

Applying a two-stage generalized synthetic control approach to quantify the heterogeneous health effects of extreme weather events: A 2018 large wildfire in California event as a case study

Noemie Letellier, Maren Hale, Kasem Salim, Yiqun Ma, Francois Rerolle, Lara Schwarz, Tarik Benmarhnia

▶ To cite this version:

Noemie Letellier, Maren Hale, Kasem Salim, Yiqun Ma, Francois Rerolle, et al.. Applying a two-stage generalized synthetic control approach to quantify the heterogeneous health effects of extreme weather events: A 2018 large wildfire in California event as a case study. Environmental Epidemiology, 2025, 9 (1), pp.e362. 10.1097/EE9.00000000000362. hal-04868399

HAL Id: hal-04868399 https://ehesp.hal.science/hal-04868399v1

Submitted on 6 Jan 2025

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers. L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.



Distributed under a Creative Commons Attribution - NonCommercial - NoDerivatives 4.0 International License

OPEN

Applying a two-stage generalized synthetic control approach to quantify the heterogeneous health effects of extreme weather events

A 2018 large wildfire in California event as a case study

Noemie Letellier^{a,b}, Maren Hale^a, Kasem U. Salim^c, Yiqun Ma^a, Francois Rerolle^a, Lara Schwarz^{a,d}, Tarik Benmarhnia^{a,b,*}

Abstract: Extreme weather events, including wildfires, are becoming more intense, frequent, and expansive due to climate change, thus increasing negative health outcomes. However, such effects can vary across space, time, and population subgroups, requiring methods that can handle multiple exposed units, account for time-varying confounding, and capture heterogeneous treatment effects. In this article, we proposed an approach based on staggered generalized synthetic control methods to study heterogeneous health effects, using the 2018 California wildfire season as a case study. This study aimed to estimate the effects of the November 2018 California wildfires, one of the state's deadliest and most destructive wildfire seasons, on respiratory and circulatory health, document heterogeneity in health impacts, and investigate drivers of this heterogeneity. We applied a two-stage generalized synthetic control method to compare health outcomes in exposed (from 8 November to 5 December 2018) versus unexposed counties and used random-effects meta-regression to evaluate the effect modification of county-level socioeconomic variables on the observed health effects of the November 2018 wildfires. We observed an increase in respiratory hospitalizations for most exposed counties when compared with unexposed counties, with significant increases in Fresno, San Francisco, San Joaquin, San Mateo, and Santa Clara counties. No effect on circulatory hospitalizations was observed. County-level sociodemographic characteristics seem to not modulate the effects of wildfire smoke on respiratory hospitalizations. This novel two-stage framework can be applied in broader settings to understand spatially and temporally compounded health impacts of climate hazards. We provide codes in R for reproducibility and replication purposes.

Keywords: Quasi-experimental method; Heterogeneous effect; Environmental justice; Climate hazards; Air pollution

^aScripps Institution of Oceanography, University of California San Diego, La Jolla, California; ^bIrset Institut de Recherche en Santé, Environnement et Travail, UMR-S 1085, Inserm, University of Rennes, EHESP, Rennes, France; ^cDepartment of Public Health, University of California Merced, Merced, California; ^dDivision of Environmental Health Sciences, School of Public Health, University of California Berkeley, Berkeley, California

N.L. and M.H. contributed equally as cofirst authors.

L.S. and T.B. contributed equally as cosenior authors.

This work had been partially funded by the Climate Action 2023 UC Innovation and Entrepreneurship Awards (R02CE6859).

Data and codes for reproducibility and replication purposes are available at the following link: https://github.com/benmarhnia-lab/Wildfires_social_vulnerability.

SDC Supplemental digital content is available through direct URL citations in the HTML and PDF versions of this article (www.environepidem.com).

*Corresponding Author. Address: Scripps Institution of Oceanography, University of California San Diego, 8885 Biological Grade, La Jolla, CA 92037. E-mail: tbenmarhnia@health.ucsd.edu (T. Benmarhnia).

Copyright © 2024 The Authors. Published by Wolters Kluwer Health, Inc. on behalf of The Environmental Epidemiology. All rights reserved. This is an open-access article distributed under the terms of the Creative Commons Attribution-Non Commercial-No Derivatives License 4.0 (CCBY-NC-ND), where it is permissible to download and share the work provided it is properly cited. The work cannot be changed in any way or used commercially without permission from the journal.

