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Climate knows no borders: Assessing the role of extreme weather events in driving adverse health outcomes in a binational United States-Mexico border region

A Dissertation submitted in partial satisfaction of the requirements
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in

Public Health (Global Health)

by

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The Dissertation of Lara Schwarz is approved, and it is acceptable in quality and form for publication on microfilm and electronically.

Chair

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Dedication

This dissertation is dedicated to Eduardo Yobani Nava Chavez, my fierce supporter, and my inspiration. He encouraged me to think about the who and why behind my research, how to be intentional with my words and actions, and to never be afraid to follow my dreams. He was my motivation for pursuing this doctoral program, my inspiration for choosing this project and work, and the driving force for my success. Through thick and thin, Eddie encouraged and supported me every step of the way and he is the reason I am here today. Thank you Eddie for your unconditional love and support, I could not have done this without you. Your memory will live on through all the people you have touched and the wisdom that I learned from you will forever continue to be at the core of my work and efforts.

Epigraph

“We didn’t cross the border, the border crossed us”
- Cesar Chavez

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List of Acronyms

ATT	Average Treatment Effect of the Treated
BHM	Bayesian Hierarchical Model
CDC	Centers for Disease Control and Prevention
COPD	Chronic Obstructive Pulmonary Disease
COVID-19	Coronavirus Disease 2019
ERR	Excess Relative Risk
GDP	Gross Domestic Product
HMS	Hazard Mapping Smoke Product
IPCC	United Nations Intergovernmental Panel on Climate Change
NAFTA	North American Free Trade Agreement
NOAA	National Oceanic and Atmospheric Administration
$PM_{2.5}$	Fine Particles (under 2.5 microns in diameter)
RR	Relative Risk
SARS-CoV-2	Severe Acute Respiratory Syndrome Coronavirus 2
SAWs	Santa Ana Winds
SES	Socioeconomic Status
US	United States

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Abstract of the Dissertation

Climate knows no borders: Assessing the role of extreme weather events in driving adverse health outcomes in a binational United States-Mexico border region

by

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Background: While the detrimental health effects of extreme heat and wildfire smoke are well established in high-income countries, there is substantially less evidence in low and middle-income settings. This dissertation research aimed to quantify the effects of extreme heat and wildfire smoke through a social vulnerability approach, using the San Diego-Tijuana border as a context to study differential impacts.

Methods: This dissertation includes three studies examining the differential impacts of extreme heat and wildfire smoke in a binational context. The first study evaluates the spatial variation in the effect of extreme heat across municipalities in Mexico using a within-community-matched design with a Bayesian Hierarchical model extension and meta-regression to explore socioeconomic drivers. In the second study, we used the San Diego-Tijuana region as a unique context to study the differential effects of wildfire smoke on cardio-respiratory hospitalizations across the border using synthetic control methods (SCM). The third study also used SCM to explore the potential role of wildfire smoke in driving COVID-19 mortality in the San Diego-Tijuana border region.

Results: In the first study, we found substantial spatial heterogeneity in the effects of heat across Mexico at the municipality level, and disadvantaged social conditions such as low education, poor housing conditions, and higher marginalization were important predictors of these differences. In the second study, wildfire smoke increased cardio-respiratory hospitalizations in the San Diego-Tijuana border region, with a higher, albeit imprecise, relative change in Tijuana likely driven by a higher poverty rate and increased social vulnerability. Lastly, in the third study, no strong effect of wildfire smoke on COVID-19 mortality was observed in either San Diego or Tijuana.

Conclusion: The results of this dissertation indicate that social vulnerability is an important factor in understanding the health risks of extreme heat and wildfire smoke. We hope that highlighting the differential susceptibility of populations to these effects can help inform binational efforts to protect those that are most vulnerable to extreme weather events which will be increasingly prevalent and severe in the context of climate change.

Chapter 1 : Introduction

1.1 Extreme weather events under climate change

Climate change has caused widespread impacts on populations at a global scale and is one of the biggest global health threats of the 21st century (Mitchell, Heaviside et al. 2016, Holsman and Lucatello 2022). From 2006-2015, the global mean surface temperature was 0.87°C higher than the average from pre-industrial times (1850-1900) (Shukla, Skeg et al. 2019). This continued to increase by 1.09 [0.95 to 1.20] °C in 2011–2020 compared to the 1850-1900 period (Pörtner, Roberts et al. 2022), and it is projected to increase at 0.2°C per decade due to continued anthropogenic carbon emissions (Masson-Delmotte, Zhai et al. 2018). For warming to stay under 1.5°C, global carbon emissions would have to decrease by 45% by 2030 (relative to 2010 levels) and reach net zero by 2050 (Masson-Delmotte, Zhai et al. 2018). As the global mean surface temperatures continue to rise, climate projections forecast more extreme temperatures, heavy precipitation, and droughts in many regions (Masson-Delmotte, Zhai et al. 2018). Furthermore, warming has been increasing more rapidly over land; global averaged land surface air temperature has increased by 1.53°C from 1999-2018 from the pre-industrial period (Shukla, Skeg et al. 2019). One of the six reasons for concern about the effects of global warming identified by the United Nations Intergovernmental Panel on Climate Change (IPCC) is the severe and widespread risks and societal impacts of extreme weather events (Masson-Delmotte, Zhai et al. 2018).

Rising global temperatures affect weather variability, which has known impacts on the occurrence and severity of extreme weather. Extreme weather events can include extreme heat events, floods, droughts, wildfires, and hurricanes (Curtis, Fair et al. 2017, Clarke, Otto et al. 2022). This dissertation will focus on extreme heat and wildfires, due to their known health impacts and high prevalence in the US and Mexico, particularly in the San Diego-Tijuana border region, in recent years (Gershunov and Guirguis 2012, Goss, Swain et al. 2020, Safford, Paulson et al. 2022) (Figure 1.1). Even a small increase in global temperatures can multiply the likelihood of extreme heat and heat waves due to increased climate variability (Clarke, Otto et al. 2022, EPA 2023). Global warming also produces dry conditions due to hotter temperatures and decreased moisture from changes in precipitation regimes, intensifying the risk for larger wildfires (EPA 2023). Wildfires and heat waves have increased in length, intensity, and severity under climate change (Gershunov and Guirguis 2012, Goss, Swain et al. 2020) particularly in the US West Coast, with record-breaking events occurring frequently in the last decade (Li, Tong et al. 2021). In any scenario, the effects of global warming will continue to be exacerbated, and it is increasingly important to study the impacts of extreme weather to better forecast these events and reduce their adverse effects.

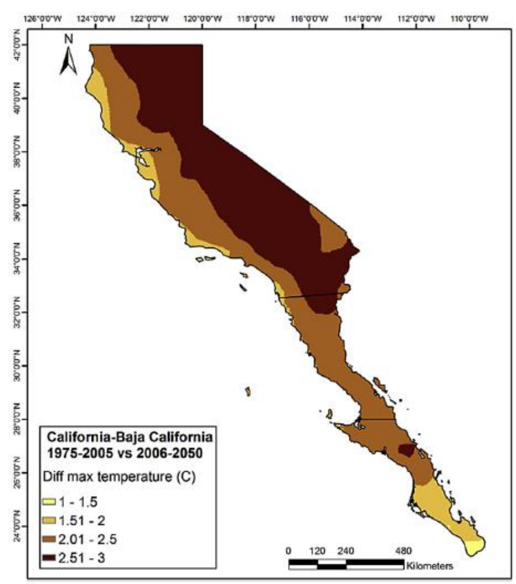


Figure 1.1: Distribution of temperature anomalies for 2006-2050 compared to the historical (1975-2005) period in California-Baja California under climate change (Vaghefi, Abbaspour et al. 2017).

1.2 Climate change and global health inequities

The countries that contribute the least to anthropogenic climate change will be the most affected by its impacts (Bathiany, Dakos et al. 2018). Poorer regions of the world will be disproportionally affected by the effects of climate change (Gasparrini, Guo et al. 2017). Globally, the majority of deaths from extreme weather events have occurred in lower-income countries, due to higher exposure and an increased vulnerability to stressors due to higher levels of poverty, lower education, and weaker healthcare systems (Mal, Singh et al. 2018). A far greater number of people susceptible to poverty will be exposed to climate-related risks as the globe continues to warm (Masson-Delmotte, Zhai et al. 2018). Additionally, socioeconomic determinants play an important role in modifying the risk of heat-related impacts making low-income contexts more susceptible to these environmental stressors (Campbell, Remenyi et al. 2018). Understanding what factors make communities at higher risk can be critical to informing targeted adaptation policies and reducing their burden and associated inequalities.

Despite this, there is much less evidence studying the impacts of extreme weather events in lower-income countries (Campbell, Remenyi et al. 2018, Green, Bailey et al. 2019). The vast majority of studies considering epidemiologic impacts of heat and wildfire smoke are focused on high-income contexts, with fewer research studies quantifying impacts in Latin America or Africa, for example (Green, Bailey et al. 2019, Marlier, Crnosija et al. 2022). It was estimated that 80% of health impact research on heat waves is focused on North America or Europe (Campbell, Remenyi et al. 2018). Research on the health effects of wildfire smoke is similar with the majority of evidence coming from the US and Australia (Liu, Pereira et al. 2015). Poor data quality and availability are often a barrier to health research in these regions; lack of data standards can further contribute to this challenge (Li, Brodsky et al. 2018). Although data from low and middle-income regions may be more limited, studying the epidemiological effects of extreme weather events in these settings is critical to understanding and addressing these impacts in the context of climate change. There is a strong need for policy-relevant evidence to inform interventions to protect populations in these highly vulnerable regions.

