Research Square

Preprints are preliminary reports that have not undergone peer review.
They should not be considered conclusive, used to inform clinical practice,
or referenced by the media as validated information.

Spatial Heterogeneity in Population Health Impacts and Vulnerability to Compound Climate Hazards: Extreme Heat and Wildfire Smoke in California

Chen Chen (chc048@ucsd.edu)
University of California San Diego
Lara Schwarz
University of California San Diego
Noam Rosenthal
University of California Los Angeles
Miriam Marlier
Columbia University
Tarik Benmarhnia
University of California San Diego

Article

Keywords:

Posted Date: July 7th, 2023

DOI: https://doi.org/10.21203/rs.3.rs-3131787/v1

License: This work is licensed under a Creative Commons Attribution 4.0 International License.
Read Full License

Additional Declarations: There is **NO** Competing Interest.

Version of Record: A version of this preprint was published at Science Advances on February 2nd, 2024.
See the published version at https://doi.org/10.1126/sciadv.adj7264.

Abstract

Extreme heat and wildfire smoke events are increasingly co-occurring in the context of climate change, especially in California. Extreme heat and wildfire smoke may have synergistic effects on population health that vary over space. We leveraged high-resolution satellite and monitoring data to quantify spatially varying compound exposures to extreme heat and wildfire smoke in California (2006–2019) at ZIP code level. We found synergistic effects between extreme heat and wildfire smoke on cardiorespiratory hospitalizations at the state level. We also found spatial heterogeneity in such synergistic effects across ZIP codes. Communities with lower education attainment, lower health insurance coverage, lower income, lower proportion of automobile ownership, lower tree canopy coverage, higher population density, and higher proportions of racial/ethnic minorities are more vulnerable to the synergistic effects. This study highlights the need to incorporate compound hazards and environmental justice considerations into evidence-based policy development to protect populations from increasingly prevalent compound hazards.

Introduction

Global exposure to extreme heat and wildfires has grown in recent years and is expected to continue intensifying in the context of climate change[1–7]. A small increase in global temperature can result in extreme local temperature[8,9]. Hotter temperatures from a warming climate coupled with lower moisture from changes in precipitation regimes also produce drier conditions, intensifying the risk for larger wildfires[9,10]. Wildfires and heat waves have increased in length, intensity, and size under climate change, particularly in the US West Coast[11–15], with record-breaking events occurring frequently in recent years[2]. As a result, populations have been increasingly exposed to co-occurring extreme heat and wildfire smoke[16].

Aside from increases in co-occurrence due to climate change, exposure to extreme heat and wildfire smoke both increase the risk of adverse health outcomes, including cardiovascular and respiratory complications. Extreme heat can lead to dehydration and vasodilation of blood vessels which can produce heat stress and pressure the thermoregulatory process, increasing pulmonary and cardiac strain[17]. It has been estimated that 1.69 million deaths globally were attributed to non-optimal temperatures (i.e., the local temperature associated with the lowest mortality rate) in 2019[18]. The inhalation of particulate matter from wildfire smoke can also produce oxidative stress and inflammation which triggers cellular damage and increases the risk of cardiopulmonary disease[19]. Global deaths attributable to fine particulate matter ($PM_{2.5}$) from smoke are estimated to be 340,000-680,000 per year[20,21]. Due to the regularity of these concurrent exposures and their similar physiological impacts, these events may act synergistically to further aggravate health effects. Communities may be overburdened by these concomitant events and developing adaptation strategies based on exposure information from both extreme heat and wildfire smoke can protect against these dual risks. However, most efforts to mitigate the adverse health impacts of extreme heat and wildfire smoke did not consider

this potential synergistic effect. For example, existing early warning systems for wildfire smoke and extreme heat are issued separately by different government agencies in California. The local National Weather Service offices issue heat advisories in advance of forecast periods of high heat[22], while the local air quality management district sends out air quality warnings to promote behavior changes based on Air Quality Index created by the U.S. Environmental Protection Agency[23]. If a synergistic effect existed between wildfire smoke and extreme heat, issuing a joint warning earlier considering the compound exposure would be beneficial. Besides, existing evaluation of climate-related health impacts generally estimates the influence of each climate hazard separately and ignores potential synergistic effects between climate hazards[24], which might underestimate the actual health burden and jeopardize the effectiveness of climate change adaptation plans.

Our understanding of the potential synergistic effects of wildfire smoke and extreme heat is limited. Previous studies have focused on compounded effects of extreme heat and ambient air pollution, while none directly explored compounded effects of extreme heat and wildfire smoke. Systematic reviews found evidence of synergistic effects for heat with $PM_{2.5}$ on all-cause mortality and respiratory and cardiovascular morbidity[24] and weak evidence of effect modification by $PM_{2.5}$ on heat-mortality association[25]. However, the increased toxicity of $PM_{2.5}$ from wildfires[26] as well as the intensity of exposure during wildfire events – often an order of magnitude larger than year-round ambient levels – produces distinct physiological responses and adaptive behaviors that warrant independent study[27].

Such compounded impacts may also have important environmental justice implications since community factors may modulate the synergistic effect of co-occurring climate hazards. Previous studies found spatial heterogeneity in health impacts associated with extreme heat events [28–30], wildfire smoke events[31,32], and effect modification of air pollution on health effects of extreme heat[33]. Certain communities have increased vulnerability to wildfire smoke[34,35] and extreme heat[25] due to socioeconomic and other vulnerability factors. For example, neighborhood-level risk factors such as crime, noise, and traffic can lead to acute and chronic changes in the functioning of body systems and increase the effect of environmental exposures such as air pollution and heat in communities with lower socioeconomic status[36–39]. Communities with lower socioeconomic status might also have lower financial capacity to guard themselves against such hazards[35]. Communities that are majority Black, Hispanic, or Native American have a 50% higher vulnerability to wildfires[34] and racially marginalized communities experience greater impacts from extreme heat[25,40]. Climate change effects may exacerbate racial disparities and disproportionately impact communities of color[40]. However, existing studies on synergistic health effects of air pollution and extreme heat usually estimate an overall measure at a regional or country level using time-series analysis or case-crossover design[24,25,33]. No study has evaluated fine-scale spatial variability in the synergistic effects or explored what community-level socio-demographic characteristics are important to explain the differential synergistic effects. Identifying the local effects of these compounded climate hazards can be used to inform appropriate measures that account for the specific vulnerability of the community to reduce related health burdens. By exploring

what community-level socio-demographics are important in explaining spatial differences in synergistic effects of two key climate hazards, we can highlight the need to incorporate environmental justice considerations into adaptation efforts towards climate change and promote health equity and provide evidence to aid decisions like siting clean air and cooling centers and targeted educational campaign.

As a highly diverse state that is heavily affected by extreme heat and wildfire smoke, California is a unique context to investigate this potential synergistic effect and explore underlying vulnerability factors. The racial/ethnic composition of California is highly diverse- according to the 2020 census, Hispanics make up the largest racial/ethnic group (39%) which is followed by White (35%), Asian American (15%), and Black (5%)[41]. Income inequality is a major concern and California has one of the largest income gaps in the country; 20% of the state's net worth is concentrated in zip codes that are home to only 2% of the population[42]. Furthermore, projections show that California will be one of the most climatologically risk-prone areas in the county in the next decades[43]. Wildfires already account for 50% of total primary fine particulate matter emissions in California, and this percentage will only increase under climate change[1,44]. Extreme heat exposure is also expected to increase and projections show that the frequency of extreme temperatures will increase by ten-fold in many California regions[45]. Approximately 68% of the state of California was exposed to both extreme heat and wildfire smoke particulate matter concurrently during the 2020 wildfire season and these co-exposures are expected to continue increasing under climate change[46,47].

In this study, we leveraged highly resolved satellite and monitoring environmental data to estimate compound exposures to extreme heat and wildfire smoke $PM_{2.5}$ from 2006 to 2019 in California. We estimated the individual and joint effect of these hazards on cardiorespiratory hospitalizations and evaluated whether synergistic effects exist in such compounded climate hazards. We estimated these effects for California overall and then used a novel spatiotemporal approach to explore heterogeneity in such synergistic effects at the ZIP code level. Lastly, we investigated the effect modification of the synergistic effects by community characteristics to highlight the environmental justice implications of these compounded impacts. This is the first study to evaluate the synergistic effects of these two climate hazards and identify vulnerable communities in California to support evidence-based mitigation and adaptation policy development.

Results

We analyzed 995 California ZIP codes with populations larger than 1000 that experienced at least one day of extreme heat alone, wildfire smoke alone, or compound exposure to both hazards. For our main analyses, we choose the 85th percentile of historical summer daily maximum heat index as the threshold for extreme heat day and > 15 $\mu g/m^3$ wildfire-specific $PM_{2.5}$ concentration as the threshold for wildfire smoke day *a priori*. These threshold values were adopted from health-based guidelines for daily $PM_{2.5}$ utilized by the World Health Organization and heatwave definition utilized by the U.S. Environmental Protection Agency[48,49].