Environmental Epidemiology (2025) 9:e362

Received 26 September, 2024; Accepted 10 December, 2024

Published online 31 December 2024

DOI: 10.1097/EE9.000000000000362

Introduction

Wildfires are becoming increasingly intense, frequent, and expansive as a result of climate change, particularly in the western United States.¹⁻⁴ One result of this increased wildfire activity is an increase in air pollution coming from wildfire smoke, with drastic spikes in wildfire-associated $PM_{2.5}$ concentration (particulate matter with an aerodynamic diameter $\leq 2.5 \mu m$).⁵ In fact, this increase in wildfire PM_{2.5} pollution has effectively reversed decades of PM_{2.5} air quality improvements achieved through policy changes across the country, particularly in the western states.^{5,6} This offsetting of public health gains has also been specifically observed within the state of California.⁷

Wildfire-associated PM_{2.5} emissions contribute to negative health outcomes, with previous studies documenting the effects

What this study adds:

This study demonstrated the utility of a two-stage generalized synthetic control method as an alternative to traditional approaches for studying the impacts of extreme events such as wildfires. We proposed a framework based on this novel quasi-experimental method to quantify the heterogeneous health effects of the 2018 California wildfires and identify its potential drivers. Such a framework can be used to understand spatially and temporally compounded health impacts of climate hazards, such as heat waves or flooding events. Understanding the drivers of the heterogeneous effects of climate-sensitive exposures is crucial to designing adaptation and emergency response strategies that prioritize vulnerable communities. on respiratory and cardiovascular health.⁸⁻¹⁵ Evidence suggests that $PM_{2.5}$ emitted from wildfires may be more harmful to human health than equivalent amounts of $PM_{2.5}$ emitted from more traditional sources of pollution (e.g., traffic, agricultural, or industrial sources).¹⁶⁻¹⁸ In addition, the contribution of wildfire smoke $PM_{2.5}$ emissions to all $PM_{2.5}$ emissions continues to increase,⁶ intensifying the health impacts of wildfires.

There is also a growing body of evidence that wildfire smoke may not impact all population subgroups equally. Several studies, using various measures, have found that wildfire smoke-related health outcomes differ based on socioeconomic status (SES), with worse outcomes for those in lower SES groups.^{11,19-22} Differential health outcomes from wildfire events have also been found between communities of differing race/ethnicity.7,20,21,23 For instance, Liu et al²⁰ found that Black Americans face a higher risk of respiratory hospitalizations from wildfire events than White Americans. In California, communities of color and communities of lower SES are at higher risk of being exposed to harmful compounding poor air quality events from wildfires and heatwaves.²⁴ Age is also an effect modifier of wildfire PM_{2.5} health impacts, with the very young and the elderly being most at risk.^{7,8,14,25-27} In this context, adaptation may be more difficult for communities and individuals of lower SES due to disparities in access to resources and care, health literacy, or simply being more likely to live near an exposure source or other sources of pollution,^{20,28,29} hence the heightened vulnerability these communities often face.

Besides heterogeneity across population subgroups, wildfire smoke health impacts may also differ spatially and temporally. Understanding the drivers of such variability may be useful to inform adaptation strategies and also to better understand the mechanisms through which wildfire smoke impacts population health. In this study, we propose a framework based on a twostage generalized synthetic control (GSC) method to quantify the heterogeneous health effects of wildfire smoke and identify its potential drivers. We use a large wildfire event that took place in 2018 in California and impacted multiple counties as a case study. The 2018 wildfire season was one of the deadliest and most destructive (in terms of area burned) in California's history to date, with several notable fires occurring across the state (though focused most strongly on Northern California), including the Mendocino Complex Fire, the Camp Fire, and the Woolsey Fire.³⁰ The November 2018 Camp Fire caused extensive damage, consuming more than 153,000 acres, resulting in the loss of 85 lives, and the destruction of over 18,000 structures. The total cost of the Camp Fire is estimated at \$16.5 billion.³¹ Simultaneously, Southern California experienced the outbreak of two distinct wildfires known as the Woolsey and Hill Fires, causing a wildfire smoke event, which we find impacted 27 counties. Using our proposed framework, we analyze if respiratory and circulatory health impacts differed across the affected areas and attempt to document the drivers of such heterogeneity. Such a framework can be extended to understanding the temporal variability of wildfire smoke events (i.e., multiple events affecting the same location) and can be used for other climate hazards such as heat waves or flooding events.32-34

We rely on the GSC, a quasi-experimental method (QEM), to study the health effects of the 2018 California wildfires. QEMs are well suited for studying the impacts of extreme events such as wildfires and offer multiple advantages over traditional epidemiologic methods³⁵ as the timing of such events can be assumed to be independent (exogenous) of the time trends of a given health outcome. This allows us to analyze wildfires as a type of natural experiment,³⁶ mimicking randomization and helping reduce the issue of residual confounding, which can be a limitation of more traditional approaches.³⁵ Specifically, GSC has several key advantages, as outlined by Xu³⁷ and Sheridan et al:³⁵ (1) it allows for counterfactuals for each treated unit and allows estimation of heterogeneous treatment effects, (2) the synthetic control is generalized to be used in the case of multiple treated units or treatment periods, (3) it improves efficiency and interpretability, and (4) it allows one to control for time-varying observed covariates. GSC methods are very useful for studying extreme events such as wildfires, allowing for an alternative approach in situations where it would be impossible to use traditional methods.³⁵ In this study, we extend the GSC method into a two-stage GSC approach to further explore the drivers of heterogeneous effects of extreme weather events.

Therefore, the aim of this study is to apply a two-stage GSC method to determine the effects of the 2018 California wildfires on respiratory and circulatory health, to document the heterogeneity in health impacts, and to explore potential drivers of this heterogeneity. We investigated the effect of modification of socioeconomic and demographic variables on respiratory hospitalizations associated with wildfires.