1.3 Overview of the epidemiological impacts of extreme weather events

Extreme heat and wildfires have a range of known public health impacts. Both extreme weather events have direct and indirect effects on human health. For example, high temperatures can increase the risk of developing heat-related health conditions or exacerbate existing conditions such as cardiovascular events, asthma, and COPD (Rossiello and Szema 2019). Wildfires can cause physical harm to those directly affected by the flames, but can also cause harmful effects through wildfire smoke inhalation exposure that often travels far beyond the wildfire's perimeters (Brey, Ruminski et al. 2018, Rossiello and Szema 2019). It has been estimated that 1.69 million (95% CI: 1.52–1.83) deaths globally were attributed to non-optimal temperatures in 2019 (Burkart, Brauer et al. 2021). Global deaths attributable to fine particulate matter ($PM_{2.5}$) from wildfire smoke amount to over 300,000 on average annually, which accounts for 8-21% of the total mortality burden from outdoor air pollution (Marlier, Crnosija et al. 2022). In the context of this dissertation, epidemiological impacts will focus on the impacts of extreme heat events through their direct and indirect biological effects and wildfires through their indirect effects from exposure to wildfire smoke. These specific pathways were selected due to their widespread impacts on populations.

1.3.1 Health effects of extreme heat

Heat waves, or extreme heat events, are the greatest cause of weather-related fatalities in the US in the last thirty years, surpassing those attributed to flooding and hurricanes combined

(NOAA 2021). A systematic review of 54 studies found heat waves to be associated with increased cardio-respiratory mortality and morbidity (Cheng, Xu et al. 2019). A 10°F increase in daily temperature was associated with a 4.3% increase in emergency respiratory hospital admissions in the Medicare population in the US (Anderson, Dominici et al. 2013). There is no universal definition for a heat wave or extreme heat event but using contextual information unique to the region and period of study to define these events can be important in maximizing the potential benefit of public health interventions (Tong and Kan 2011, McElroy, Schwarz et al. 2019). Studying extreme heat events, as compared to ambient temperature, has policy-relevant applications due to its distinct thresholds that can be used to activate early warning systems or action plans (McElroy, Schwarz et al. 2019). A unique regional definition for extreme heat events is crucial to reducing health impacts as the threshold can activate a response including interventions to promote the capacity of the population to cope with these events, which can target vulnerable populations (Benmarhnia, Bailey et al. 2016). Although extensive evidence exists on the epidemiological impacts of extreme heat, the majority of research is focused on high-income countries that have extensive resources and strong healthcare systems (Green, Bailey et al. 2019).

Heat stress can affect multiple biological systems and increase the risk of cardiovascular disease, respiratory disease, genitourinary disease, or mental illness (Bouchama, Aziz et al. 2017, Ebi, Capon et al. 2021). Exposure to high ambient temperature can cause heat stress and the induction of heat shock proteins which increase thermoregulation and a cellular stress response that is activated to prevent cellular damage and hyperthermia (Bouchama, Aziz et al. 2017). Heat-related injuries are related to cytotoxicity caused by exposure to high temperature, the inability of the body to increase the expression of heat shock proteins, and heat-related inflammation (Bouchama, Aziz et al. 2017). Thermoregulation during extreme heat events can lead to increases in cardiac effort and cardiovascular stress (Ebi, Capon et al. 2021). Exposure to heat is associated with higher odds of being hospitalized due to dehydration, heat illness, ischemic stroke, acute renal failure, and diabetes (Basu, Pearson et al. 2012).

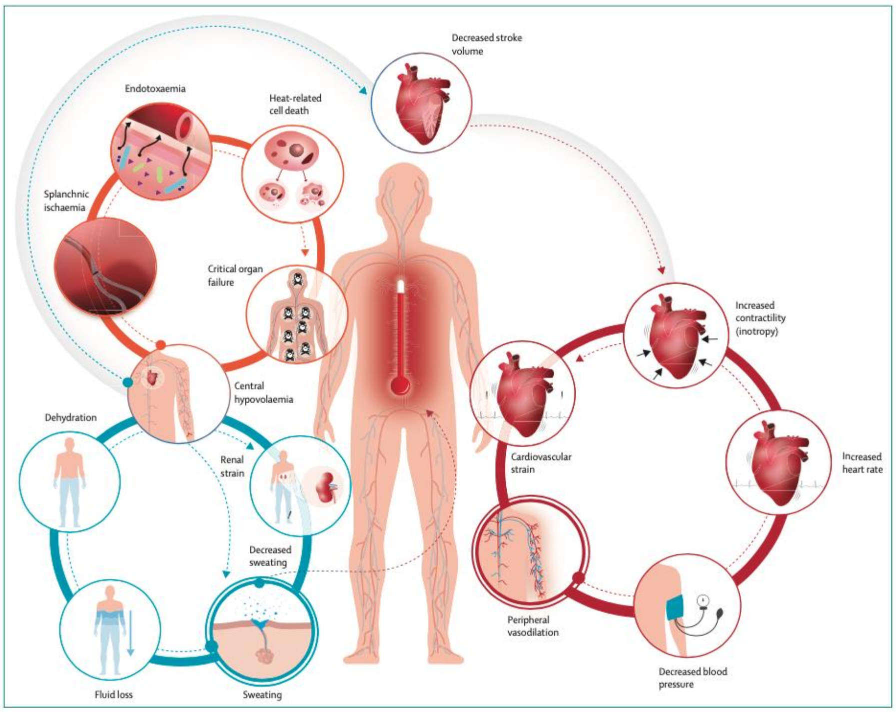


Figure 1.2: Physiological pathways of the effects of heat stress on human health (Ebi, Capon et al. 2021).

On the other hand, high temperature has been shown to be negatively associated with aneurysms, hemorrhagic stroke, and hypertension (Basu, Pearson et al. 2012). The physiologic responses to heat are associated with vasodilation which can lead to blood pressure reduction, which explains why high heat events have been shown to increase hospitalizations due to hypotension but reduce hospital admissions from hypertension (Basu, Pearson et al. 2012). Although the full mechanism of the effect of heat on the human body continues to be studied and understood, negative health impacts on the cardiovascular and respiratory systems have been well established in the literature (Ishigami, Hajat et al. 2008, Bobb, Obermeyer et al. 2014, Vaidyanathan, Malilay et al. 2020, Liu, Varghese et al. 2022). Overall, acute exposure to extreme heat increases morbidity and mortality in the majority of populations and studies (Hajat, Armstrong et al. 2005, Deschenes and Moretti 2009, Åström, Bertil et al. 2011, Carleton and Hsiang 2016, Green, Bailey et al. 2019, Burkart, Brauer et al. 2021).

1.3.2 Wildfire smoke and cardio-respiratory effects

Global mortality from wildfire smoke is estimated to be 339,000 deaths per year (Johnston, Henderson et al. 2012). Wildfire smoke includes high concentrations of ambient particulate matter such as $PM_{2.5}$, particles under 2.5 microns in diameter, which can be composed of ions, organic compounds, or other materials (Valavanidis, Fiotakis et al. 2008). In Southern California, the Santa Ana winds (SAWs) are associated with driving wildfires, particularly in the fall after dry and warm summers (Westerling, Cayan et al. 2004). While SAWs reduce $PM_{2.5}$ in the context of no wildfire event, they are associated with increased particulate matter exposure in areas downwind of wildfires during an event (Aguilera, Gershunov et al. 2020). $PM_{2.5}$ is associated with a range of adverse health effects (Berger, Malig et al. 2018, Yang, Ruan et al. 2019). A systematic review including 45 studies on the impact of wildfires on respiratory health found that 90% of studies reported an increased risk of respiratory morbidity due to wildfire smoke exposure (Liu, Pereira et al. 2015). Impacts have also been found on cardiovascular health outcomes (Chen, Samet et al. 2021). There is strong evidence of the adverse health effects of wildfire smoke, yet the majority of research has been conducted in the US and Australia, with little evidence from other contexts (Liu, Pereira et al. 2015).

Globally, exposure to ambient air pollution drives 3.3 million premature deaths every year (Lelieveld, Evans et al. 2015). Particulate matter is known to exacerbate existing conditions, and increase morbidity and mortality from various causes and conditions (Valavanidis, Fiotakis et al. 2008, Yang, Ruan et al. 2019). The widespread health burden from air pollution exposure has been well documented in the literature, with effects including respiratory disease, cardiovascular disease, allergenic diseases, and diabetes, affecting individuals throughout the life course from developing fetuses to elderly populations (Mannucci, Harari et al. 2015). $PM_{2.5}$ exposure has a strong association with adverse health outcomes due to its small diameter and ability to penetrate deeply into the lung alveoli (Yang, Ruan et al. 2019). The effect of wildfire-specific $PM_{2.5}$ is strongly associated with respiratory health effects; exposure can result in declining lung function such as triggering asthma and/or chronic obstructive pulmonary disease (COPD) symptoms (Reid, Brauer et al. 2016).