From 2006 to 2019, we observed 206,302 (4.06% among all ZIP code-days) extreme heat alone ZIP code-days, 32,089 (0.63%) wildfire smoke alone ZIP code-days, and 5,423 (0.11%) compound exposure ZIP code-days (Table 1). Although we included data for the entire year, most compound exposure days occurred between June and November (eTable 1). Years with > 1 day of compound exposure per ZIP code are 2008 (2.14 days) and 2017 (1.68 days) (eTable 2). ZIP codes with higher numbers of compound exposure days were in the northern mountains and central valley, likely driven by the higher occurrence of wildfires in surrounding mountains (Fig. 1A). Indeed, the northern mountain and central valley areas had more days with wildfire smoke alone during the study period than other regions (Fig. 1C). Since we defined extreme heat days using percentiles of historical summer daily maximum heat index from the year 1980 to the year 2005, the total number of days with extreme heat alone was different across ZIP codes and more days occurred in the coastal region and the southern desert (Fig. 1B). This could be a result of rapidly increasing temperatures during recent decades and consistently high temperatures coupled with a minimum cutoff value of 80°F and a maximum cutoff value of 105°F for the extreme heat definition. Indeed, the ZIP code-specific threshold values for extreme heat were higher in the central valley and the southern desert (eFigure 1). Across all years and ZIP codes in the study, we observed 18,143,419 cardiorespiratory hospitalizations.

When estimating statewide effect estimates using a time-stratified case-crossover design that did not consider spatial heterogeneity, we observed a relative excess risk due to interaction (RERI) of 0.04 (95% CI: 0.01, 0.06) for same-day exposure and hospitalization, suggesting a positive synergistic effect on the additive scale (Fig. 2A and eTable 3). In other words, we found a higher health impact due to interactions of wildfire smoke and extreme heat than the sum of health impacts from the individual hazards separately. As more stringent definitions were used for either hazard, there were fewer exposed ZIP code-days for each exposed category (Table 1), and RERI point estimates were higher with wider confidence intervals (Fig. 2A and eTable 3). RERI for previous-day exposure and hospitalization (lag 1) was similar (Fig. 2A and eTable 3). Although the synergistic effect on the additive scale (difference in effect estimates) is more relevant to public health than the synergistic effect on the multiplicative scale (ratio in effect estimates), we estimated the latter as a sensitivity analysis and found a similar pattern (eFigure 2 and eTable 3). Besides, we observed odds ratios (ORs) of 1.01 (95% confidence interval (CI): 1.00, 1.01), 1.03 (95% CI: 1.02, 1.03), and 1.07 (95% CI: 1.05, 1.09) for individual effects of extreme heat and wildfire smoke alone, and joint effect of combined exposure to both hazards, respectively (Fig. 2B and eTable 3). Similarly, ORs of individual and joint effects increased with definition stringency for both same-day and lag-1 metrics (Fig. 2B and eTable 3). ORs of previous-day exposure and hospitalization (lag 1) were similar for wildfire smoke and combined exposure but lower for extreme heat.

To allow the synergistic effect to vary across space, we utilized a within-community matched design (see details in the methods section) to calculate ZIP code-specific rate ratios for individual and joint effects of extreme heat and wildfire smoke, as well as the corresponding ZIP code-specific RERIs. We failed to estimate RERI in four ZIP codes because no hospitalization was observed in selected control days of these ZIP codes, which is expected given the small population (< 3500). To account for spatial autocorrelation, we leveraged spatial information across the remaining 991 ZIP codes with a spatial

Bayesian hierarchical model (BHM) and calculated the post-pooling ZIP code-specific RERIs and noise-to-signal ratios (Fig. 3), which were of similar patterns as the pre-pooling estimates (eFigure 3A). The median ZIP code-specific RERIs after incorporating the spatial information was 0.11 (interquartile range [IQR]: -0.14, 0.35), indicating positive synergistic effects between wildfire smoke and extreme heat among most ZIP codes in our study. We also observed strong spatial heterogeneity in ZIP code-specific RERIs, with positive synergistic effects in the northern mountain, central valley, and large coastal metropolitan areas such as Los Angeles and the Bay Area, and antagonistic effects in the northern coast (Fig. 3).

To explore how community characteristics might explain the observed heterogeneity in ZIP code-specific synergistic effects, we ran meta-regressions using 918 ZIP codes after removing missing data. Communities with lower synergistic effects had higher education attainment, higher health insurance coverage, higher income, higher proportion of automobile ownership, higher tree canopy coverage, and higher proportion of White residents (Fig. 4). On the other hand, we observed higher synergistic effects among communities with higher population density, and higher proportions of Black, Asian, Latino, Native American, and Pacific Islander residents. Since AC prevalence varies drastically across California due to the varied climate zones (eFigure 4A), we also evaluated the effect modification of AC prevalence on synergistic effects by climate zone, and found lower synergistic effects among communities with higher AC prevalence in 11 out of 15 climate zones (not enough data for estimation in Brawley), with exceptions for Eureka, San Jose, Santa Maria and LA Civid Center (eFigure 4B).

To assess the robustness of our conclusions, we conducted extensive sensitivity analyses. First, we included all 1772 California ZIP codes in the statewide case-crossover analysis. The spatial distribution of compound exposure days is similar to the main analysis (eFigure 5A), and so were the RERI estimates (eTable 3). Second, using three different control selection and estimation methods for the within-community matched designs to obtain ZIP code-specific estimates, we observed similar pre- and post-pooling synergistic effect estimates in spatial patterns in all matched designs explored (eFigure 3 and eFigure 6). Inferences for effect modification of synergistic effects by community characteristics were also similar except for air conditioning prevalence (eFigure 7). Last, inferences remained the same for effect modification of synergistic effects by community characteristics under different analytical decisions: 1) using HUD-crosswalk to convert census tract data to ZIP code level for community characteristics, 2) incorporating minimal prior knowledge into the spatial BHM, and 3) ignoring potential spatial autocorrelation (eFigure 8).

Discussion

Using daily time-series dataset of compound exposures and cardiorespiratory hospitalizations for 995 ZIP codes in California from 2006 to 2019, we found evidence of synergistic effects between extreme heat and wildfire smoke at the state level. In other words, we observed a higher statewide joint effect when both hazards co-occur compared to the sum of individual effects of either hazard alone. Furthermore, using a within-community matched design and a spatial-temporal model, we also found that such synergistic effects vary spatially within California, with higher values in the northern mountains,

central valley, and large coastal metropolitan areas. This spatial heterogeneity is correlated with socioeconomic and demographic characteristics; we observed higher synergistic effects in communities less affluent, more crowded, or with higher proportions of racial/ethnical minority residents. In 11 out of 15 California climate zones, AC prevalence was negatively associated with the synergistic effect. Our results are robust to various climate hazard definitions and analytical methods. These results support the need to incorporate consideration of synergistic effects in evaluation of health impacts and development of action plans and adaptation efforts. Our results could also aid decision-making for targeted efforts in communities with higher vulnerability toward the synergistic effects.

This is the first study that explicitly evaluated the synergistic effects of extreme heat and wildfire smoke events while exploring spatial heterogeneity and environmental justice implications of such impacts. Although we cannot directly compare with previous studies due to our unique focus on wildfire smoke instead of all-source $PM_{2.5}$, our findings are consistent with previous studies qualitatively. A systematic review found evidence supporting the synergistic effects of heat and air pollutants (ozone and particulate matter) on all-cause mortality, non-accidental mortality, and morbidity outcomes[24]. Synergistic effects between air pollution and heat were further supported by recent studies, including a global study that found higher effects of extreme heat on cardiorespiratory mortality in areas with higher levels of PM_{10}, $PM_{2.5}$, $O_{3,}$ and NO_2[33], and a California study that found positive RERI between extreme $PM_{2.5}$ exposure and extreme heat for all-cause mortality[50].

Our finding that hospitalizations on days with concurrent extreme heat and wildfire smoke events exceeded the combined hospitalizations from days with either hazard alone, motivates the consideration of compound climate hazards in public health planning. Although government agencies are becoming more aware of the increase in concurrent exposure to wildfire smoke and extreme heat, and some attempted to promote individual behavior changes specific to such compound exposure to mitigate adverse health impacts[51,52], a better understanding of the magnitude of the synergistic effect could promote more proactive top-down initiatives to protect public health. For example, the health impact of the compound exposure in days with wildfire $PM_{2.5}$ above 15 $\mu g/m^3$ (WHO 24-hour standard) is close to the health impact of the wildfire smoke alone in days with wildfire $PM_{2.5}$ above 35 $\mu g/m^3$ (U.S. EPA 24-hour standard). In other words, a joint early warning system using more stringent standards (e.g., 15 $\mu g/m^3$ instead of 35 $\mu g/m^3$) to account for the synergistic effect is needed to achieve the same level of protection using less stringent standards in days with single hazard when compound exposures exist.