Methods

Data sources

Hospitalization data for the study came from the patient discharge data and emergency department data collected by the California Department of Health Care Access and Information. We estimated daily counts of respiratory hospitalizations based on the International Classification of Diseases, Tenth Revision (ICD-10-CM) primary diagnosis codes of diseases of the respiratory system (J00–J99) and of cardiovascular hospitalizations based on primary ICD-10 codes of diseases of the circulatory system (I00–I99).³⁸

Wildfire smoke PM_{2.5} data were estimated using an ensemble model based on a multiple imputation approach.³⁹ This model incorporated data from the US 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 Surface Meteorological (gridMET) reanalysis product, and other land-use variables from the National Land Cover Database. The details for this methodology were previously described by Aguilera et al.³⁹ Briefly, Aguilera et al applied a suite of machine learning models, including gradient boosting, random forest, and deep learning, alongside a diverse set of predictors, such as air monitor data, aerosol optical depth, land cover, and meteorological conditions, to estimate ZIP code tabulation areas (ZCTA)-specific daily PM₂₅ concentrations from all sources. This ensemble model demonstrated high model prediction capabilities with an R^2 of 0.86. Subsequently, they employed a chained random forest algorithm to impute nonwildfire PM_{2.5} concentrations for ZCTA days impacted by smoke plumes. The difference between the ensemble model's estimated daily PM2.5 concentrations and the imputed nonwildfire PM_{2.5} concentrations in each ZCTA is defined as wildfire-specific PM2.5. Other meteorological data (including maximum temperature, precipitation, relative humidity, shortwave radiation, and wind velocity) were estimated from the gridMET ~4-km daily dataset. All meteorological data were averaged from zip code level daily estimates to the county level.

County-level sociodemographics for California counties from the 2019 American Community Survey were used for exploring differential vulnerability to wildfire smoke impacts. Variables considered to be important and included in the analysis were the following: population over 55 years and over (%), population over 65 years and over (%),population over 85 years and over (%), median age, population with a high school degree or higher (%), population unemployed (%), median income, population female (%),population non-Hispanic White (%), population non-Hispanic Black (%), population Asian (%), and population Hispanic (%).

Table 1.

Descriptive statistics (mean) of climate exposures and hospitalizations before and after the start of wildfire smoke exposure (8 November) in exposed counties

	Before wildfire (13 September–7 November 2018)		During wildfire (8 November–5 December 2018)	
	Exposed counties (n = 27)	Unexposed counties (n = 31)	Exposed counties (n = 27)	Unexposed counties (n = 31)
Climatic variables				
Mean wildfire smoke	0.2	3.0	25.5	3.2
PM _{2.5} (µg/m ³)				
Mean max temperature (K)	299.0	297.0	289.8	289.0
Precipitation (mm)	0.4	0.3	4.2	3.9
Specific humidity (g/m ³)	0.0059	0.0055	0.0048	0.0041
Shortwave radiation	196.1	197.3	106.2	118.3
(W/m ²)				
Wind velocity (m/s)	3.3	3.1	2.9	3.4
Health data				
Mean daily respiratory	265	413	388	512
hospitalizations				
Mean daily circulatory	168	273	173	282
hospitalizations				

Stage 1: generalized synthetic control analysis by county

The study period lasted 3 months, from 13 September to 5 December 2018. To quantify the effect of the November 2018 wildfires on hospitalizations in California, a synthetic control approach was used for counties exposed to wildfire smoke during this period. For this case study, a county was considered to be exposed if the average wildfire-PM₂₅ was higher

than 10 μ g/m³ during the exposed period, defined as the 4 weeks following the initial wildfire smoke exposure (i.e., from 8 November to 5 December 2018). No county had more than 10 μ g/m³ wildfire-PM_{2.5} in the pre-exposure period, that is, from 13 September to 7 November 2018, levels were 0.2 μ g/m³ on average. Therefore, no county was excluded from the analysis because of pre-exposure.

In summary, the GSC methodology is a quasi-experimental approach that uses the timing of the wildfire smoke exposure to quantify its effect.^{35,40} The trend in the "treated" unit, or exposed county, before the wildfire smoke event occurs is used to identify a counterfactual of weighted controls that were not exposed to wildfire smoke. Controls are decomposed with calendar time, lagged outcomes (in the pre-exposure period), and time-varying covariates (including maximum temperature, precipitation, humidity, shortwave radiation, and wind), and an interactive fixed effects model is applied to identify a suitable control based on this time series in the pretreatment period.³⁵ This informs a reweighting approach in which weights for control units are selected based on these decomposed estimates and are used to impute hypothetical trends for the treated unit if they had not been treated by predicting the outcome in the treated unit during the posttreatment period.35,37 As a result, each treated unit (i.e., exposed county) has its own synthetic control, which is constructed from a weighted combination of nonexposed counties. Any difference between the treated unit and its synthetic control after the treatment occurs, the Average Treatment Effect among the Treated (ATT), can be attributed to the wildfire smoke event. Covariates included in the GSC model are maximum temperature (K), precipitation (mm), humidity (g/m³), shortwave radiation (W/m²), and wind (m/s).