There are several proposed mechanisms by which inhaled fine particulate matter can affect the biological system. Neurochemical reactions between the lung and nervous system can cause blood pressure to increase and heart rhythms to change, increasing the risk of cardio-respiratory issues (Cascio 2018). Oxidative stress and inflammation are also known effects of particulate matter exposure due to the generation of reactive oxygen species from the inhalation of these particles (Valavanidis, Fiotakis et al. 2008). This inflammatory damage can trigger cellular damage and increase risk of cardiopulmonary disease (Valavanidis, Fiotakis et al. 2008). Furthermore, the smallest particles can cross the alveolar membrane to the bloodstream and cause systemic effects on the human biological system (Yang, Ruan et al. 2019). The pulmonary response to these stressors can affect airway function and decrease resilience to viral and bacterial infections (Cascio 2018). A systematic review indicates sufficient evidence to demonstrate the adverse health effects of wildfire-specific particulate matter on all-cause mortality and respiratory morbidity (Cascio 2018). A subsequent review studying the impacts of wildfire smoke on cardiovascular health finds exposure to wildfire-related particulate matter to be a driver of adverse cardiovascular effects (Chen, Samet et al. 2021).

1.3.3 Wildfire smoke and COVID-19 effects

COVID-19 infections can range from being asymptomatic to causing premature death. However, it is estimated that one in five infected persons develop severe disease (Aliberti, Covinsky et al. 2021). Elderly persons are at higher risk of complications of COVID-19, and up to 80% of deaths from the disease occur in older adults (Aliberti, Covinsky et al. 2021). Furthermore, older persons from low-income communities are at an even higher risk for COVID-19 mortality as they are more likely to suffer from other health conditions, increasing the risk of complications (Calderón-Larrañaga, Dekhtyar et al. 2020). Unhealthy behaviors can also increase risk of disease severity; for example, smokers are at increased risk of severe COVID-19 (Reddy, Charles et al. 2020). In the US, African Americans have a higher risk of COVID-19 infection and death, which can be partly attributable to economic inequality and chronic stress related to racial discrimination (Chowkwanyun and Reed Jr 2020).

SARS-CoV-2, the virus that causes COVID-19 disease, can cause a wide variety of symptoms ranging from loss of taste and smell to chest tightness and fever (Struyf, Deeks et al. 2020). In severe infections, the virus can cause alveolar damage in the lung and interstitial pneumonia (Aguiar, Lobrinus et al. 2020). A systematic review of predictive symptoms found that dyspnea was predictive of severe infection, while COPD, cardiovascular disease, and hypertension symptoms were predictors of admission to intensive care units (Jain and Yuan 2020). Wildfire smoke has been shown to affect the risk of these health issues; therefore, it is plausible that exposure to these events may modify the risk of severe COVID-19 or drive increased mortality. Political responses to the pandemic including stay-at-home orders may increase disparities in exposure to wildfire smoke; households that have accessibility to air filtration systems, for example, may be able to cope with the environmental stressor while those without them will be at increased risk. Understanding this dual burden of these concurrent public health crises can be important to allocate resources and protect vulnerable populations.

Due to the established associations between air pollution and respiratory disease outcomes, wildfire-specific $PM_{2.5}$ has been suggested as a driver of severe outcomes of COVID-19 infection (Henderson 2020, Zhou, Josey et al. 2021, Ademu, Gao et al. 2022, Schwarz, Dimitrova et al. 2022, Yu and Hsueh 2023). Air pollution can weaken the respiratory system and reduce the ability to produce an immune response, which can enable viral entry and replication (Bourdrel, Annesi-Maesano et al. 2021). Additionally, as air pollution and COVID-19 affect the same biological systems and organs, it could increase the risk of more severe infection due to their dual effects on the respiratory and cardiovascular systems (Bourdrel, Annesi-Maesano et al. 2021). Air pollution has also been found to increase the expression of the alveolar angiotensin-converting enzyme 2 (ACE2), an important receptor for the host defense against COVID-19 disease (Katoto, Brand et al. 2021). While numerous studies have considered the role of particulate matter exposure in driving COVID-19 mortality (Cole, Ozgen et al. 2020, Liang, Shi et al. 2020, Wu, Nethery et al. 2020), few have considered wildfire smoke as a specific exposure (Schwarz, Dimitrova et al. 2022, Yu and Hsueh 2023). Our previous work has shown that wildfire smoke increased COVID-19 case fatality ratios in several counties in the San Francisco Bay Area (Schwarz, Dimitrova et al. 2022). Yu & Hsueh (2023) also investigated the effect of wildfire smoke on COVID-19 during the 2020 wildfire season and found that $PM_{2.5}$ during this time increased COVID-19 infections and deaths, while this effect was attenuated in counties with more hospital resources (Yu and Hsueh 2023). Other studies have found a modifying effect of acute respiratory infections on air pollution-related impacts, such as severe acute respiratory syndrome (SARS) and influenza (Wong, Yang et al. 2008, Xu, Hu et al. 2013, Horne, Joy et al. 2018). Hypothetical models have found that wildfire smoke of moderate magnitude and intensity has the potential to increase the impacts of COVID-19 by 10% (Henderson 2020). Understanding the role of wildfire smoke and air pollution In modulating the severity of COVID-19 disease is critical to forecasting and informing hospitals and the healthcare system of increases in the need for hospital beds during peak pollution events.

Further studies have considered the role of acute air pollution exposure more generally in driving COVID-19 disease and outcomes. A systematic review of epidemiological studies on this topic found that four of six studies considering the effect of $PM_{2.5}$ on COVID-19 mortality observed a positive association (Sheppard, Carroll et al. 2022). Another critical review on the association between air pollutants and COVID-19 from 2022 presented evidence that demonstrated an association between air pollution and COVID-19 mortality and infectivity (Yates, Zhang et al. 2022). However, the ecological nature of many studies on this topic can be considered a weakness that prevents them from providing evidence of a causal effect (Villeneuve and Goldberg 2020). There are methodological challenges in studying this association due to the ecological fallacy and threat of unmeasured confounders in this proposed association (Benmarhnia 2020, Bhaskar, Chandra et al. 2020). However, novel methodologies that adjust for confounding by design can be applied to the study of acute environmental events such as wildfires smoke to further explore this association. This allows the consideration of air pollution from wildfire smoke as a natural experiment within a causal framework. The application of causal inference methods to this question can not only highlight the potential role of wildfire smoke in driving COVID-19 mortality but can also provide evidence for how particulate matter in general may interact to increase disease severity. Using the random occurrence of wildfire smoke spatially and temporally as a natural experiment is an opportunity to study this association and promote the importance of further exploring this research question (Sheridan, McElroy et al. 2022).

1.4 Differential susceptibility to extreme weather events

Populations may have different levels of exposure to the same environmental hazard; for example, communities with low SES are disproportionally living in areas with higher air pollution exposure (Hajat, Hsia et al. 2015). This indicates a first level of environmental injustice, or when communities do not have "equal protection and equal enforcement of environmental laws and regulations" (Bullard 2005). There is also a second level of injustice that goes beyond exposure levels. For the same level of exposure, populations can also be differentially *susceptible* to a given environmental hazard. It is well known that susceptibility to extreme weather events varies with certain population socio-demographics showing increased risk of being harmed by these exposures (Gronlund 2014, Cakmak, Hebbern et al. 2016, Chi, Hajat et al. 2016, O'lenick, Winquist et al. 2017). It is particularly important to identify susceptible populations as prioritizing these groups can be hugely effective in maximizing the potential benefit of environmental health policies and actions through a health equity approach.

1.4.1 Extreme heat

The elderly, children, and those with low SES are particularly susceptible to the health effects of extreme heat (Wilson, Black et al. 2011, Benmarhnia, Deguen et al. 2015, Xu, Crooks et al. 2017, Cheng, Xu et al. 2018). The vulnerability of the elderly population may be due to the reduced ability of these populations to thermoregulate, increasing stress on the pulmonary and cardiovascular systems, and subsequently negative health outcomes (Basu and Ostro 2008). Additionally, the elderly are more susceptible due to the increased prevalence of underlying medical conditions that can limit their ability to respond physiologically to heat as well as mental disorders that may alter risk perceptions and protective behaviors (Åström, Bertil et al. 2011).

Generally, lower SES and ethnic minority groups are also more likely to live in warmer neighborhoods that have high settlement density, sparse vegetation, and no open space which are aspects of the built environment that can increase heat stress (Harlan, Brazel et al. 2006, Hsu, Sheriff et al. 2021). Neighborhoods with green space have been shown to attenuate the health effects of heat (Gronlund, Berrocal et al. 2015, Lungman, Cirach et al. 2023). Racial minorities and communities of low SES are also more likely to have poorer physical health, less likely to have health insurance, more likely to live in neighborhoods with high levels of crime and sparse vegetation, and have lower air conditioning ownership (Gronlund 2014). Many factors may contribute to this increased risk including but not limited to housing characteristics, linguistic isolation, or increased physiological susceptibility due to other social and/or biological stressors (Gronlund 2014, Jones, Dunn et al. 2021). Weathering or accelerated biological aging due to psychosocial stress also plays a role in the differential health effects we observe as it affects susceptibility to environmental hazards (Forrester, Jacobs et al. 2019).