More importantly, we found spatial heterogeneity in the synergistic effects of extreme heat and wildfire smoke events across California, with higher synergistic effects in communities with lower education attainment, lower health insurance coverage, lower income, lower proportion of automobile ownership, lower tree canopy coverage, higher population density, and higher proportions of racial and ethnic minorities. This is consistent with vulnerable communities identified separately for wildfire and extreme heat in previous studies[25,34,36,40]. These results confirmed spatial variations in the effects of extreme weather events and shed light on how to understand such heterogeneity and develop targeted

interventions toward vulnerable subpopulations. For example, we observed higher synergistic effects in communities with higher proportions of racial/ethnic minority groups, who may be more vulnerable to the impacts of such compounded impacts due to the intersection with other social determinants of health such as lack of access to health care, lower financial capacity to protect themselves against exposure to the hazards, lower awareness of the compound hazards, or higher prevalence of comorbidities. Although uncertainty exists in the mechanism behind such vulnerability, updating existing heat action plans to incorporate considerations of wildfire smoke could still help mitigate the joint effects of compound hazards, such as implementing focused educational outreaches and establishing new clean air and cooling centers near the most vulnerable subpopulations.

There are a few limitations in this study that should be explored in future research. First, we identified wildfire smoke day using a threshold value for daily wildfire-specific $PM_{2.5}$ concentrations while ignoring other harmful components of wildfire smoke, which might cause underestimation in the joint effect and individual effect of wildfire smoke. Second, being exposed to ambient air pollution or extreme heat for multiple consecutive days might lead to greater health impacts (i.e., excess effect from long heatwaves or cumulative effect of air pollution)[53,54], which we did not consider in this study due to the limited size of our sample. Third, we focused on acute effects of extreme heat and wildfire smoke on unscheduled cardiorespiratory hospitalizations, while both hazards could have long-term health impacts or less clearly defined health outcomes like increased mental stress. Exploring the potential synergistic effects of both hazards on different time scales and mental health outcomes warrants future research. Fourth, although we accounted for seasonality and confounding from variables that are stable within two months by design in estimating ZIP code-specific synergistic effects, we could not rule out the possibility of residual confounding. However, consistent results from different control selections (e.g., yearly matching controlled for seasonality in outcomes more stringently than the monthly matching in the main analysis) and estimation methods (e.g., Poisson method assigned the same weights to all control days) alleviated this concern (eFigure 7). Last, we assumed isotropy (i.e., same spatial relationships regardless of direction) in the spatial Bayesian hierarchical model due to methodological limitation, which might not hold in data with complex geographies and climates like California. Yet, this potential bias is likely stable over time and would have a limited impact on our final inferences.

Conclusion

Extreme heat and wildfire smoke are both harmful exposures that are increasingly co-occurring in the context of climate change. As the number of compound exposure days increases, the synergistic effects between extreme heat and wildfire smoke identified in this study will become more important for accurate health burden estimation and should be incorporated in the development of the new hazard warning system. For example, a joint warning system could offset the excess risk due to the synergistic effect by considering exposure to both climate hazards and issuing health warnings at lower air pollution levels when extreme heat co-occurs. Moreover, we found spatially varying synergistic effects between wildfire smoke and extreme heat on cardiorespiratory hospitalization and identified vulnerable communities to

such effects in California. This finding highlights the need to incorporate environmental justice considerations into evidence-based mitigation and adaptation policy development, which could guide the siting of clean air and cooling centers and the implementation of focused educational outreaches.

Methods

Data sources

We studied the synergistic effects of two climate-related hazards, extreme heat and wildfire smoke, in California ZIP codes from 2006 to 2019 that satisfied the following criteria: 1) having a population larger than 1000 in the 2010 U.S. decennial census (statistical power consideration); and 2) having at least one day in each of the four exposure categories (required for ZIP code-specific effect estimates; details in the climate hazards section below). We chose the ZIP code as the spatial unit for analysis given the availability of health data.

Health outcome

We calculated the ZIP code-specific daily sum of unscheduled hospitalizations by cause using the Patient Discharge Data and Emergency Department Data collected by the California Department of Health Care Access and Information[55]. We estimated the counts of cardiorespiratory hospitalization, the sum of circulatory and respiratory hospitalizations, based on primary diagnosis codes (see Supplementary materials for the list of codes included to identify the cause-specific hospitalizations).

Climate hazards

We identified wildfire smoke ZIP code-days as days in which the daily wildfire-specific $PM_{2.5}$ concentration in the ZIP code is higher than a pre-specific threshold. We explored four threshold values—>0 $\mu g/m^3$, 5 $\mu g/m^3$ (2021 air quality guideline for annual $PM_{2.5}$ by World Health Organization[48]), 15 $\mu g/m^3$ (2021 air quality guideline for 24-hour $PM_{2.5}$ by World Health Organization[48]), and 35 $\mu g/m^3$ (National Ambient Air Quality Standard for 24-hour $PM_{2.5}$ by U.S. Environmental Protection Agency[56]). Although adverse health impacts were observed below such thresholds[57,58], maintaining $PM_{2.5}$ concentrations lower than these threshold values are considered sufficient to protect public health from a regulatory perspective and serves as a good starting point to dichotomize the wildfire-specific $PM_{2.5}$. Most local air quality management agencies also issue air quality warnings or promote “action days” if the standards were exceeded[23]. The daily time-series dataset of ZIP code-specific wildfire-specific $PM_{2.5}$ concentration was previously developed and details were reported elsewhere[59]. Briefly, this dataset estimated daily total and non-wildfire-specific $PM_{2.5}$ concentration using an ensemble model-based novel multiple imputation approach with a prediction R^2 of 0.78 in the test set by incorporating data from U.S. Environmental Protection Agency’s Air Quality System monitors, aerosol optical depth from NASA satellite

measurements, smoke plume observations from the NOAA Hazard Mapping System, meteorological variables from the Gridded Meteorological (GRIDMET) reanalysis product, and other land-use variables from the National Land Cover Database.

We identified extreme heat ZIP code-days as days in which the daily maximum heat index of the ZIP code is higher than a ZIP code-specific threshold, which is similar to the definition of heatwave day threshold used by the U.S. Environmental Protection Agency[49]. We calculated the ZIP code-specific threshold as the 85th or 95th percentile of the summertime (July and August) daily maximum heat index from the year 1980 to the year 2005 in the ZIP code, which captured unusually hot days in each ZIP code and allowed adaptation and acclimation to local climates. In other words, this definition emphasizes the influence of climate change in recent decades by allowing ZIP codes with larger increases in heat index during the study period compared to the historical period to have more extreme heat days. Besides, we utilized the daily maximum heat index as the threshold, which combines maximum absolute temperature and minimum relative humidity, proxies biological heat stress, and is of higher health relevance than absolute temperature[60,61]. We obtained daily temperature and humidity from the GRIDMET reanalysis product at a 4km resolution for the calcualtion[62]. Since most heat index algorithms produce numerically similar results, we choose the National Weather Service's Weather Prediction Center's adaptation of the Rothfusz regression model to calculate heat index[63,64]. To avoid implausible threshold values, we also replaced ZIP code-specific threshold values higher than 105°F or lower than 80°F with absolute cutoff values of 105°F or 80°F to define extreme heat days[47]. Details of the implementation of this algorithm in Google Earth Engine were reported elsewhere[47].

Combining designations of extreme heat ZIP code-day and wildfire smoke ZIP code-day, we categorized ZIP code-days within California into four types of ZIP code-days: extreme heat alone, wildfire smoke alone, compound exposure to both hazards and no exposure to either hazard (control/unexposed). These exposure categories were used in selecting ZIP codes for the study and in ZIP code-level matched design to evaluate spatial heterogeneity in synergistic effects. We summarized spatial distribution and the total number for the three types of exposed days.