Regarding our causal identification assumptions,⁴¹ we ensured that: (1) geographical units eligible for the pool of control groups had not been exposed to the smoke event; (2) differences in the incidence rates of hospital admissions between





Figure 1. Mean smoke exposure for California zip codes during 2018 wildfires, 8 November–5 December 2018.

Exposed Counties November 2018



Figure 2. California counties considered exposed to wildfire smoke during the November 2018 wildfires.

the treated units and the obtained synthetic control groups were null or close to zero in the pre-exposure period, and (3) no other shocks coincidently took place during the wildfire smoke event (i.e., common shock assumption). With these causal identification assumptions being met, we used our estimates to infer the causal effects of the wildfire smoke event on the outcomes of interest. Our main estimand of interest is the ATT.

Stage 2: random-effects meta-regression

Results from the synthetic control analysis for each exposed county were extracted for further analysis. The ATT and standard error for each county were population adjusted for a rate of hospitalizations attributable to wildfire smoke per 10,000 population. Standardized sociodemographic variables were estimated by taking the difference in the county-level measure from the mean across counties and dividing by the interquartile range. A random-effect meta-regression was applied to evaluate the effect modification for each of these variables on the observed effect of wildfire smoke.

Codes for reproducibility and replication purposes are available at the following link: https://github.com/benmarhnia-lab/ Wildfires_social_vulnerability.

Results

Descriptive information

Meteorological exposures and hospitalizations were assessed before (13 September–7 November 2018) and during the wildfire smoke exposure (8 November–5 December 2018, see details in Figure S1; http://links.lww.com/EE/A319) in exposed and unexposed counties (Table 1). For hospitalization variables, there was a notable increase in mean daily respiratory hospitalizations in both exposed (from 265 to 388) and unexposed counties (from 413 to 512) after the start of the wildfire. Mean daily circulatory hospitalization only slightly increased in both exposed (from 168 to 173) and unexposed counties (from 273 to 282) following the start of the wildfire.

Figure 1 displays the mean smoke exposure for California zip codes during the 2018 wildfires, while Figure 2 displays the California counties that we considered to be exposed to wildfire smoke during the 2018 wildfires for the purposes of this study. Counties that were determined to be exposed are: Alameda, Butte, Colusa, Contra Costa, Fresno, Glenn, Kings, Lake, Marin, Mendocino, Merced, Napa, Placer, Sacramento, San Francisco, San Joaquin, San Mateo, Santa Clara, Santa Cruz, Solano, Sonoma, Stanislaus, Sutter, Tehama, Tulare, Yolo,



Figure 3. Results of synthetic control analysis of the effect of November 2018 wildfires on respiratory hospitalizations in California for counties exposed to wildfire smoke.

and Yuba (Table S1; http://links.lww.com/EE/A319). Figure S2; http://links.lww.com/EE/A319 shows the average weekly wild-fire smoke in exposed and unexposed counties, and Figure S3; http://links.lww.com/EE/A319 the number of days with wildfire smoke above 10 µg/m³ per week in exposed counties, from 13 September to 5 December 2018.

Sociodemographic mean and standard deviations were calculated for the wildfire smoke-exposed counties (Table S3; http:// links.lww.com/EE/A319). On average, there was a greater percentage of White people (69.7%) than Asian (10.7%), Black (3.8%), or Hispanic (30.1%) populations among exposed counties. Exposed counties had on average, 50.3% women among their population. The median exposed income in exposed counties was \$68,097 and the median age was 38 years old. Additionally, there was an unemployment rate of 7.3% among the exposed counties. Notably, 28.2% of the exposed counties had an average age of 55 years or older, 15.6% had an average age of 65 years or older, and 1.9% had an average age of 85 years or older. Around 56.6% of the population in exposed counties were, on average, high school graduates or higher.

Main results for stage 1: health effects of wildfire event: findings from a generalized synthetic control analysis

Using a reweighting approach to predict the outcome in the treated unit during the posttreatment period, we were generally able to find good matches for synthetic controls (i.e., difference ~0) in other unexposed California counties. The analysis included 27 exposed and 31 unexposed counties. Overall, we observed an increase in respiratory hospitalizations for most exposed counties when compared with unexposed counties (Figure 3); however, only a few counties showed precise effects

of wildfire smoke. The following exposed counties were found to have significant increases in respiratory hospitalizations: Fresno (ATT of 193.7; 95% confidence interval [CI]: 78.1, 309.2), San Francisco (ATT of 97.9; 95% CI: 11.1, 184.7), San Joaquin (ATT of 113.1; 95% CI: 16.3, 209.9), San Mateo (ATT of 107.9; 95% CI: 5.6, 210.2), and Santa Clara (ATT of 207.9; 95% CI: 110.6, 305.1) (Figure 4, Figure S4; http://links.lww. com/EE/A319, and Table S2; http://links.lww.com/EE/A319). There was no effect found in circulatory hospitalizations in exposed counties when compared with the synthetic controls (Figure S5; http://links.lww.com/EE/A319).