Understanding which socio-demographic characteristics make a neighborhood particularly at-risk can be used to target resources in susceptible areas before and during a period of extreme heat and maximize the potential effectiveness in decreasing the adverse effects and promoting health equity. Accounting for these known community-level vulnerabilities can be used to effectively estimate the expected burden of heat waves and extreme heat events to prepare for and prioritize at-risk populations. Characterizing differential susceptibility is critical to estimating the health impacts of these events in understudied regions of the world; by considering community-level characteristics that are known risk factors for the health effects of heat, we can better understand health impacts in these regions and inform policies to reduce their burden.

1.4.2 Wildfire smoke

Many neighborhood and individual-level factors can increase the susceptibility of populations to air pollution and, specifically, wildfire smoke. Age and gender can play a role in the observed effects; some studies found an increased risk of asthma-related symptoms from wildfire smoke exposure in women than men (Liu, Pereira et al. 2015). An increased susceptibility was also found among those 65+ years of age (Liu, Wilson et al. 2017). Children also had an increased risk of emergency department visits during the 2007 wildfires in San Diego, with young children under the age of 1 showing a 243% increase in asthma visits during the peak fire period (Hutchinson, Vargo et al. 2018). Another study attributed 16 excess pediatric respiratory visits per day to wildfire $PM_{2.5}$ from the Lilac Fire that affected the region in 2017 (Leibel, Nguyen et al. 2020). Wildfire-$PM_{2.5}$ drives a 30% (95% CI: 26.6-33.4) increase in pediatric respiratory hospital admissions in a hospital network in San Diego County (Aguilera, Corringham et al. 2021).

SES is also well documented as an effect modifier[1] in the associations between air pollution and various health effects (Cakmak, Hebbern et al. 2016, Chi, Hajat et al. 2016, O'lenick, Winquist et al. 2017). Socio-economic factors may increase susceptibility to air pollution impacts by increasing the risk of other conditions such as asthma and/or affecting

[1] A variable that changes the magnitude of the effect of exposure on outcome.

development and resistance to other disease threats (Neidell 2004). A study conducted in North Carolina estimated that counties with a higher poverty level had twice the risk of having an emergency department visit following exposure to wildfire smoke than counties with lower poverty levels (Rappold, Cascio et al. 2012). The same study showed that income inequality in a county was a risk factor for increased emergency department visits due to smoke exposure (Rappold, Cascio et al. 2012). Neighborhood-level risk factors faced by those living in low-income neighborhoods may increase their susceptibility to environmental hazards (Clougherty and Kubzansky 2009). Stressors, such as crime, noise, and traffic can lead to acute and chronic changes in the functioning of body systems and increase the effect of exposures such as wildfire smoke on the biological system (Chi, Hajat et al. 2016).

By revealing these environmental health inequities, and identifying which communities are particularly susceptible, resources can be allocated in a manner that promotes health and environmental equity. Warning systems to forecast wildfire smoke exposure have the potential to decrease the burden of these exposures; smoke-related public health messaging to stay indoors can be adapted and prioritize at-risk populations (Fish, Peters et al. 2017). Although there is a need for more research to evaluate the effectiveness of these measures on protecting population health, understanding which characteristics make a neighborhood or area susceptible to the effects of wildfire smoke is critical to the activation and effectiveness of any public health intervention.

1.5 Evidence of extreme heat effects in Mexico

When compared to the vast literature on heat-related health impacts in the US (Marmor 1975, Anderson, Dominici et al. 2013, Bobb, Obermeyer et al. 2014, Benmarhnia, Deguen et al. 2015, Gronlund, Berrocal et al. 2015, Huang, Skidmore et al. 2020, Vaidyanathan, Malilay et al.

2020, Jones, Dunn et al. 2021, Khatana, Werner et al. 2022) and even research specific to California (Basu and Ostro 2008, Basu, Pearson et al. 2012, Guirguis, Gershunov et al. 2014, Guirguis, Basu et al. 2018, McElroy, Schwarz et al. 2019, Schwarz, Malig et al. 2019, Schwarz, Hansen et al. 2021), there is a much smaller number of studies quantifying the health effects of extreme heat in Mexico. Yet some studies have considered the effects of extreme temperature on mortality in specific urban centers such as Mexico City and Monterrey (O'Neill, Hajat et al. 2005, Bell, O'Neill et al. 2008), the effect of high temperature on specific outcomes such as diarrheal diseases (Vargas and Magaña 2020) and suicide rates (Burke, González et al. 2018), and three studies have looked at temperature and mortality nationwide (Cohen and Dechezleprêtre 2017, Cohen and Dechezleprêtre 2022). Other studies have considered its synergistic effects with air pollution (Mendez-Astudillo, Caetano et al. 2022) and projected extreme heat under climate change scenarios (Cueto, Martínez et al. 2010) focusing on exposure-level vulnerability. The available evidence exploring the effects of extreme heat in Mexico will be summarized in this section.

Many studies investigating heat-related effects in Mexico have considered heat-mortality effects focusing on specific urban centers such as Monterrey and Mexico City. O'Neill et al (2005) studied the association between apparent temperature and mortality in both Monterrey and Mexico City assessing the influence of controlling for air pollution and respiratory epidemics (O'Neill, Hajat et al. 2005). They found a 27.2% higher mortality [95% CI: 20.0%, 34.7%] in Monterrey on days with an apparent temperature of 35/36°C when compared to days of 25/26°C after controlling for the season, day of the week, and public holidays while no effect was found in Mexico City (0.3 [95% CI: −2.0%, 2.7%] (O'Neill, Hajat et al. 2005). A few years later, Bell et al. (2008) applied a case-crossover approach to study heat-related mortality in three cities including Mexico City, and explore vulnerability factors (Bell, O'Neill et al. 2008). A 1.26 (−0.39 to 2.93) percentage increase in mortality was observed at the 95th percentile of mean apparent temperature compared with the 75th percentile (Bell, O'Neill et al. 2008). Recent work evaluating the city-level effect of the impact of extreme temperature on mortality in Latin American cities included 92 cities in Mexico and found increased risks with high temperatures, and particularly high effects in the coastal cities of Mexico (Kephart, Sánchez et al. 2022). Another study expanded on this dataset to consider effect modification by socio-demographics across 9 Latin American counties including Mexico and found unexpected associations where cities with higher poverty levels and income inequality were found to have lower impacts of heat (Bakhtsiyarava, Schinasi et al. 2023).

Some work has also investigated specific disease outcomes such as diarrheal disease and suicide rates. Vargas & Magaña (2020) associated weekly average temperatures in Mexico City with acute diarrheal diseases and found that weekly maximum temperatures above average increased reports of hospital discharges for diarrheal diseases reported by the Federal Commission for Health Risk Management one or two weeks later (Vargas and Magaña 2020). Burke et al. (2018) studied the effect of temperature on suicide rates in the US and Mexico, showing a 2.1% increase in suicide rates in Mexican municipalities for a 1 °C increase in monthly average temperature; this was higher than the 0.7% increase observed in US counties (Burke, González et al. 2018). Agüero (2014) used Mexican's nationally representative health and nutrition survey to study the effect of extreme temperature during the life course on adult height finding infancy and adolescence to be important periods for the effects of extreme heat (Agüero 2014).

Few studies have considered the effects of extreme heat at a national level. Guerrero Compean (2013) studied the relationship between extreme temperature and mortality rates, concluding that extreme heat drove increases in mortality and rural areas of Mexico are particularly susceptible (Guerrero Compeán 2013). Subsequent work by Cohen and Dechezleprêtre (2022) explored the impact of temperature on mortality in Mexico and showed that 3.8 percent of deaths in the country are caused by suboptimal temperature, finding that the majority are driven by cold temperatures as shown in Figure 1.3 (Cohen and Dechezleprêtre 2022). The authors use binned temperature ranges to study these effects in Mexico (Cohen and Dechezleprêtre 2022). However, variations in the observed effects may be driven by regional-level differences in the population composition and temperature distributions; using local temperature distributions has been found to be important to best estimate the public health impacts of extreme heat (McElroy, Schwarz et al. 2019).

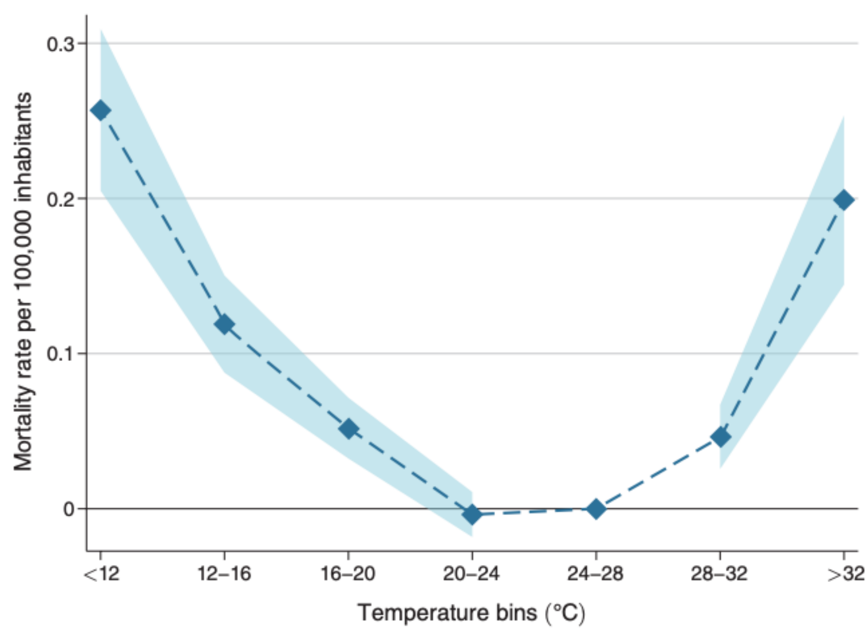


Figure 1.3: Impact of temperature ranges on 31-day cumulative mortality rate in Mexico relative to the 24°C–28°C category (Cohen and Dechezleprêtre 2022).