Community characteristics

To explore the effect modification of spatial heterogeneities in synergistic effects from extreme heat and wildfire smoke by community characteristics, we obtained ZIP code level community characteristics from the U.S. Decennial Census in 2010[65] and the Healthy Places Index (HPI) report version 3.0[66,67]. All community characteristics were coded in a way that higher values indicate better socioeconomic status or fewer racial and ethnic minority residents. Specifically, we included variables for race/ethnicity (proportion of White, Black, Asian, Latino, Native American, Pacific Islander), employment (proportion of employment among those ages 20–64), education attainment (proportion of 25 and older with a bachelor degree or higher), health insurance coverage (proportion of insured among those aged 18–64), income (proportion of the population with an income that is greater than 200% of the federal poverty level

and per capita income in U.S. dollars), population density per 10,000 population, assets and utilities (percentage of households with central air conditioning [AC] or access to an automobile), and tree canopy coverage (population-weighted percentage of area with tree canopy). Most socioeconomic variables are based on the averages of the American Community Survey in 2015–2019 summarized by the HPI while racial/ethnical variables are based on the Decennial Census survey in 2010. Details of all data sources are summarized in eTable 4. Since California has a highly varied climate with drastically different average temperatures, we also obtained the designation of ZIP codes into 16 climate zones in California from the Pacific Energy Center for stratified analysis[68].

Although the HPI provided community characteristics at ZIP code level, they did not provide details on their crosswalk from the census tract (the spatial unit where most survey data was measured) to the ZIP code (the spatial unit for our health outcome). As a sensitivity analysis, we calculated the ZIP code level community characteristics manually from census-tract values except for population density and AC prevalence, which were available at ZIP code level from other data sources (see eTable 4). We downloaded the census tract-level HPI data for the relevant indicators[67], census tract population sizes from the U.S. Decennial Census in 2010[65], and the U.S. Department of Housing and Urban Development crosswalk file[69]. Specifically, we calculated the ZIP code-level values as weighted averages of census tract-level values. The weight is the census tract population within the ZIP code, which was calculated as the product of the census tract population and the ratio of the census tract addresses that fall within the ZIP code. For automobile ownership, we created an ordinal variable with ten categories based on deciles of ZIP code's automobile ownership percentile among census tracts within each ZIP code.

Statistical analyses

State-level case-crossover analysis

We first evaluated the synergistic effect of extreme heat and wildfire smoke on the risk of daily cardiorespiratory hospitalizations at the state level using the time-stratified case-crossover design and the metric relative excess risk due to interaction (RERI). The time-stratified case-crossover design is a widely used method in evaluating short-term health impacts of environmental hazards, which compared exposures in days with an event to exposures in the same weekdays in other weeks of the month without the event to account for time-invariant confounding and estimates odds ratio (OR)[70,71]. An OR larger than one indicates an increase in the risk of hospitalization from exposure to environmental hazards. RERI quantifies the relative difference between the joint effect of two co-occurring hazards (extreme heat and wildfire smoke) and the sum of individual effects of the two hazards[72]. A positive RERI value indicates an increase in risk due to interaction between the two hazards. We used > 15 $\mu g/m^3$ daily wildfire-specific $PM_{2.5}$ concentration as the threshold for wildfire smoke and 85th percentile historical daily maximum heat index as the threshold for extreme heat in the definition of hazards for main analysis.

Specifically, for each ZIP code-day that had cardiorespiratory hospitalizations, we first identified controls as the same weekdays from other weeks of the same month and year in the same ZIP code. Next, we applied conditional logistic models to estimate the statewide OR for the effect of extreme heat alone, wildfire smoke alone, and the combined exposure to both hazards on cardiorespiratory hospitalizations by including an interaction term between indicators for either hazard. The conditional logistic model accounted for the matching procedure by comparing the exposures of each matched case and control set and calculating a weighted average across all matched sets. The OR approximates the effect of the climate hazard (compound or individual) on the risk of hospitalization; in other words, an OR larger than one indicates a detrimental effect of the climate hazard (compound or individual) on the risk of hospitalization. Since this study design controls for covariates that do not vary markedly within a month, such as age, race, and sex, as well as time-varying covariates like season[73,74], we did not include covariates other than indicators for the hazards of interest and an interaction term between the two hazards. Effects of individual hazard alone (OR_{H0S1} and OR_{H1S0}) were exponentiated coefficients from the conditional logistic model, while the joint effect of both hazards (OR_{H1S1}), or effect of compound climate hazards, was calculated as the exponentiated sum of three coefficients (two for individual hazards and one for the interaction term) in the conditional logistic model. Since assessing interaction on the additive scale has been recommended as the appropriate scale to inform potential public health benefits of hypothetical interventions[72,75], we evaluated whether a synergistic effect exists between extreme wildfire smoke and heat on the additive scale using the RERI in our main analysis. We calculated the RERI as (OR_{H1S1} -1) - (OR_{H0S1}-1) - (OR_{H1S0}-1), where subscript H1 indicates days with extreme heat and S0 indicates days without wildfire smoke. We also assessed interaction on the multiplicative scale using the ratio of the odds ratio (exponentiated coefficient for the interaction term) as a secondary analysis. We calculated the 95% confidence intervals for RERI and the joint effect using the delta method[72]. We used the “survival” for conditional logistic regression and the “msm” package for the delta method[76,77].

ZIP code-level matched design with spatial Bayesian hierarchical model

Since the state-level analysis assumed the same effect of extreme heat and wildfire smoke (individual, joint, or synergistic) across all ZIP codes while spatial heterogeneity might exist, we applied a modified version of the previously developed method that utilizes within-community matched design to estimate ZIP code-specific effects and spatial Bayesian hierarchical model (BHM) to incorporate considerations of spatial autocorrelation[78].

In the within-community matched design, we quantified the ZIP code-specific effects of the climate hazards on cardiorespiratory hospitalizations for each ZIP code separately. For each ZIP code, we first identified matched controls for three types of exposed days separately (extreme heat alone, wildfire smoke alone, and compound exposure to both hazards). For each exposed day, controls are days of the same year and ZIP code, not exposed to either hazard and within the window of 30 calendar days before

or after the exposed day[78]. To reduce the spill-over effect, we excluded days within three days of any exposed days (either extreme heat or wildfire smoke) from the potential controls[79,80]. Next, we calculated the rate ratio for each exposed day as the ratio of hospitalization counts in the exposed day divided by the weighted average of the counts of hospitalization in all selected control days, with weights equal to the inverse distance to the exposed day (i.e., 1/number of days to exposed day). Since this study design resembles a matched cohort design, we directly calculated the ZIP code-specific rate ratios for extreme heat alone (RR_{H1S0}), wildfire smoke alone (RR_{H0S1}), and combined exposure to both hazards (RR_{H1S1}) as the average rate ratios from all corresponding pairs of matched exposed days and control days in each ZIP code. We used the ratio of the hospitalization counts to approximate the rate ratio because the population size of a ZIP code is unlikely to change dramatically within two months. Last, we calculated the ZIP code-specific synergistic effects, RERI, as (RR_{H1S1} -1) - (RR_{H0S1}-1) - (RR_{H1S0}-1). This within-community matched design accounted for potential confounding that does not vary remarkably within two months by design (e.g., population composition regarding sex and age) while giving more weight to control days closer to the exposed day in calculation reduced the potential influence of seasonal trend. We removed ZIP codes from the next-step analysis if the estimation of individual or joint effects failed.

Since areas closer together are more likely to be exposed to the same wildfire smoke or extreme heat events, we expect the ZIP code-specific RERIs to be more similar among closer ZIP codes. To increase the precision of our ZIP code-specific estimates, we used a spatial BHM to leverage this spatial autocorrelation in our estimates. The theoretical development of this model was described elsewhere[78]. Based on the empirical semivariogram, we selected the spherical shape for the covariance structure and specified starting values of the covariance structure as 2, 0.75, and 2 for sill, nugget, and range, respectively. We also specified the priors as inverse gamma distributions (2 for shape and 1/starting value for scale) for the sill and nugget, and uniform distribution (0.001 to 6) for the range; the tuning parameters as one-twentieth of the starting values. We used 10,000 Monte Carlo Markov chain samples with 75% burn-in to estimate parameters and sample weights in the spatial BHM. We recovered sample weights in the BHM to obtain pooled ZIP code-specific RERIs, which incorporated information from spatial autocorrelation into the pre-pooling ZIP code-specific RERIs. We also computed the signal-to-noise ratio (SNR) as the ratio between the mean of the recovered samples (either for the parameters or for the weights) and the corresponding standard deviation of the recovered samples, representing the precision of the estimates. This method assumes isotropy (i.e., the same spatial relationship in all directions). We used the “spBayes” package in R for the spatial BMH[81].

Effect modification by community characteristics

To evaluate the potential effect modification of community characteristics on the synergistic effect, we ran meta-regressions of the pooled ZIP code-specific RERIs on each community characteristic selected separately. We reported results as the increase in RERI per interquartile range change in the community characteristics. For AC prevalence, we also evaluated the effect modification for each climate zone separately because AC prevalence varies dramatically across climate zones in California (eFigure 4A). We conducted meta regressions using the “meta” package[82].