Heterogeneity in health impacts: findings from a randomeffect meta-regression

Meta-regression was applied using results from the synthetic control analysis for exposed counties to evaluate the effect modification for each of these county-level socioeconomic variables on the observed effect of 2018 wildfires in California on respiratory hospitalizations (Figure 5). We found no evidence that the county-level sociodemographic variables modified the effects of wildfire smoke on respiratory hospitalizations.

Discussion

This study proposed an analytical framework based on a twostage GSC method as an alternative to traditional approaches for assessing the heterogeneous health effects of extreme events such as wildfire and exploring their potential drivers. Using the 2018 California wildfire season, one of the deadliest and most destructive wildfires in California's history, as a case study, we



Figure 4. ATT and 95% CI by county for the effect of 2018 wildfires on respiratory hospitalizations.

found an increase in respiratory hospitalizations in most counties that were exposed to wildfire smoke when compared with unexposed counties. In particular, Fresno, San Francisco, San Joaquin, San Mateo, and Santa Clara counties faced significant increases in hospitalizations. No effect of wildfire smoke was observed for circulatory-related hospitalizations. We found no evidence that sociodemographic characteristics at the county level modified the effects of wildfire smoke on respiratory hospitalizations.

Understanding the drivers of the heterogeneous effects of climate-sensitive exposures, such as wildfire smoke events, is important for several reasons. First, documenting these vulnerabilities, as well as resilience factors, is essential to designing adaptation and emergency response strategies that prioritize vulnerable communities and reduce the uneven burden they face.⁴² For instance, in the event of a wildfire where the main vulnerable population is elderly or of low SES with lower-than-average internet accessibility, social media posts would likely not be an appropriate or effective method for disseminating alerts.⁴³ Other vulnerable populations could require communication in languages other than English.44,45 Second, understanding the heterogeneous impacts of wildfire events is important for planners to be able to determine how to allocate resources proportionately to expected impacts ahead of or in the aftermath of a disaster.46,47 Finally, it also helps us to gain a better understanding of the compounded impacts of wildfires with other concurring risks. We did not aim at comprehensively investigating such mechanisms but rather highlight how the approach we propose can be used in various settings including for studying

the compounded impacts of extreme weather events and infectious diseases.

In this study, the health impacts of major California wildfires in 2018 are investigated using QEM, more specifically GSC. The GSC method is a powerful approach that combines synthetic control techniques with interactive fixed-effect models, as introduced by Xu.³⁷ The GSC approach was found to provide accurate estimates across a range of simulation scenarios compared with more traditional methods such as difference-in-differences and synthetic control methods.48 The GSC method proves especially advantageous when applied to the assessment of extreme weather events³⁵ such as wildfires, as such events often exhibit widespread impacts, causing treatment effects to vary significantly across different regions, and frequently coincide with other environmental exposures. Using GSC to estimate the impact of wildfires allows for indirect confounding adjustment and explicit definition of a counterfactual trend and does not require detailed individual-level data. Furthermore, this approach also accommodates multiple exposed units and accounts for both time-varying confounding and heterogeneous treatment effects

We analyzed potential factors that may drive heterogeneous effects across affected counties by considering a second stage to quantify what modulates the amplitude of the ATT identified in the first stage. This approach can be seen as a type of staggered intervention similar to the approach that has been proposed by Callaway and Sant'Anna⁴⁹ for staggered difference-indifferences. When enough never-treated units (units that are never exposed) are available to build synthetic control groups



Figure 5. Results of meta-regression of change in effects of wildfire smoke on respiratory hospitalizations for standardized increase in county-level sociodemographic variables during November 2018 wildfires in California.

for each treated unit, such an approach can be implemented. In our example, we capitalized on the spatial variability of the impacts to evaluate effect modification. Yet, this approach could be extended to multiple events or staggered interventions over multiple treated units. For example, wildfires affecting the same area (or different areas) at different times can be a good opportunity to understand if (and why) the health impacts of wildfire smoke vary over time. In such settings, it is necessary to estimate an ATT for each event and for each exposed county. In the second stage (i.e., a random-effect meta-regression), it will be therefore necessary to include a fixed effect at the county level to consider the dependence of the effect estimates within the same area. It is important to note that one potential question of interest can be related to quantifying the differential effects across multiple events and in such a situation, a variable capturing the order of the wildfire smoke event within an area can be included in the meta-regression stage.

In the case study presented in this article, we focused on spatially compounding impacts, but this approach can also be used to explore temporally compounding impacts, ⁵⁰ when a succession of hazards leads to differential impacts. Previous studies based on traditional time series modeling have also relied on a similar two-stage approach to explore the drivers of the heterogeneous effects of environmental exposures across space.^{51,52} Our approach is different as we focus on specific events and, besides time-fixed effect modifiers, we can also incorporate time-varying effect modifiers in the second stage. For example, consider multiple wildfire smoke events (or any other extreme weather events such as extreme heat events) affecting multiple areas, it would be possible to analyze each wildfire smoke event's features (e.g., quantity of wildfire-PM_{2.5}, temperature, concentration of other background pollutants during the event, and infectious disease patterns) that may modulate the effects.