Other research has considered spatial vulnerability to extreme heat and combined risk with other environmental health and projected impacts under climate change scenarios. Collins et al. (2013) studied the fine-scale vulnerability to the combined risks of extreme heat, peak ozone, and floods at a small spatial scale in the El Paso-Ciudad Juárez border region (Collins, Grineski et al. 2013). This study applied GIS-based spatial assessment methods to identify spatial vulnerability to these environmental hazards for children, focusing on exposure. Projections in Mexicali have shown that the city will continue to experience longer, more frequent, and more severe days of extreme heat in the next decades (Cueto, Martínez et al. 2010). For example, in a medium-high emissions scenario (A2), heat days are projected to increase by 93% in the 2020s, 226% in the 2050s, and 407% in the 2080s (Cueto, Martínez et al. 2010). This is consistent with other studies projecting increases in extreme heat exposure at a global scale in the context of climate change (Russo, Dosio et al. 2014). To our knowledge, no study has considered the fine-scale spatial variation in the health effects of heat or explored community-level factors that can explain heterogeneous effects.

1.6 Environmental epidemiology in a border context

The US-Mexico border region is characterized by rapid growth, high migration, economic intensification, and climate change, making it a region with high social and environmental vulnerability (Wilder, Garfin et al. 2013). Exposure to ambient hazards such as wildfire smoke may be similar on both sides of the border, but effects may vary due to contextual differences across the border. Borders are a unique area to explore differential impacts of extreme weather events due to climatological uniformity and socio-demographic/neighborhood level heterogeneity. Smoke produced from wildfires in the Southern California-Baja California Norte area affects populations in the entire region, so understanding the burden of these events is critical in addressing this global health concern. Results can be used to inform harmonized warning systems to protect populations from the health effects of these extreme weather events.

1.6.1 Historical context of the San Diego-Tijuana border region

The native inhabitants of the San Diego-Tijuana border region are the Kumeyaay who lived here for 10,000 years before the Europeans arrived; during this time, the area was considered one region not separated by any border, wall, or politics. Spanish colonizers arrived in San Diego in 1542 and it was stolen from the Kumeyaay and taken under Spanish rule. The Mexican independence then occurred in 1821 and San Diego was taken under Mexican control (Sparrow 2001). It stayed under Mexican rule for 27 years until 1848 when the people living in the US overthrew the Mexican government. The Treaty of Guadalupe Hidalgo was ratified by US Congress concluding the war and establishing the border between the US-Mexico, California-Baja California, and San Diego-Tijuana. This separated the Kumeyaay tribes by an artificial boundary through their ancestral land despite their common language, history, and cultural traditions (Kada and Kiy 2004). They were left without the right to cross the border, even though a mountain sacred for their cultural traditions is on the US side with many of the tribe's people living on the Mexican side of the border (Luna-Firebaugh 2002, Kada and Kiy 2004). Throughout this period, the Kumeyaay were forced off their ancestral lands and nearly all Kumeyaay land was stolen and became private or US government-owned.

Although the cities of San Diego and Tijuana are close in proximity and have economic ties, the history of each of their development and growth differ. In 1850, shortly after the armed conflict with Mexico, California's state constitution was accepted and it became the thirty-first state; San Diego became a city that same year (Sparrow 2001). In 1974, a Mexican customs crossing was set up for the flow of goods between San Diego and what we now know as Tijuana, and in 1910 the entire population of Tijuana did not exceed 700 (Sparrow 2001). The city provided low-cost labor, access to activities that were not legal in the US, and looser regulations, and developed as a direct response to fulfill the needs of the population living in San Diego (Sparrow 2001). Tijuana was officially named in 1929 when the population was approximately 11,000 inhabitants (Sparrow 2001). Although the development of Tijuana as a city was a reaction to the growth of San Diego as an urban center, it was not until the 1970s that Mexican and US policies started considering each other (Sparrow 2001).

During World War II there was a shortage of labor and the US government allowed Mexican workers to legally cross the border to work mostly in agricultural jobs under the Bracero program (Mandeel 2014). However, the program was stopped in 1964 when it was deemed that the US economy no longer needed this labor (Mandeel 2014). This resulted in many unemployed Mexican workers at the border and the Border Industrialization Program was established in response, which invested in *maquiladoras* in Mexico providing manufacturing by Mexican labor with aims to attract foreign investment and produce jobs in the northern border region (Schwartz 1987).

This binational context became a unique setting because although the San Diego-Tijuana border is one local region in many ways, state and local governments on both sides are not allowed to formally work with each other as the government structures require federal governments to conduct foreign relations (Sparrow 2001). In response, quasi-governmental entities have been established out of need such as certain border environmental resource issues that cannot be adequately managed without the cooperation of both authorities (Sparrow 2001). The International Boundary and Water Commission, for example, was a bilateral organization composed of leaders in the foreign ministries of Mexico and the US established in 1889 to settle issues of boundary alterations due to changes in the course of rivers but evolved to focus on regional water resource management challenges (Brown 2005). Cross-border planning started in the 1960s and the two cities started initiatives and planning meetings for developing infrastructure at the border (Mendoza and Dupeyron 2020). In 1992, the Integrated Environmental Plan for the Mexican-US border region was established which was the first comprehensive border environmental cooperation in which the environmental protection agencies of both the US and Mexico committed financial investment to the border area and its environment (Agency, Urbano et al. 1992).

Globalization has been a driving force for the economic growth of the San Diego-Tijuana border region, but the government has failed to create region-wide efforts. There is a lack of power of local governments to implement structures and processes to work together to govern the border region. The author Sparrow (2001) argued that because the relations between San Diego and Tijuana are driven by economic interests, there is a lack of sense of belonging for both cities for it to truly become one bi-national city and region. The socio-economic context of the San Diego and Tijuana has continued to co-evolve over the last decades. The North American Free Trade Agreement (NAFTA) was established in 1994 and synchronized business cycles between Tijuana and San Diego and allowed economic ties to be further strengthened (Mendoza and Dupeyron 2020). After 9/11 the US border shifted more focus on securing the border, and the San Diego-Tijuana border region experienced contrasting forces of increased economic integration while experiencing the effects of increased border enforcement (Mendoza and Dupeyron 2020).

With the 2008-2009 economic recession, the unemployment rate in the city of San Diego was very high, many workers sought out jobs in Tijuana. This is still true in the current day where Tijuana has a lower unemployment rate than San Diego as it has a high level of employment in the maquiladora industry (Mendoza and Dupeyron 2020). The recession also increased deportations of Mexican workers from the US which added pressure to border urban centers including Tijuana (Mendoza and Dupeyron 2020). Manufacturing industry remains an important share of the Gross Domestic Product (GDP) of Tijuana, which manufactures and assembles imported products that are then re-exported to the US; almost 16% of exports from the US to Mexico come from California, and 70% of those pass through Baja California (Mendoza and Dupeyron 2020).

1.6.2 Current context of the San Diego-Tijuana border region

The San Diego-Tijuana border is one of the busiest international crossings in the world (Mendoza and Dupeyron 2020). San Diego and Tijuana are two major coastal cities, making this region the largest bi-national conurbation shared between the US and Mexico and the fourth-largest in the world (Mendoza and Dupeyron 2020). Tijuana has grown exponentially in the last 20 years. In 1990, the population was 747,381 but this increased to 1.5 million people by 2010 (Mendoza and Dupeyron 2020). In 2021, San Diego County was estimated to have a population of 3.3 million while the Municipality of Tijuana was home to 1.9 million residents in 2020 (INEGI 2020, UN 2021). Border crossings have also increased drastically in the last 10 years; in the major port of entry, San Ysidro pedestrian border crossings increased by 57% from 2004 to 2014 (Mendoza and Dupeyron 2020).

Tijuana is more socially deprived than San Diego with a higher poverty rate and lower education levels (INEGI 2010, Census Bureau 2011, Rosa, Haines et al. 2023). Income distribution in Mexico has been one of the most unequal in the world, with the poorest populations earning less than 4% of the total national income (Vargas-Hernández and Reza, 2010). In 2010, the GDP of San Diego County was over 1,222,000 million dollars, while the GDP of the state of Baja California (including Tijuana) was just over 26,000 million dollars (Mendoza and Dupeyron 2020). While poverty levels differ between San Diego and Tijuana, low-income populations on both sides suffer from a lack of access to healthcare services that meet their needs (Vargas-Hernández and Reza, 2010). Urban poverty is rising in Tijuana with half of the new residents living in communities without inadequate infrastructure. Additionally, the cost of living is high. Many US residents seek healthcare across the border and some estimates show that 25 to 40 percent of US residents travel to Mexico to bring back prescription pharmaceuticals (Vargas-Hernández and Reza, 2010).