Sensitivity analyses

To evaluate the robustness of our state-level estimates towards the inclusion of ZIP codes, we conducted the time-stratified case-crossover analysis using all California ZIP codes (1772) after removing two ZIP codes due to exposure data missingness (one for extreme heat and the other for wildfire smoke). We also explored seven combinations of hazard definitions other than the definition used in the main analysis (threshold of > 0 $\mu g/m^3$, 5 $\mu g/m^3$, 15, and 35 $\mu g/m^3$ daily wildfire-specific $PM_{2.5}$ concentration for wildfire smoke; threshold of 85th and 95th percentiles of historical daily maximum heat index for extreme heat). Last, we conducted the above analyses using the exposure of the previous day (lag1).

For ZIP code-specific RERIs, we explored three different within-community matched designs with varying assumptions (yearly weighting, monthly Poisson, and yearly Poisson) other than the within-community matched design described in the main analysis (monthly Poisson). The first part of the method name describes the control identification method while the second part describes the estimation method. Specifically, in the “yearly” methods, we adopted the control identification method used by Liu et al. 2017 studying wildfire smoke events[79]. We identified matched controls for each exposed day as days of the same ZIP code, not exposed to either hazard and within the window of seven calendar days before or after the exposed day in a different year. This control identification method provides better control for seasonal trends by design than the “monthly” method used in the main analysis but might experience more inter-year confounding. For “yearly weighting”, the calculation of the rate ratio is the same as the main analysis except that the unit for the distance between matched control and the exposed day is year instead of day. We also adopted a new rate ratio calculation method modified from Liu et al. 2017[79], which takes a random sample of four controls from the matched controls of each exposed day and runs a Poisson regression of the count of hospitalization on an indicator of exposed among all matched pairs in each ZIP code (“Poisson”). Compared to the weighting method that gives more weight to days closer to the event, the Poisson method treats all matched controls equally. We leveraged spatial information into these estimations through the spatial BHM while restricting the analyses to ZIP codes that succeeded in all four matched designs and had a plausible RERI (< 50). We also evaluated effect modification by community characteristics for all matched designs explored.

Last, we evaluated the robustness of the combination of our spatial BHM and effect modification evaluation method by conducting three analyses other than the main analysis: 1) we used the HUD crosswalk dataset for meta-regression to confirm the robustness towards community characteristic dataset (HUD crosswalk); 2) we ran the spatial BHM using flat priors for the sill and nugget to introduce minimal prior information into the Bayesian model (inverse gamma distributions with shape and scale equal to 0.001) (flat prior); and 3) we ignored the potential spatial autocorrelation and ran linear regressions of ZIP code RERI from the within-community matched design and community characteristics (non-spatial linear).

All analyses were performed in R Studio with R version 4.1.0[83]. The R code to replicate these analyses is available at the following link: https://github.com/suthlam/synergistic_effect_wildfire_extremeheat_ca.git

References

1. Ford, B. *et al.* Future Fire Impacts on Smoke Concentrations, Visibility, and Health in the Contiguous United States. Geohealth 2, 229–247 (2018).
2. Li, Y. *et al.* Dominance of Wildfires Impact on Air Quality Exceedances During the 2020 Record-Breaking Wildfire Season in the United States. *Geophysical Research Letters* 48, e2021GL094908 (2021).
3. Perkins, S. E., Alexander, L. V. & Nairn, J. R. Increasing frequency, intensity and duration of observed global heatwaves and warm spells. Geophysical Research Letters 39, (2012).
4. Smith, T. T., Zaitchik, B. F. & Gohlke, J. M. Heat waves in the United States: definitions, patterns and trends. Clim Change 118, 811–825 (2013).
5. Tebaldi, C. & Wehner, M. F. Benefits of mitigation for future heat extremes under RCP4.5 compared to RCP8.5. Climatic Change 146, 349–361 (2018).
6. Krawchuk, M. A., Moritz, M. A., Parisien, M.-A., Dorn, J. V. & Hayhoe, K. Global Pyrogeography: the Current and Future Distribution of Wildfire. PLOS ONE 4, e5102 (2009).
7. Senande-Rivera, M., Insua-Costa, D. & Miguez-Macho, G. Spatial and temporal expansion of global wildland fire activity in response to climate change. Nat Commun 13, 1208 (2022).
8. Clarke, B., Otto, F., Stuart-Smith, R. & Harrington, L. Extreme weather impacts of climate change: an attribution perspective. Environ. Res.: Climate 1, 012001 (2022).
9. US EPA, O. Climate Change Indicators in the United States. https://www.epa.gov/climate-indicators (2023).
10. Abatzoglou, J. T., Williams, A. P. & Barbero, R. Global Emergence of Anthropogenic Climate Change in Fire Weather Indices. Geophysical Research Letters 46, 326–336 (2019).
11. Gershunov, A. & Guirguis, K. California heat waves in the present and future. Geophysical Research Letters 39, (2012).
12. Goss, M. *et al.* Climate change is increasing the likelihood of extreme autumn wildfire conditions across California. Environ. Res. Lett. 15, 094016 (2020).
13. Williams, A. P. *et al.* Observed Impacts of Anthropogenic Climate Change on Wildfire in California. Earth's Future 7, 892–910 (2019).
14. Westerling, A. L. Increasing western US forest wildfire activity: sensitivity to changes in the timing of spring. Philosophical transactions of the Royal Society of London. Series B, Biological sciences 371, 20150178–20150178 (2016).
15. Iglesias, V., Balch, J. K. & Travis, W. R. U.S. fires became larger, more frequent, and more widespread in the 2000s. Science Advances 8, eabc0020 (2022).

16. Hanberry, B. B. Compounded Heat and Fire Risk for Future U.S. Populations. Sustainability 12, 3277 (2020).
17. Ebi, K. L. *et al.* Hot weather and heat extremes: health risks. Lancet 398, 698–708 (2021).
18. Burkart, K. G. *et al.* Estimating the cause-specific relative risks of non-optimal temperature on daily mortality: a two-part modelling approach applied to the Global Burden of Disease Study. The Lancet 398, 685–697 (2021).
19. Black, C., Tesfaigzi, Y., Bassein, J. A. & Miller, L. A. Wildfire smoke exposure and human health: Significant gaps in research for a growing public health issue. Environ Toxicol Pharmacol 55, 186–195 (2017).
20. Johnston, F. H. *et al.* Estimated global mortality attributable to smoke from landscape fires. Environ Health Perspect 120, 695–701 (2012).
21. Roberts, G. & Wooster, M. J. Global impact of landscape fire emissions on surface level PM2.5 concentrations, air quality exposure and population mortality. Atmospheric Environment 252, 118210 (2021).
22. National Weather Service. NWS HeatRisk. https://www.wrh.noaa.gov/wrh/heatrisk/?wfo=sgx.
23. Action Days | AirNow.gov. https://www.airnow.gov/aqi/action-days/.
24. Anenberg, S. C., Haines, S., Wang, E., Nassikas, N. & Kinney, P. L. Synergistic health effects of air pollution, temperature, and pollen exposure: a systematic review of epidemiological evidence. Environmental Health 19, 130 (2020).
25. Son, J.-Y., Liu, J. C. & Bell, M. L. Temperature-related mortality: a systematic review and investigation of effect modifiers. Environ. Res. Lett. 14, 073004 (2019).
26. Aguilera, R., Corringham, T., Gershunov, A. & Benmarhnia, T. Wildfire smoke impacts respiratory health more than fine particles from other sources: observational evidence from Southern California. Nature Communications 12, 1493 (2021).
27. Marlier, M. E., Crnosija, N. & Benmarhnia, T. Wildfire smoke exposures and adult health outcomes. in *American Geophysical Union* (2022).
28. Curriero, F. C. *et al.* Temperature and Mortality in 11 Cities of the Eastern United States. Am J Epidemiol 155, 80–87 (2002).
29. Bennett, J. E., Blangiardo, M., Fecht, D., Elliott, P. & Ezzati, M. Vulnerability to the mortality effects of warm temperature in the districts of England and Wales. Nature Clim Change 4, 269–273 (2014).
30. Gasparrini, A. *et al.* Small-area assessment of temperature-related mortality risks in England and Wales: a case time series analysis. The Lancet Planetary Health 6, e557–e564 (2022).
31. Aguilera, R. *et al.* Respiratory hospitalizations and wildfire smoke: a spatiotemporal analysis of an extreme firestorm in San Diego County, California. Environ Epidemiol 4, e114 (2020).
32. Reid, C. E. *et al.* Differential respiratory health effects from the 2008 northern California wildfires: A spatiotemporal approach. Environ Res 150, 227–235 (2016).