Our findings are consistent with prior research, as we observed respiratory effects associated with exposure to wildfire smoke but found no such association with cardiovascular outcomes. Previous studies have consistently found positive associations between exposure to wildfire smoke and an increase in emergency departments or physician visits for respiratory outcomes, or an exacerbation of asthma and chronic obstructive pulmonary disease.^{10,26,53–55} In contrast, studies focusing on the effects of wildfire smoke on cardiovascular health display a lack of consistent findings, with the majority of studies not identifying any association between wildfire smoke and outcomes related to cardiovascular diseases.¹⁰ A study using generalized estimating equations found that the 2003 Southern California wildfire storm led to a 17% increase in daily respiratory admissions after the fires compared with the prefire period.8 Another study, using the GSC approach, found that the 2007 southern California wildfire storm resulted in an 18% increase in respiratory hospitalizations.³⁵ In this case study, we did not identify heterogeneous effects of wildfire smoke. Such findings may largely be attributed to a lack of statistical power as we assessed effect modification based on county-level vulnerability factors across 27 exposed counties. Nevertheless, our main goal was to illustrate how such a framework can be employed to explore such patterns.

Regarding our causal identification assumptions, we ensured that: (1) geographical units eligible as potential control groups were not exposed to the smoke event; (2) differences in hospital admission incidence between the treated units and the synthetic control groups were negligible or nonexistent during the pre-exposure period, and (3) no other coinciding shocks occurred place during the wildfire smoke event. Overall, we believe these assumptions are met in this case study. We were generally successful in identifying well-matched synthetic controls, with minimal differences (close to zero), in other unexposed counties in California. Moreover, the common shock assumption should be satisfied, ensuring that the observed effects can be attributed solely to that wildfire event (and no other shocks). However, our classification of counties may have led to misclassification of exposure. Counties classified as unexposed may, in reality, have been exposed to low levels of wildfire-PM2.5, as no counties remained completely unaffected by the massive 2018 wildfire event. In addition, it is worth mentioning that some spillover effects may be present as some counties may experience a slight increase in smoke exposure, which can lead to more hospitalizations. In parallel, as we used the place of residence for each hospital admission, it is also possible that some misclassifications may occur as some individuals may not be necessarily admitted in their county of residence.

This study presents other limitations and areas for future development. First, we analyzed the effects of wildfire smoke on health at the county level in order to have sufficient statistical power. We acknowledge that the county level is not the ideal scale for such an analysis as the average treatment effect is averaged across relatively large areas. Assessing the spatial variation in the impact of wildfire smoke exposure within a county could lead to more nuanced results. Moreover, we did not consider spatial dependency between geographical units that could be leveraged in a Bayesian spatial model to improve the statistical precision of the variance and deal with spatial autocorrelation. Combining Bayesian Hierarchical models with GSC methods in such a framework constitutes a promising area for future research. Finally, we did not consider other air pollutants emitted by wildfires (e.g., O₂) or other factors besides wildfire smoke that could lead to increased respiratory hospitalizations. For example, we know that extreme weather events such as heat waves may co-occur with wildfire events and have synergistic health effects,⁵⁶ yet this was not addressed in the present study, which mostly aimed at illustrating an analytical framework.

Conclusion

This study aimed to demonstrate a novel analytical framework, based on QEMs, particularly well suited to assessing the health impacts of extreme weather events and the drivers of their heterogeneous effects. We evaluated the respiratory and circulatoryrelated hospitalizations associated with an extreme wildfire event at the county level in California, using a two-stage GSC method. We found that the November 2018 wildfires resulted in increased respiratory hospitalizations in most of the exposed California counties with important variability across counties. We explored multiple effect modifiers to explain such variability. This framework can be used in broader settings to understand spatially and temporally compounded health impacts of climate hazards.

Conflicts of interest statement

The authors declare that they have no conflicts of interest with regard to the content of this report.