There are now many actors that work on border issues in the region, including private organizations, non-governmental organizations, and governmental entities (Mendoza and Dupeyron 2020). However, a contrast remains in the vision of local stakeholders of the San Diego-Tijuana border as one region while the US government pushes national security, preventing it from becoming fully integrated (Mendoza and Dupeyron 2020). Following NAFTA, local non-governmental agencies such as the Environmental Health Coalition argue that policies and committees established to counteract its adverse effects on communities and the environment have not been effectively implemented and that local agencies have insufficient authority to enforce some of these agreements (Mendoza and Dupeyron 2020). Additionally, there is a lack of awareness at the federal level of what the local issues and local agencies lack decision-making power since international borders are managed federally (Sparrow 2001, Mendoza and Dupeyron 2020). Many local organizations consider the US economic policies to be mistreating the Mexican labor force by using them as a disposable labor supply and succumbing them to poor working conditions and treatment; they advocate for a strong need for additional support and resources for these migrant populations (Mendoza and Dupeyron 2020).

1.6.3 Climate in the San Diego-Tijuana border region

The San Diego-Tijuana border region is between a Mediterranean and semi-arid climate (Peel, Finlayson et al. 2007). Most of the annual precipitation occurs in the winter, from November to March, and is subject to high variability, driving increasingly frequent droughts and floods (Wilder, Garfin et al. 2013). The Southern California coast experiences moderate temperature year-round with average maximum temperatures of 25°C, 20°C, and 22°C in the fall, winter, and spring, respectively (Schwarz, Malig et al. 2019). The region is also characterized by micro-climates, with a high range in temperatures between the coastal and inland areas (McElroy, Schwarz et al. 2019), daily maximum temperature can differ by 10-20°F in these areas (Rosa 2020).

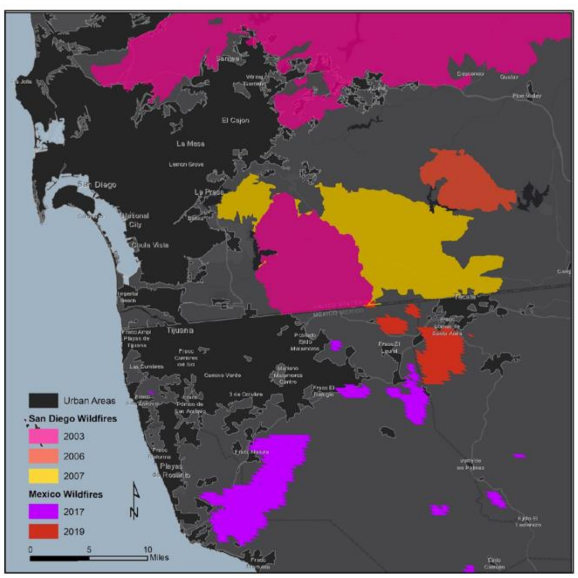


Figure 1.4: Extent of the largest wildfires by area burned in San Diego and recent wildfires in northern Baja California (Rosa 2020).

The region is affected by SAWs, dry down-sloping winds rooted in cold air masses over the elevated Great Basin, which affect the region primarily between September and May (Guzman-Morales and Gershunov 2015). The SAWs heat by compression as they descend to the sea and often lead to increased ambient temperatures during the typically ‘colder’ fall, winter, and spring seasons (Schwarz, Malig et al. 2019). SAWs are associated with some of the hottest temperatures recorded in the Southern California coastal region. SAWs are also linked to the ignition and spread of wildfires, and spreading the smoke burden during these events (Aguilera, Gershunov et al. 2020). In October 2007, for example, the region faced a large record-breaking event, which ignited thirteen different wildfires from Los Angeles to Tijuana; this was exacerbated by SAWs (Petersen 2011). This event as well as other more recent wildfires in the region highlight the vulnerability of the region to this climatic threat. The area has experienced many record-breaking wildfire events in recent years (Figure 1.4), and this is projected to continue increasing in the context of climate change.

As San Diego and Tijuana cities are located less than 20 miles from the border, exposure to extreme weather events may be similar on both sides of the border. Wildfire smoke plumes can extend far beyond the wildfire’s perimeter and fires igniting on either side of the border can cause unhealthy air quality for residents of both San Diego and Northern Baja California (Brey, Ruminski et al. 2018). This makes it an ideal region to explore the public health manifestation of wildfire smoke in a border context.

1.6.4 Review of epidemiologic evidence in the San Diego-Tijuana border region

While both sides of the border region are affected by the health impacts of extreme weather events, there are significant disparities in evidence between San Diego and Tijuana. Numerous studies have been conducted to understand the epidemiological effects of extreme heat and wildfire smoke on California as a whole (Ebi, Exuzides et al. 2004, Ostro, Roth et al. 2009, Guirguis, Gershunov et al. 2014, Aguilera, Corringham et al. 2021) and in San Diego specifically (Guirguis, Basu et al. 2018, Hutchinson, Vargo et al. 2018, Aguilera, Hansen et al. 2020). Contrastingly, little to no research has been conducted in Tijuana or Baja California to understand these impacts. The proximity of these cities and the discrepancy in available evidence on this topic highlights the need to find strategies to adapt research tools and methods to each context; understanding the impacts of extreme weather events in regions with limited epidemiological data will become increasingly important.

In San Diego and California, it has been well established that wildfire smoke drives adverse health outcomes (Kunzli, Avol et al. 2006, Richardson, Champ et al. 2012, Kochi, Champ et al. 2016, Reid, Jerrett et al. 2016, Aguilera, Hansen et al. 2020, Aguilera, Corringham et al. 2021, Heaney, Stowell et al. 2022). An evaluation of the health effects of a major wildfire event that occurred in Southern California in 2003 showed increased eye and respiratory symptoms, medication use, and physician use for children in communities in Southern California (Kunzli, Avol et al. 2006). Recent work in Southern California has shown that $PM_{2.5}$ from wildfire smoke can drive up to 10 times more respiratory hospitalizations than non-wildfire $PM_{2.5}$ (Aguilera, Corringham et al. 2021). A study specific to San Diego County found a 30% (95% CI: 26.6% to 33.4%) increase in emergency and urgent care visits at Rady’s Children’s Hospital network for each 10-unit increase in $PM_{2.5}$ from wildfire smoke (Aguilera, Corringham et al. 2021). A study evaluating the economic impact of the 2007 wildfires showed that it drove medical costs by over $3.4 million (Kochi, Champ et al. 2016). These are a few of the numerous studies in San Diego and California that demonstrate the health impacts of wildfire smoke and highlight the need to inform policies to limit the harmful effects of this exposure.

The strong health effects of wildfire smoke observed in San Diego County indicate the need to understand and reveal these impacts in Tijuana. Studying these effects in Tijuana is critical to informing early warning systems and addressing this research gap. Ideally, forecasting systems for wildfire smoke will consider environmental risk factors on both sides of the border and inform warning systems and action plans to protect populations in the entire region.

1.7 Dissertation overview and specific aims

As wildfires and extreme heat become more severe and frequent in the context of climate change, quantifying the public health implications of these events in diverse regions with varying socioeconomic structures and vulnerabilities is increasingly urgent (Gershunov and Guirguis 2012, Goss, Swain et al. 2020). Exposure to extreme heat and wildfire smoke causes adverse effects on population health, driving increased morbidity and mortality (Åström, Bertil et al. 2011, Liu, Pereira et al. 2015, Green, Bailey et al. 2019). Exposure to extreme heat is ubiquitous across regions and can trigger dangerous physiological responses such as inflammation, heat cytotoxicity, and vasodilation, increasing the risk of cardio-pulmonary disease and death (Cramer and Jay 2016, Mora, Counsell et al. 2017). Wildfires are episodic events that produce wildfire smoke which is associated with declining lung function, oxidative stress, and inflammation (Reid, Brauer et al. 2016, Chen, Samet et al. 2021). While low and middle-income regions of the world are disproportionally affected by extreme weather, there is much less evidence of epidemiological impacts in these settings than in high-income contexts (Green, Bailey et al. 2019, Marlier, Crnosija et al. 2022).