33. Rai, M. *et al.* Heat-related cardiorespiratory mortality: effect modification by air pollution across 482 cities from 24 countries. Environment International 107825 (2023) doi:10.1016/j.envint.2023.107825.
34. Davies, I. P., Haugo, R. D., Robertson, J. C. & Levin, P. S. The unequal vulnerability of communities of color to wildfire. PLOS ONE 13, e0205825 (2018).
35. Burke, M. *et al.* Exposures and behavioural responses to wildfire smoke. Nat Hum Behav 1–11 (2022) doi:10.1038/s41562-022-01396-6.
36. Bell, M. L., Zanobetti, A. & Dominici, F. Evidence on vulnerability and susceptibility to health risks associated with short-term exposure to particulate matter: a systematic review and meta-analysis. Am J Epidemiol 178, 865–876 (2013).
37. Chi, G. C. *et al.* Individual and Neighborhood Socioeconomic Status and the Association between Air Pollution and Cardiovascular Disease. Environ Health Perspect 124, 1840–1847 (2016).
38. Clougherty, J. E. & Kubzansky, L. D. A Framework for Examining Social Stress and Susceptibility to Air Pollution in Respiratory Health. Environ Health Perspect 117, 1351–1358 (2009).
39. Gronlund, C. J. Racial and socioeconomic disparities in heat-related health effects and their mechanisms: a review. Curr Epidemiol Rep 1, 165–173 (2014).
40. Berberian, A. G., Gonzalez, D. J. X. & Cushing, L. J. Racial Disparities in Climate Change-Related Health Effects in the United States. Curr Envir Health Rpt 9, 451–464 (2022).
41. California's Population. Public Policy Institute of California https://www.ppic.org/publication/californias-population/.
42. Income Inequality in California. Public Policy Institute of California https://www.ppic.org/publication/income-inequality-in-california/.
43. KC, B., Shepherd, J. M., King, A. W. & Johnson Gaither, C. Multi-hazard climate risk projections for the United States. Nat Hazards 105, 1963–1976 (2021).
44. Hurteau, M. D., Westerling, A. L., Wiedinmyer, C. & Bryant, B. P. Projected Effects of Climate and Development on California Wildfire Emissions through 2100. Environ. Sci. Technol. 48, 2298–2304 (2014).
45. Mastrandrea, M. D., Tebaldi, C., Snyder, C. W. & Schneider, S. H. Current and future impacts of extreme events in California. Climatic Change 109, 43–70 (2011).
46. AghaKouchak, A. *et al.* Climate Extremes and Compound Hazards in a Warming World. Annual Review of Earth and Planetary Sciences 48, 519–548 (2020).
47. Rosenthal, N., Benmarhnia, T., Ahmadov, R., James, E. & Marlier, M. E. Population co-exposure to extreme heat and wildfire smoke pollution in California during 2020. Environ. Res.: Climate 1, 025004 (2022).
48. World Health Organization. *WHO global air quality guidelines: particulate matter (PM2.5 and PM10), ozone, nitrogen dioxide, sulfur dioxide and carbon monoxide*. (World Health Organization, 2021).

49. US EPA, O. Climate Change Indicators: Heat Waves. https://www.epa.gov/climate-indicators/climate-change-indicators-heat-waves (2021).
50. Rahman, M. M. *et al.* The Effects of Co-Exposure to Extremes of Heat and Particulate Air Pollution on Mortality in California: Implications for Climate Change. Am J Respir Crit Care Med rccm.202204-0657OC (2022) doi:10.1164/rccm.202204-0657OC.
51. Canada, H. Wildfire smoke 101: Combined wildfire smoke and heat. https://www.canada.ca/en/health-canada/services/publications/healthy-living/combine-wildfire-smoke-heat.html (2021).
52. Wildfire Smoke | Los Angeles County Department of Public Health - Environmental Health. http://www.publichealth.lacounty.gov/eh/safety/wildfire-smoke.htm.
53. Anderson, G. B. & Bell, M. L. Heat waves in the United States: mortality risk during heat waves and effect modification by heat wave characteristics in 43 U.S. communities. Environ. Health Perspect. 119, 210–218 (2011).
54. Qiu, X. *et al.* Inverse probability weighted distributed lag effects of short-term exposure to PM2.5 and ozone on CVD hospitalizations in New England Medicare participants - Exploring the causal effects. Environ Res 182, 109095 (2020).
55. HCAI - Department of Health Care Access and Information. *HCAI* https://hcai.ca.gov/.
56. US EPA, O. NAAQS Table. US EPA https://www.epa.gov/criteria-air-pollutants/naaqs-table (2014).
57. Pinault, L. *et al.* Risk estimates of mortality attributed to low concentrations of ambient fine particulate matter in the Canadian community health survey cohort. Environ Health 15, 18 (2016).
58. Di, Q. *et al.* Air pollution and mortality in the Medicare population. New England Journal of Medicine 376, 2513–2522 (2017).
59. Aguilera, R. *et al.* A novel ensemble-based statistical approach to estimate daily wildfire-specific PM2.5 in California (2006–2020). Environment International 171, 107719 (2023).
60. Anderson, G. B., Bell, M. L. & Peng, R. D. Methods to Calculate the Heat Index as an Exposure Metric in Environmental Health Research. Environ Health Perspect 121, 1111–1119 (2013).
61. Jacklitsch, B. *et al.* NIOSH criteria for a recommended standard: occupational exposure to heat and hot environments. (2016).
62. Abatzoglou, J. T. Development of gridded surface meteorological data for ecological applications and modelling. International Journal of Climatology 33, 121–131 (2013).
63. National Weather Service. Heat Index Equation. https://www.wpc.ncep.noaa.gov/html/heatindex_equation.shtml (2014).
64. Rothfusz, L. P. *The Heat Index 'Equation' (or, More Than You Ever Wanted to Know About Heat Index)*. (1990).
65. US Census Bureau. 2010 Census. https://web.archive.org/web/20100320084325/http://2010.census.gov/2010census/ (2010).

66. Maizlish, N. *et al.* California Healthy Places Index: Frames Matter. Public Health Rep 134, 354–362 (2019).
67. Data & Reports – California Healthy Places Index. https://healthyplacesindex.org/data-reports/.
68. Commission, C. E. Climate Zone tool, maps, and information supporting the California Energy Code. *California Energy Commission* https://www.energy.ca.gov/programs-and-topics/programs/building-energy-efficiency-standards/climate-zone-tool-maps-and (current-date).
69. HUD USPS ZIP Code Crosswalk Files | HUD USER. https://www.huduser.gov/portal/datasets/usps_crosswalk.html.
70. Tong, S., Wang, X. Y. & Guo, Y. Assessing the Short-Term Effects of Heatwaves on Mortality and Morbidity in Brisbane, Australia: Comparison of Case-Crossover and Time Series Analyses. PLOS ONE 7, e37500 (2012).
71. Wei, Y. *et al.* Short term exposure to fine particulate matter and hospital admission risks and costs in the Medicare population: time stratified, case crossover study. BMJ 367, l6258 (2019).
72. VanderWeele, T. J. & Knol, M. J. A Tutorial on Interaction. Epidemiologic Methods 3, 33–72 (2014).
73. Levy, D., Lumley, T., Sheppard, L., Kaufman, J. & Checkoway, H. Referent Selection in Case-Crossover Analyses of Acute Health Effects of Air Pollution: Epidemiology 12, 186–192 (2001).
74. Janes, H., Sheppard, L. & Lumley, T. Overlap bias in the case-crossover design, with application to air pollution exposures. Stat Med 24, 285–300 (2005).
75. Benmarhnia, T., Hajat, A. & Kaufman, J. S. Inferential challenges when assessing racial/ethnic health disparities in environmental research. Environmental Health 20, 7 (2021).
76. Therneau, T. survival: A Package for Survival Analysis in R. (2022).
77. Jackson, C. Multi-State Models for Panel Data: The msm Package for R. Journal of Statistical Software 38, 1–28 (2011).
78. Schwarz, L. *et al.* Spatial variation in the joint effect of extreme heat events and ozone on respiratory hospitalizations in California. *PNAS* 118, (2021).
79. Liu, J. C. *et al.* Wildfire-specific Fine Particulate Matter and Risk of Hospital Admissions in Urban and Rural Counties: Epidemiology 28, 77–85 (2017).
80. Bobb, J. F., Obermeyer, Z., Wang, Y. & Dominici, F. Cause-Specific Risk of Hospital Admission Related to Extreme Heat in Older Adults. JAMA 312, 2659–2667 (2014).
81. Finley, A. O., Banerjee, S. & Gelfand, A. E. spBayes for Large Univariate and Multivariate Point-Referenced Spatio-Temporal Data Models. Journal of Statistical Software 63, 1–28 (2015).
82. Balduzzi, S., Rücker, G. & Schwarzer, G. How to perform a meta-analysis with R: a practical tutorial. Evidence-Based Mental Health 22, 153–160 (2019).
83. R Core Team. R: A language and enviromment for statistical computing. (2021).