References

- Dennison PE, Brewer SC, Arnold JD, Moritz MA. Large wildfire trends in the western United States, 1984–2011. *Geophys Res Lett*. 2014;41:2928–2933.
- 2. Abatzoglou JT, Williams AP. Impact of anthropogenic climate change on wildfire across western US forests. *Proc Natl Acad Sci U S A*. 2016;113:11770–11775.
- Parks SA, Abatzoglou JT. Warmer and drier fire seasons contribute to increases in area burned at high severity in western US forests from 1985 to 2017. *Geophys Res Lett.* 2020;47:e2020GL089858.
- Zhuang Y, Fu R, Santer BD, Dickinson RE, Hall A. Quantifying contributions of natural variability and anthropogenic forcings on increased fire weather risk over the western United States. *Proc Natl Acad Sci U S A*. 2021;118:e2111875118.
- Childs ML, Li J, Wen J, et al. Daily local-level estimates of ambient wildfire smoke PM2.5 for the contiguous US. *Environ Sci Technol*. 2022;56:13607–13621.
- 6. Burke M, Childs ML, de la Cuesta B, et al. The contribution of wildfire to PM2.5 trends in the USA. *Nature*. 2023;622:761–766.
- Thilakaratne R, Hoshiko S, Rosenberg A, Hayashi T, Buckman JR, Rappold AG. Wildfires and the changing landscape of air pollution-related health burden in California. *Am J Respir Crit Care Med.* 2023;207:887–898.
- Delfino RJ, Brummel S, Wu J, et al. The relationship of respiratory and cardiovascular hospital admissions to the southern California wildfires of 2003. Occup Environ Med. 2009;66:189–197.
- Alman BL, Pfister G, Hao H, et al. The association of wildfire smoke with respiratory and cardiovascular emergency department visits in Colorado in 2012: a case crossover study. *Environ Health*. 2016;15:64.
- Reid CE, Brauer M, Johnston FH, Jerrett M, Balmes JR, Elliott CT. Critical review of health impacts of wildfire smoke exposure. *Environ Health Perspect*. 2016;124:1334–1343.
- Reid CE, Jerrett M, Tager IB, Petersen ML, Mann JK, Balmes JR. Differential respiratory health effects from the 2008 northern California wildfires: a spatiotemporal approach. *Environ Res.* 2016;150:227–235.
- 12. Gan RW, Ford B, Lassman W, et al. Comparison of wildfire smoke estimation methods and associations with cardiopulmonary-related hospital admissions. *GeoHealth*. 2017;1:122–136.
- 13. Liu JC, Wilson A, Mickley LJ, et al. Wildfire-specific fine particulate matter and risk of hospital admissions in urban and rural counties. *Epidemiology*. 2017;28:77–85.
- Hutchinson JA, Vargo J, Milet M, et al. The San Diego 2007 wildfires and Medi-Cal emergency department presentations, inpatient hospitalizations, and outpatient visits: an observational study of smoke exposure periods and a bidirectional case-crossover analysis. *PLoS Med*. 2018;15:e1002601.
- Leibel S, Nguyen M, Brick W, et al. Increase in pediatric respiratory visits associated with Santa Ana wind–driven wildfire smoke and PM2.5 levels in San Diego County. Ann Am Thorac Soc. 2020;17:313–320.
- Wegesser TC, Pinkerton KE, Last JA. California wildfires of 2008: coarse and fine particulate matter toxicity. *Environ Health Perspect*. 2009;117:893–897.
- 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. *Nat Commun.* 2021;12:1493.
- Aguilera R, Corringham T, Gershunov A, Leibel S, Benmarhnia T. Fine particles in wildfire smoke and pediatric respiratory health in California. *Pediatrics*. 2021;147:e2020027128.
- Rappold AG, Cascio WE, Kilaru VJ, et al. Cardio-respiratory outcomes associated with exposure to wildfire smoke are modified by measures of community health. *Environ Health*. 2012;11:71.
- Liu JC, Wilson A, Mickley LJ, et al. Who among the elderly is most vulnerable to exposure to and health risks of fine particulate matter from wildfire smoke? *Am J Epidemiol.* 2017;186:730–735.
- Kondo MC, De Roos AJ, White LS, et al. Meta-analysis of heterogeneity in the effects of wildfire smoke exposure on respiratory health in North America. Int J Environ Res Public Health. 2019;16:960.
- 22. Reid CE, Considine EM, Watson GL, Telesca D, Pfister GG, Jerrett M. Effect modification of the association between fine particulate air pollution during a wildfire event and respiratory health by area-level measures of socio-economic status, race/ethnicity, and smoking prevalence. *Environ Res Health*. 2023;1:025005.
- Heaney A, Stowell JD, Liu JC, Basu R, Marlier M, Kinney P. Impacts of fine particulate matter from wildfire smoke on respiratory and cardiovascular health in California. *GeoHealth*. 2022;6:e2021GH000578.
- Masri S, Jin Y, Wu J. Compound risk of air pollution and heat days and the influence of wildfire by SES across California, 2018–2020:

implications for environmental justice in the context of climate change. *Climate*. 2022;10:145.