Environmental epidemiological research demonstrating the adverse effects of extreme weather events is extensive in San Diego and California (Guirguis, Gershunov et al. 2014, Aguilera, Hansen et al. 2020, Aguilera, Corringham et al. 2021, Schwarz, Hansen et al. 2021), but evidence is lacking in Tijuana and Mexico. Few studies have quantified the association between extreme heat and mortality in Mexico (Agüero 2014, Cohen and Dechezleprêtre 2022) and none have considered the spatial variation in these effects. Due to the widespread impacts of extreme heat, there is a need for a comprehensive assessment of the effects of extreme heat in Mexico; we apply a spatial model to study this and understand what socio-demographics are driving this heterogeneity. In contrast, wildfires are episodic events that are not prevalent across Mexico. Border regions are a unique setting to explore the effects of wildfire smoke as wildfires igniting on either side of the border can cause harmful smoke exposure to the entire region. The San Diego-Tijuana region is one of the most densely populated international borders, and the largest bi-national urban center shared between the US and Mexico (Mendoza and Dupeyron 2020). Yet, the socioeconomic context differs between San Diego and Tijuana; Mexico is ranked much lower (74th) than the US (17th) on the United Nations Development Programme Human Development Index (UNDP 2020). Furthermore, Tijuana is ranked to have the 4th worst quality of life index out of all Mexican cities while San Diego is ranked the 5th richest city in the US (Rawes 2015, Gallardo Del Ángel 2017). Due to a similar climatology and differing social conditions at the regional scale, the San Diego-Tijuana border region is a unique context to study the epidemiological impacts of environmental exposures and associated vulnerabilities Moreover, given the known health effects of extreme weather events, it has been hypothesized that exposures such as a wildfire smoke may be a driver of severe COVID-19 outcomes (Henderson 2020). We use the San Diego-Tijuana border region as a case study to explore differential susceptibility to wildfire smoke on cardio-respiratory hospitalizations and COVID-19 mortality.

This dissertation aims to fill knowledge gaps on the effects of extreme weather events in an understudied binational context. This dissertation will investigate social vulnerability to the effects of extreme heat and wildfire smoke by 1) exploring the determinants of spatial variation of heat effects on mortality across Mexico and 2) using the San Diego-Tijuana border as a natural experiment to understand the differential effects of wildfire smoke.

The specific aims that will be addressed are as follow:

AIM 1: Examine the socio-demographic predictors of vulnerability to extreme heat at the municipality level across Mexico

AIM 2: Quantify the differential effects of wildfire smoke on cardio-respiratory hospital admissions in the San Diego-Tijuana border region

AIM 3: Explore the potential role of wildfire smoke in affecting COVID-19 mortality in the San Diego-Tijuana border region

Understanding the differential vulnerability to the impacts of extreme weather events is critical to informing evidence-based early warning systems to protect populations from these increasingly prevalent exposures and decrease their burden. Extreme heat is pervasive across regions and countries; revealing the social factors that predict differential expressions of its effect in a country with limited evidence can be used to prioritize efforts and policies for those that are most vulnerable. Studying the role of wildfire smoke in driving hospitalizations in a border context can improve our understanding of the underlying social vulnerabilities to these impacts. Results are important to understand the public health implications of these events and can be used to inform harmonized early warning systems to activate measures to protect populations. Lastly, this dissertation will reveal the potential role of wildfire smoke in driving COVID-19 mortality, shedding light on a poorly understood relationship. Findings can provide evidence to warrant the exploration of these questions and inform the utility of these methods in other border contexts and understudied populations.

Chapter 2 : Socio-demographic predictors of vulnerability to extreme heat across Mexico

2.1 Abstract

Extreme heat is projected to increase in the context of climate change and a greater number of people in low-income settings will be exposed to climate-related risks in the next decades. Yet most of the evidence of the health impacts of extreme heat is from high-income countries. Understanding the effects of extreme heat across diverse settings is critical as social determinants play an important role in modifying heat-related risks. Previous work evaluated the effects of temperature extremes on mortality in Mexico overall; we expand on this by applying a fine-scale spatial analysis to understand variation in its effect and explore what factors are driving heterogeneity. Data on daily mortality were extracted from death certificates from the Mexican Secretary of Health for all 2457 municipalities from 1998-2020. Municipality-specific extreme heat events were defined at the 95th and 99th percentile of population-weighted daily maximum and minimum temperature. A within-community matched design with a Bayesian Hierarchical model (BHM) was applied to study the effect of extreme heat on mortality spatially across Mexico. A random-effect meta-regression was applied using output from the BHM to understand which municipality-level socio-demographics from the 2010 Mexican Census were driving the observed spatial heterogeneity. Results showed an increased risk for all extreme heat events in Mexico with substantial differences across regions; the overall excess relative risk (ERR) ranged between 0.17 and 0.34 for the different measures and the 99th percentile of minimum temperature had the highest precision (ERR: 0.32, 95% CI: 0.23, 0.41). Municipalities with older populations, higher marginalization, lower education, and poorer housing conditions showed greater heat-related health effects. Understanding the differential health risks of extreme heat in Mexico is critical to prioritize at-risk populations in action plans to reduce its burden.

2.2 Introduction

Heat waves are becoming more frequent and severe on a global scale and are projected to continue increasing under all climate change scenarios- over 35% of the global population will be exposed to severe heat waves at least every 5 years if global warming increases by 2°C from pre-industrial times (Meehl and Tebaldi 2004, Dosio, Mentaschi et al. 2018, Shukla, Skeg et al. 2019). Exposure to extreme heat causes increases in morbidity and mortality; in 2019, high temperature accounted for 0.54% of all mortality, or over 300,000 deaths globally (Song, Pan et al. 2021). The majority of deaths from extreme heat events have occurred in lower-income areas, due to higher exposure as well as increased vulnerability to stressors due to higher levels of poverty, lower education, and weaker healthcare systems (Mal, Singh et al. 2018). Furthermore, a far greater number of people susceptible to poverty will be exposed to climate-related risks as global warming continues to increase (Masson-Delmotte, Zhai et al. 2018).

Despite this, there are much fewer studies on the health impacts of extreme heat events in low and middle-income countries than in high-income settings (Campbell, Remenyi et al. 2018, Green, Bailey et al. 2019, Ebi, Capon et al. 2021). Although extensive evidence exists on the epidemiological impacts of extreme heat or heat waves, the majority of research is focused on high-income countries with very few research studies quantifying impacts in Latin America or Africa (Green, Bailey et al. 2019). A review of 188 articles found that 80% of heat-related health impact research on heat waves is focused on North America or Europe (Campbell, Remenyi et al. 2018). Out of the studies conducted in North America included in this review, none were from Mexico (Campbell, Remenyi et al. 2018). Studying the epidemiological effects of extreme heat events in diverse settings and between and across continents is critical to understanding and addressing these impacts in the context of climate change. There is a strong need for policy-relevant evidence to inform interventions to protect populations in these highly vulnerable regions.

It is particularly important to understand the differential health risks of extreme heat in diverse settings as the effect of heat varies across population socio-demographics. The elderly and those with low SES are particularly susceptible to the health effects of extreme heat (Wilson, Black et al. 2011, Benmarhnia, Deguen et al. 2015, Xu, Crooks et al. 2017, Cheng, Xu et al. 2018). The risk of heat-related illnesses can be exacerbated by physiological conditions such as having pre-existing health conditions as well as the decreased behavioral capacity to respond and adapt to this health risk (Ebi, Capon et al. 2021). Many factors may contribute to increased risk including but not limited to housing characteristics, linguistic isolation, or increased physiological susceptibility due to other social and/or biological stressors (Gronlund 2014, Jones, Dunn et al. 2021). The vulnerability of the elderly population may be due to their lack of ability to thermoregulate and a higher prevalence of underlying medical conditions that can limit their ability to physiologically respond to heat (Son, Liu et al. 2019). Mental disorders can also alter risk perceptions and prevent elderly individuals from taking precautions against the effects of heat (Åström, Bertil et al. 2011).

Lower SES and ethnic minority groups are also more likely to live in warmer neighborhoods that have high settlement density, sparse vegetation, and no open space which are aspects of the built environment that can increase heat stress (Harlan, Brazel et al. 2006, Hsu, Sheriff et al. 2021). Communities from low SES are also more likely to have poorer physical health, less likely to have health insurance, more likely to live in neighborhoods with high levels of crime, and have lower air conditioning ownership (Gronlund 2014). Weathering or accelerated biological aging due to psychosocial stress can also play a role in the differential health effects that are observed between populations (Forrester, Jacobs et al. 2019).

Understanding community-level vulnerabilities can be important to effectively estimate the expected burden of extreme heat to prepare for and prioritize at-risk populations. Informing heat action plans that are activated based on epidemiological evidence is most effective in reducing the burden of heat-related health impacts (Benmarhnia, Schwarz et al. 2019). Activating actions such as the dissemination of heat advice on how to best protect oneself during an extreme heat event, sending alerts, and ensuring cooling centers are accessible for those that don't have access to air conditioning can be critical in reducing the burden of heat (Lowe, Ebi et al. 2011, Bedi, Adams et al. 2022). Community-level characteristics can be important in explaining spatial variations in health risk that are observed across regions (Schwarz, Hansen et al. 2021). Socio-demographic characteristics that are known to increase the vulnerability to extreme heat can be used to target resources in susceptible areas before and during an event and maximize its potential effectiveness in decreasing the health burden and promoting health equity (Benmarhnia, Bailey et al. 2016).

While there is little epidemiological evidence studying the impacts of extreme heat on health in Mexico as compared to the extensive body of literature to investigate these impacts in the US, there are a few studies that have explored these associations. Guerrero Compean (2013) studied the relationship between extreme temperature and mortality rates, concluding that extreme heat drove increases in mortality and identifying rural areas of Mexico as particularly susceptible (Guerrero Compeán 2013). Subsequent work by Cohen and Dechezleprêtre (2022) explored the impact of temperature on mortality in Mexico and showed that 3.8 percent of deaths in the country are caused by suboptimal temperature, but find that the majority are driven by cold temperatures (Cohen and Dechezleprêtre 2022). The authors use temperature bins considering >32°C as hot days to study these effects in Mexico (Cohen and Dechezleprêtre 2022). Variations in the observed effects may be driven by regional-level differences in the population composition and temperature distributions. Using thresholds of extreme heat defined based on local temperature distributions has been found to be important to best estimate the public health impacts of extreme heat (McElroy, Schwarz et al. 2019).