Table

Table 1. List of climate hazard definitions explored in state-level estimates and the corresponding number of ZIP code-days among 995 ZIP codes in California, 2006-2019. The extreme heat threshold is based on the percentile of the historical summer daily maximum heat index value. The wildfire smoke threshold is based on wildfire-specific $PM_{2.5}$ ($\mu g/m^3$).

Definition	Extreme heat threshold	Wildfire smoke threshold	# of ZIP code-days with exposure (%)		
			Extreme heat alone	Wildfire smoke alone	Compound
EH85_WF0	85^{th}	>0	150,310 (2.95)	448,190 (8.81)	61,415 (1.21)
EH85_WF5	85^{th}	5	194,161 (3.82)	116,128 (2.28)	17,564 (0.35)
EH85_WF15	**85^{th}**	**15**	**206,302 (4.06)**	**32,089 (0.63)**	**5,423 (0.11)**
EH85_WF35	85^{th}	35	210,174 (4.13)	11,266 (0.22)	1,551 (0.03)
EH95_WF0	95^{th}	>0	68,675 (1.35)	482,235 (9.48)	27,372 (0.54)
EH95_WF5	95^{th}	5	88,258 (1.73)	125,903 (2.47)	7,789 (0.15)
EH95_WF15	95^{th}	15	93,408 (1.84)	34,873 (0.69)	2,639 (0.05)
EH95_WF35	95^{th}	35	95,272 (1.87)	12,042 (0.24)	775 (0.02)

Figures

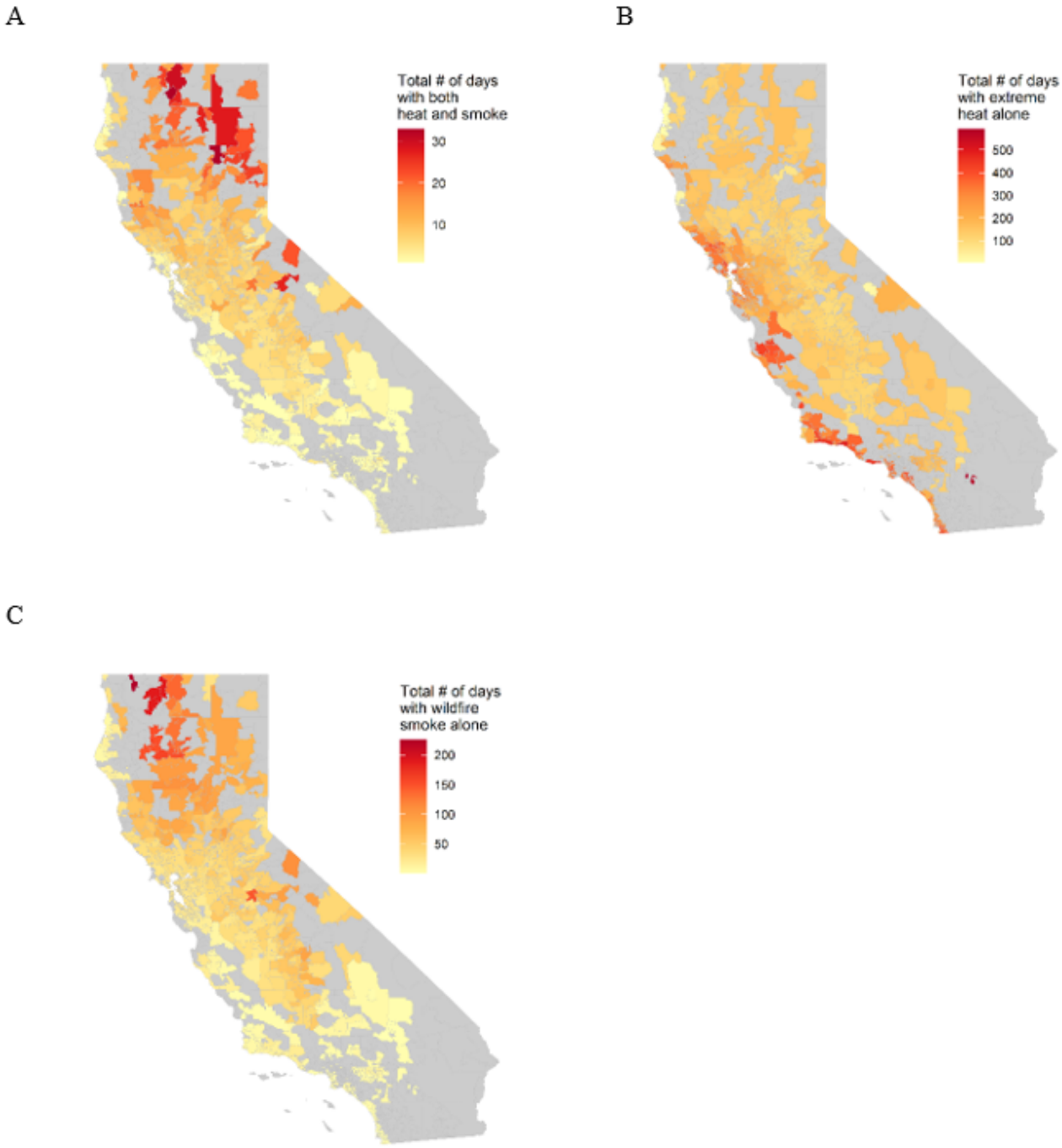


Figure 1

Spatial distribution of the total number of days with A) compound exposure, B) extreme heat alone, and C) wildfire smoke alone in 995 California ZIP codes from 2006 to 2019 under the main analysis definition for climate hazards (85^{th} percentile for extreme heat and 15 $\mu g/m^3$ for wildfire $PM_{2.5}$).

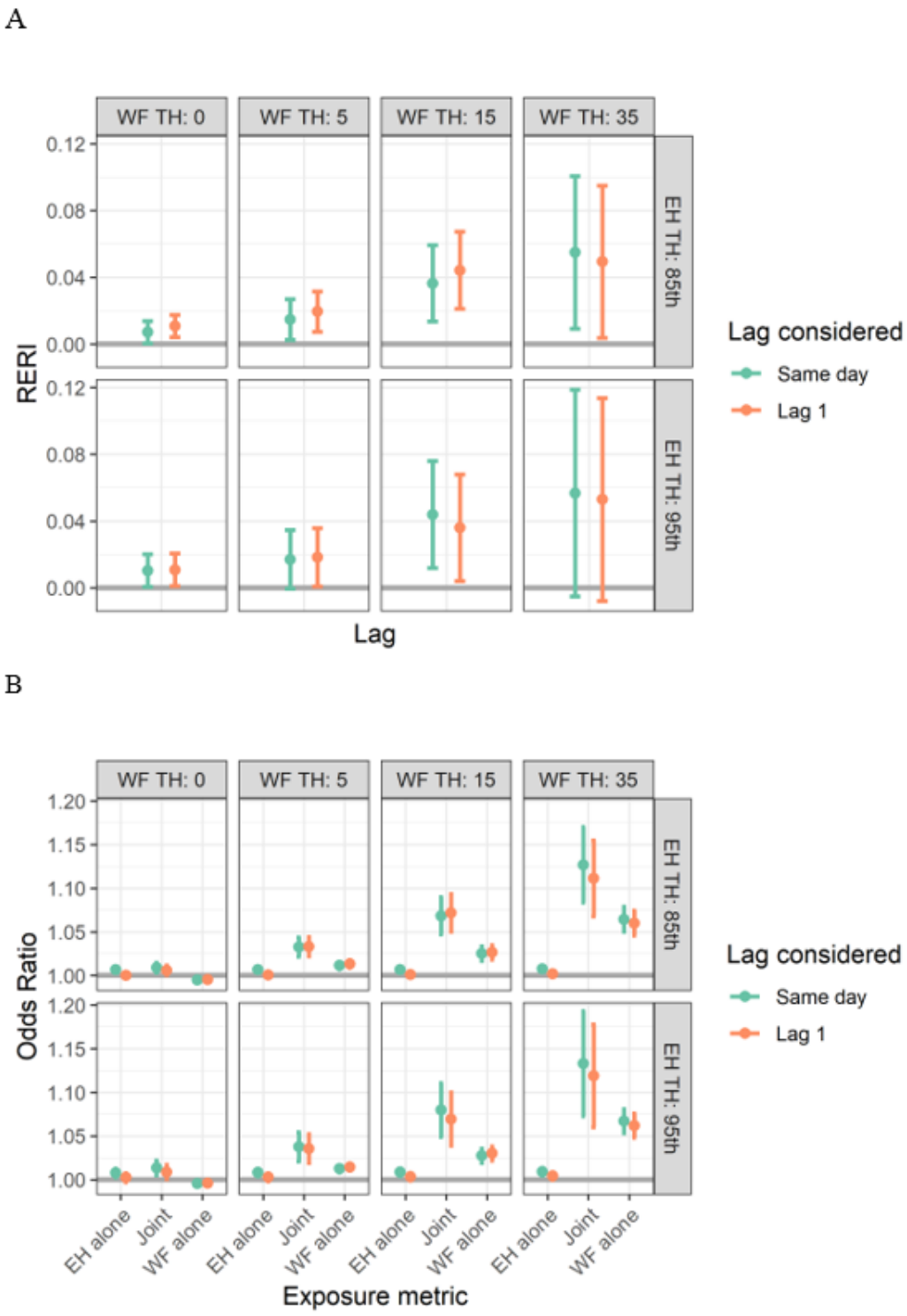


Figure 2

State-level estimates by varying definitions of climate hazards for A) additive synergistic effect of wildfire smoke and extreme heat summarized in relative excess risk due to interaction (RERI), and B) associations between risk of cardiorespiratory hospitalization and wildfire smoke alone, extreme heat alone and joint of both climate hazards. Note: numerical results are available in eTable 3.