- Ignotti E, Valente JG, Longo KM, Freitas SR, Hacon SdeS, Netto PA. Impact on human health of particulate matter emitted from burnings in the Brazilian Amazon region. *Rev Saude Publica*. 2010;44:121–130.
- Liu JC, Pereira G, Uhl SA, Bravo MA, Bell ML. A systematic review of the physical health impacts from non-occupational exposure to wildfire smoke. *Environ Res.* 2015;136:120–132.
- 27. Resnick A, Woods B, Krapfl H, Toth B. Health outcomes associated with smoke exposure in Albuquerque, new Mexico, during the 2011 Wallow Fire. *J Public Health Manag Pract*. 2015;21:S55–S61.
- Cutter SL. Vulnerability to environmental hazards. Prog Human Geogr. 1996;20:529–539.
- Sudore RL, Mehta KM, Simonsick EM, et al. Limited literacy in older people and disparities in health and healthcare access. J Am Geriatr Soc. 2006;54:770–776.
- 2018 Fire Season Incident Archive | CAL FIRE. 2019. Available at: https://www.fire.ca.gov/incidents/2018/. Accessed 1 February 2024.
- Zimmerman, J. Service Assessment: November 2018 Camp Fire. 2020. Available at: https://www.weather.gov/media/publications/assessments/ sa1162SignedReport.pdf. Accessed 1 February 2024.
- 32. Sheridan SC, Allen MJ. Changes in the frequency and intensity of extreme temperature events and human health concerns. *Curr Clim Change Rep.* 2015;1:155–162.
- Alari A, Letellier N, Benmarhnia T. Effect of different heat wave timing on cardiovascular and respiratory mortality in France. Sci Total Environ. 2023;892:164543.
- 34. Rerolle F, Arnold BF, Benmarhnia T. Excess risk in infant mortality among populations living in flood-prone areas in Bangladesh: a cluster-matched cohort study over three decades, 1988 to 2017. Proc Natl Acad Sci U S A. 2023;120:e2218789120.
- Sheridan P, McElroy S, Casey J, Benmarhnia T. Using the generalized synthetic control method to estimate the impact of extreme weather events on population health. *Epidemiology*. 2022;33:788–796.
- Craig P, Katikireddi SV, Leyland A, Popham F. Natural experiments: an overview of methods, approaches, and contributions to public health intervention research. *Annu Rev Public Health*. 2017;38:39–56.
- Xu Y. Generalized synthetic control method: causal inference with interactive fixed effects models. *Polit Anal.* 2017;25:57–76.
- DiSantostefano J. International classification of diseases 10th revision (ICD-10). J Nurse Pract. 2009;5:56–57.
- Aguilera R, Luo N, Basu R, et al. A novel ensemble-based statistical approach to estimate daily wildfire-specific PM2.5 in California (2006– 2020). *Environ Int.* 2023;171:107719.
- Abadie A, Diamond A, Hainmueller J. Synthetic control methods for comparative case studies: estimating the effect of California's tobacco control program. J Am Stat Assoc. 2010;105:493–505.

- 41. Nianogo RA, Benmarhnia T, O'Neill SA. Comparison of quasiexperimental methods with data before and after an intervention: an introduction for epidemiologists and a simulation study. *Int J Epidemiol*. 2023;52:1522–1533.
- 42. Fish JA, Peters MDJ, Ramsey I, Sharplin G, Corsini N, Eckert M. Effectiveness of public health messaging and communication channels during smoke events: a rapid systematic review. J Environ Manage. 2017;193:247–256.
- Macnamara J. The Hazelwood coal mine fire: lessons from crisis miscommunication and misunderstanding. *Case Stud Strateg Commun.* 2015;4:54–87.
- 44. Gerety RM. Farm workers in wildfire areas aren't always aware of evacuation plans. NPR. 2015. Available at: https://www.npr. org/2015/09/01/436525793/farm-workers-in-wildfireareas-arent-always-aware-of-evacuation-plans. Accessed 20 December 2024.
- Davies IP, Haugo RD, Robertson JC, Levin PS. The unequal vulnerability of communities of color to wildfire. *PLoS One.* 2018;13:e0205825.
- Morrow BH. Identifying and mapping community vulnerability. Disasters. 1999;23:1–18.
- Ojerio R, Moseley C, Lynn K, Bania N. Limited involvement of socially vulnerable populations in federal programs to mitigate wildfire risk in Arizona. Nat Hazards Rev. 2011;12:28–36.
- O'Neill S, Kreif N, Sutton M, Grieve R. A comparison of methods for health policy evaluation with controlled pre-post designs. *Health Serv Res.* 2020;55:328–338.
- Callaway B, Sant'Anna PHC. Difference-in-differences with multiple time periods. J. Econom. 2021;225:200–230.
- Zscheischler J, Martius O, Westra S, et al. A typology of compound weather and climate events. Nat Rev Earth Environ. 2020;1:333–347.
- Zhao R, Gao Q, Hao Q, et al. The exposure-response association between humidex and bacillary dysentery: a two-stage time series analysis of 316 cities in mainland China. *Sci Total Environ*. 2021;797:148840.
- 52. Sera F, Gasparrini A. Extended two-stage designs for environmental research. *Environ Health*. 2022;21:41.
- Cascio WE. Wildland fire smoke and human health. Sci Total Environ. 2018;624:586–595.
- 54. Borchers Arriagada N, Horsley JA, Palmer AJ, Morgan GG, Tham R, Johnston FH. Association between fire smoke fine particulate matter and asthma-related outcomes: systematic review and meta-analysis. *Environ Res.* 2019;179:108777.
- Doubleday A, Sheppard L, Austin E, Isaksen TB. Wildfire smoke exposure and emergency department visits in Washington State. *Environ Res Health*. 2023;1:025006.
- Anenberg SC, Haines S, Wang E, Nassikas N, Kinney PL. Synergistic health effects of air pollution, temperature, and pollen exposure: a systematic review of epidemiological evidence. *Environ Health*. 2020;19:130.