixed effects models have been increasingly applied in environmental epidemiology in recent years (58, 59). In our study, the main model can be expressed as

$$\begin{aligned}\text{Mortality Rate}_{c,y,m} &= \alpha_c + \theta_{y,m} + \delta_{s,y} + \eta_{c,m} \\ &+ \sum_{b=1}^{B} \left(\beta_b Smoke\ \text{PM}_{2.5}\ Bins^{b}_{c,y,m} \right) \\ &+ \beta NonSmoke\ \text{PM}_{2.5\ c,y,m} \\ &+ ns\left(Temperature_{c,y,m}, df = 5 \right) + \varepsilon_{c,y,m}\end{aligned}$$

where $\text{Mortality Rate}_{c,y,m}$ represents the nonaccidental or other cause-specific age-adjusted mortality rates in county c, year y, and month m. $Smoke\ \text{PM}_{2.5}\ Bins^{b}_{c,y,m}$ is a dummy for whether the moving average of smoke $PM_{2.5}$ concentration of the current and previous 11 mo in county c, year y, and month m falls into the

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concentration range of bin b. α_c refers to time-invariant county effects, and $\theta_{y,m}$ refers to time-varying effects that are common in all counties. By introducing the indicators for each county and each year-month, this 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 (60). Fixed effects at the state by year level ($\delta_{s,y}$) and at the county by month of year level ($\eta_{c,m}$) account for regional long-term trend and seasonality in exposure and outcomes. *NonSmoke* $PM_{2.5}{}_{c,y,m}$ is the 12-mo moving average of nonsmoke $PM_{2.5}$ concentrations in county c, year y, and month m. Current-month air temperature was controlled by a flexible natural cubic spline with five degrees of freedom (df). $\varepsilon_{c,y,m}$ is the error term. We weighted models using the population size in each county to improve the precision of our estimates (61). Heteroskedasticity-robust SE were used to compute 95% CI. Associations were considered statistically significant at α of 0.05 with a Bonferroni correction given as α/m, where m is the number of examined specific causes of death (17 specific causes). Only specific causes with estimates consistent in direction across smoke $PM_{2.5}$ concentration bins and statistically significant after Bonferroni correction were included in further analysis.

In subgroup analyses, to estimate the association between long-term smoke $PM_{2.5}$ exposure and monthly mortality rates by sex, age, and race and ethnicity, we used an expanded dataset nesting the subgroups, interacted the subgroup variable with all terms in the model, and reported the statistical significance of the interaction term between the subgroup variable and smoke $PM_{2.5}$. To account for multiple comparison, Bonferroni correction was also performed in subgroup analyses ($m = 3$ subgroups $\times$ 5 major causes of mortality). Furthermore, we explored the interaction between extreme heat and smoke $PM_{2.5}$ by interacting the current-month number of extreme heat days and bins of 12-mo moving average concentration of smoke $PM_{2.5}$ in the model. In addition, we also conducted stratified analysis by distance to fire (close, far) to investigate its potential modification effect. We tested the lag pattern in the effects of smoke $PM_{2.5}$ by extending the 12-mo moving average of smoke $PM_{2.5}$ concentration to 24 and 36, representing longer-term smoke $PM_{2.5}$ in the past up to 3 y.

Based on the estimated coefficients of smoke $PM_{2.5}$ bins (β_b) for each cause, which can be interpreted as the changes in mortality rate associated with being in those bins of smoke $PM_{2.5}$ concentration compared to the reference bin (0 to 0.1 $\mu g/m^3$), we calculated the number of deaths attributable to smoke $PM_{2.5}$ (attributable number, AN) in each county in each month by $AN_{c,m} = \beta_b \times Population_{c,m}$, where β_b is the estimated coefficient of the corresponding smoke $PM_{2.5}$ bin (b) in that month and $Population_{c,m}$ is the total population in county c, month m. This calculation relied on two key assumptions. First, this approach assumes homogeneity within each smoke $PM_{2.5}$ bin, disregarding the variation within the bin. In this study, the 12-mo moving average concentrations of smoke $PM_{2.5}$ were divided into nine narrowly defined bins, each with a relatively small concentration range. Therefore, the estimate of each bin is likely to well represent the average effects of smoke $PM_{2.5}$ within that specific concentration range. This assumption was further tested by using finer bins and a nonlinear curve to smoke $PM_{2.5}$ in sensitivity analyses (see below; *SI Appendix*, Figs. S8 and S9). In addition, by using the regression coefficients to estimate attributable deaths, we assume a causal relationship between smoke $PM_{2.5}$ concentration and mortality rates. Traditionally, health impact assessments for long-term exposure use exposure-response functions estimated from cohort studies. However, to the best of our knowledge, no published cohort studies have reported the association between long-term wildland fire smoke $PM_{2.5}$ exposure and cause-specific mortality for the total population across the entire contiguous United States. Similar to a previous study (62), we applied the estimates from a panel fixed effects model to the calculation of attributable mortality burden. Our statistical model accounted for unmeasured temporal and spatial confounders by the year-month and county fixed effects and unmeasured confounders that vary both over time and space by the space–time interaction terms. Therefore, the observed association is unlikely to be primarily driven by unmeasured confounding factors. Spatial and temporal randomization tests were performed to test this assumption (see below; *SI Appendix*, Fig. S10). In addition, unlike cohort studies that commonly focus on people identified by specific characteristics (e.g., older adults), our study design allows us to cover the entire population across all age groups. This makes our estimates more suitable for health impact assessments of the general population.

Several sensitivity analyses were performed to test the robustness of our results: a) we used different choices of fixed effects in the model; b) we additionally adjusted for dew point temperature in the model; c) we removed nonsmoke $PM_{2.5}$ or current-month air temperature from the model; d) an alternative four or six dfs was used in the natural cubic spline of air temperature; e) we adjusted for 12-mo moving average of air temperature instead of current-month air temperature; f) we used mortality count as the outcome variable and performed a quasi-Poisson model; g) we used finer bins of smoke $PM_{2.5}$ concentration; and h) we used a natural cubic spline with knots at 0, 0.1, 0.3, 0.5, 1, and 5 $\mu g/m^3$ to model wildland fire smoke $PM_{2.5}$ concentration.

In addition, to assess the likelihood of model misspecification influencing our main results, we performed a spatial randomization test and a temporal randomization test. In the spatial randomization test, we randomized the smoke $PM_{2.5}$ exposure for 2,000 times across county while keeping their de facto year-month; in the temporal randomization test, we randomized the exposure variable for 2,000 times across year-month while keeping the corresponding counties. Such placebo tests are commonly used to detect spatial and temporal dependence due to model misspecification in panel models (63, 64).

Data, Materials, and Software Availability. Some study data are available. All environmental data, including wildfire smoke, air pollution, and weather, are publicly accessible. Mortality data can be accessed through applications at the National Center for Health Statistics (https://www.cdc.gov/nchs/nvss/index.htm) (51).

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