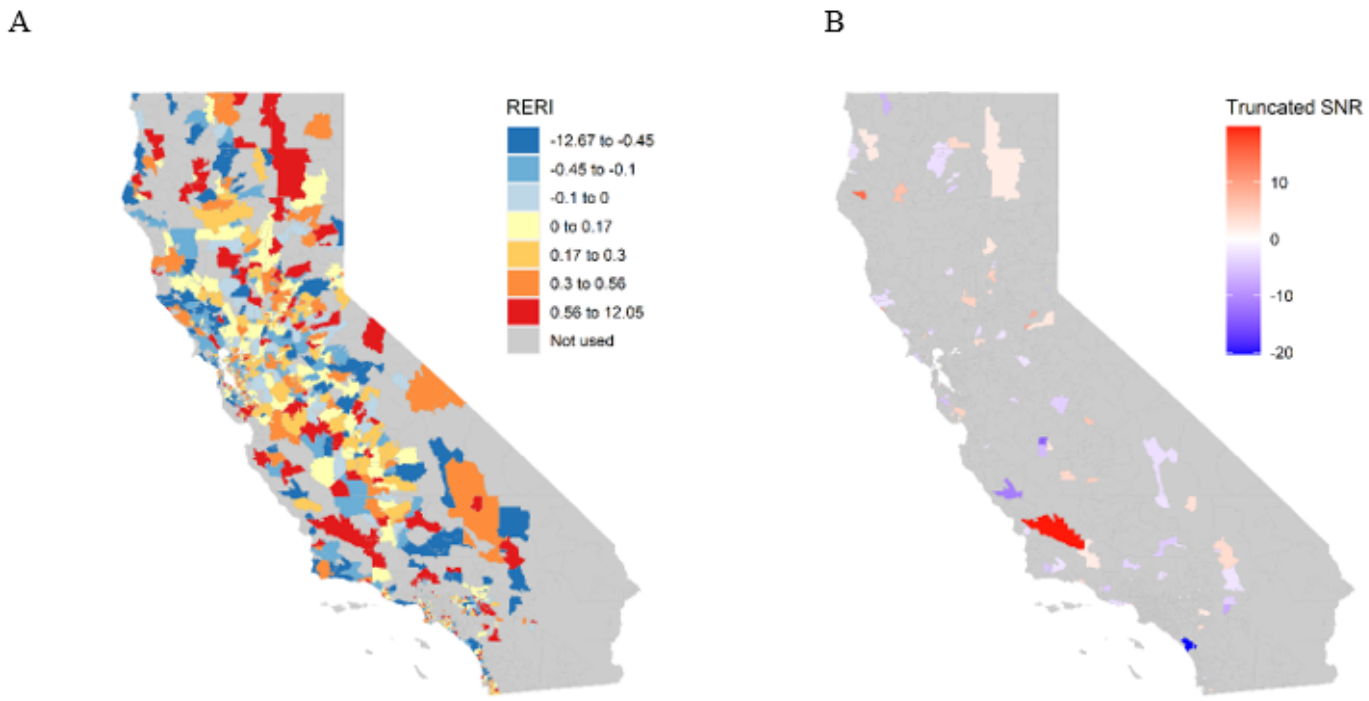


Figure 3

Spatial distribution of ZIP code-level A) pooled additive synergistic effect of wildfire smoke and extreme heat summarized (RERI) estimated using monthly weighting method under the main definition for climate hazards; and B) corresponding signal noise ratio (SNR) for the pooled estimates with absolute values smaller than 2 marked as missing (grey), which represents the significance of the effect estimates. Note: four ZIP codes were removed due to no hospitalization in control days and failure in the estimation of ZIP code-specific RERI. Color categories in A are based on septiles of the RERIs.

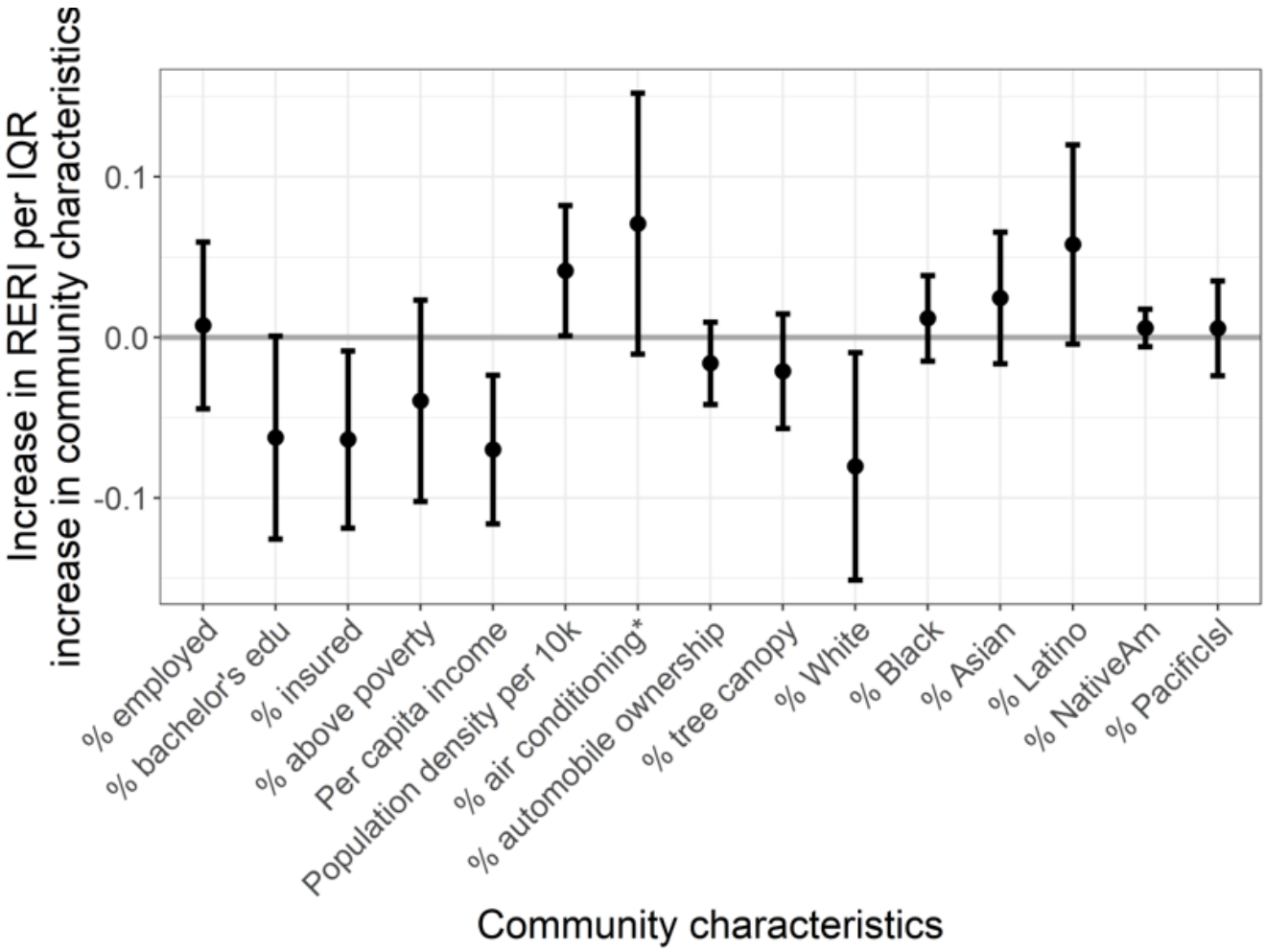


Figure 4

Effect modification of community characteristics on the additive synergistic effect of wildfire smoke and extreme heat (increase in RERI per interquartile range [IQR] increase in community characteristics). RERIs were estimated using monthly weighting method under the main definition for climate hazards.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- compoundeffectwfehnssupplementary.docx