We expand on this work to consider local thresholds of extreme heat and examine heterogeneity in these effects using a spatial model. First, we estimate a spatially-resolved measure of extreme heat using a local temperature distribution at the municipality level. Second, we examine the spatial variation in the effects of these extreme heat events on mortality across municipalities in Mexico using a within-community matched design and Bayesian Hierarchical model (BHM). Third, we explore what municipality-specific socio-demographic characteristics are important predictors of the observed spatial differences in the effects of extreme heat on mortality.

2.3 Methods

2.3.1 Data sources

Mortality counts were extracted from death certificates from the Mexican Secretary of Health and estimated daily from 1998 to 2020 for all 2457 municipalities in Mexico (http://www.dgis.salud.gob.mx/contenidos/basesdedatos/da_defunciones_gobmx.html) (Secretaria de Salud 2021). Due to 2020 corresponding to the start of the COVID-19 pandemic which drove much higher death counts than in previous years, it was excluded and a sensitivity analysis was conducted with this year included.

Daily maximum and minimum 2-meter air temperature raster data were extracted from the Daymet V4: Daily Surface Weather and Climatological Summaries (https://developers.google.com/earth-engine/datasets/catalog/NASA_ORNL_DAYMET_V4) at a 1km resolution (Thornton, Shrestha et al. 2022). Temperature raster layers were overlayed with 100x100 population grids from WorldPop and population-weighted values were estimated for each municipality and day using rgee (Tatem 2017, Aybar, Wu et al. 2020). This produced daily population-weighted temperature estimates; extreme heat days were defined at the 95th and 99th percentile of the population-weighted maximum and minimum temperature distribution (to consider both daytime and nighttime extreme heat events) for each of the 2456 municipalities in Mexico.

2.3.2 Statistical analysis

2.3.2.1 Within-community matched design

A within-community matched design (Aguilera, Hansen et al. 2020, Schwarz, Hansen et al. 2021) was applied to study the effect of extreme heat events on daily mortality at the municipality level in Mexico. This approach considers each extreme heat day in each municipality as a specific event and identifies control days (within a specific window to control for seasonality and long-term trends) that are used as a comparison to estimate a measure of relative risk (RR) during event days as compared to days in which the event did not occur using mortality counts. All municipalities with less than 500 deaths during the entire study period (1998-2019) were excluded to ensure results were not driven by extremes due to small sample sizes, these excluded municipalities had a population of less than 20,000 and those excluded had an average of 2,788 residents. For each definition of extreme heat, all days that were more than 3 days away from an extreme heat day and within 60 days of each extreme heat event were considered as potential controls. Excluding 3 days after the extreme heat day was to eliminate the potential lagged effect of heat from the selection of controls, the effects of extreme heat on mortality in Mexico have been shown to last 2-3 days and subside after 3 days as shown in Supplementray Figure 2.1 (Cohen and Dechezleprêtre 2022). An inverse time weighting scheme was applied in which control days closer in time to the exposed day were given a stronger weight than those that were further. A measure of RR was then calculated by taking the total number of deaths on the extreme heat event divided by the weighted average on all control days. A municipality-level measure of RR was estimated by taking an average for all the extreme heat events in each municipality. The excess relative risk (ERR) was then estimated by subtracting 1 from the RR. A time-stratified case-crossover analysis was also used to quantify the effect of heat in Mexico overall using an alternative approach (Lu and Zeger 2007).

2.3.2.2 Bayesian hierarchical model

We used spatial information to increase the precision of our results and account for spatial autocorrelation. Similar to previously published work by coauthors we used a spatial BHM for this purpose (Aguilera, Hansen et al. 2020, Schwarz, Hansen et al. 2021). The ERR estimates for all municipalities obtained from the within-community matched design analysis were used as the response variable in a spatial linear model. The BHM was fit using the spBayes package in R (Finley, Banerjee et al. 2007). We computed population-weighted centroids for each municipality in Mexico using Worldpop 1 kilometer grids from 2010 which were then used in the Bayesian model (Tatem 2017). An empirical semivariogram was fit to estimate the starting values for the spatial parameters: sill ($\sigma 2$), nugget ($\tau 2$), and range (ϕ). Prior distributions and tuning parameters were approximated based on the semivariogram and an inverse gamma distribution. Monte Carlo Markov sampling was applied with 10,000 samples, and 75% were used for burn-in. To estimate the statistical precision of the point estimates, we computed the signal-to-noise ratio (SNR) from the model output, which represents the ratio between the mean and standard deviation of recovered samples. The overall effects of extreme heat in Mexico were assessed by taking the mean and standard deviation of the recovered samples of the intercept from the BHM, and 95% credible intervals were estimated with two standard deviations above and below the mean. The SNR was mapped for each municipality to represent statistical precision. This gives a visual representation of areas where estimates of ERR are precise. A conventional cutoff was used of $|SNR| > 2$ to represent precision. This methodology assumes isotropy or a homogenous spatial relationship in all directions.

2.3.2.3 Meta-regression

A meta-regression was applied using the output from the BHM to understand what municipality-level factors are important predictors in the observed spatial heterogeneity. Data on socio-demographics at the municipality level was collected from the 2010 Census of Population and Housing from the National Institute of Statistics and Geography of Mexico (INEGI 2010). Socio-demographic variables at the municipality level considered to be relevant for heat-related impacts were population size, percentage of persons without schooling, percentage of persons illiterate, the median level of schooling, crowding (percentage with 3 or more people living per room), percentage without electricity, percentage with no refrigerator or tv, percentage with no amenities (no radio, television, refrigerator, washing machine, car, computer, fixed telephone, cell phone or internet), percentage of women, percentage of population 65+ years of age, median age and a marginalization score. The marginalization score is developed by the Mexican National Institute of Statistics and Geography using information about a municipality’s educational level, health, housing, assets and income to estimate the level of social deficiency that is endured by the population (INEGI 2010). Each socio-demographic variable was considered in a meta-regression, using the spatial estimate and variance from the BHM. Average minimum and maximum temperature for the study period (1998-2019) were also considered as predictors to consider the role of differential temperature profiles in predicting heat-related effects. Effect estimates and standard deviation were taken from each model to represent the important of each variable in predicting spatial distribution of heat effects across Mexico. For reproducibility purposes, all datasets and code used for this project are provided in the following repository: https://github.com/benmarhnia-lab/spatial_heat_Mexico.

2.4 Results

Mexico is composed of 2456 municipalities in 31 states. Additional information about the age and gender distribution of deaths is included in Supplementary Table 2.1). After excluding municipalities with less than 500 deaths in the 1998-2019 study period, 1740 municipalities were analyzed. The average daily mortality count across these municipalities was 0.86 and was higher on days of extreme heat (ranging between 0.89 and 0.92 for all four measures of extreme heat) (Table 2.1). Results of the time-stratified case-crossover showed a positive precise effect of heat for all extreme heat definitions considered (Supplementary Table 2.2). The temperature distribution varies by state and municipality although the warmer months usually fall within the March-October period (Supplementary Figure 2.2). The temperature threshold for daytime extreme heat events ranges between 25 °C and 45 °C while the threshold for nighttime extreme heat events ranges from 10°C to 30°C (Figure 2.1).

Overall, we observed an effect of extreme heat on all-cause mortality in Mexico for each definition of extreme heat. For the four metrics of extreme heat events (99^{th} maximum, 95^{th} maximum, 99^{th} minimum, 95^{th} minimum), we observe a range in ERR from 0.17 and 0.34 with the 99th percentile of minimum temperature measure showing the highest precision (ERR: 0.32, 95% credible interval: 0.23, 0.41). (Supplementary Table 2.2). The precision varies geographically and by extreme heat measure, with few municipalities showing precise values (defined by |SNR| > 2) for extreme heat events at the 99th percentile of minimum and maximum temperature (Supplementary Figure 2.3). Results of the within-community matched design showed substantial spatial heterogeneity in the effects of extreme heat, including some areas showing an ERR of up to 5 with other areas even showing a negative ERR (Figure 2.2). We observe particularly strong effects of extreme heat in the eastern coastal regions of Mexico as well as some hotspots on the western coast. Results were consistent across all measures of extreme heat and in the sensitivity analysis including 2020 (Supplementary Figure 2.4 & 2.5).

When investigating what socio-demographics are predictors of the spatial variation observed, we find that education level is inversely predictive of heat-related effects- as a municipality's education level increases, decreased effects of extreme heat are observed (Figure 2.3). The effect of extreme heat on mortality is greater in municipalities that have a higher percentage of individuals without schooling and illiteracy, and the impacts are less in municipalities with a higher median schooling level. Similar trends are found for certain housing-related characteristics; a higher percentage of crowded households (3+ persons per room) and households with no electricity, increase heat-related risks (Figure 2.3). Interestingly, the percentage of households without a television or refrigerator, a measure of household wealth, and the percentage of households with no amenities are not important predictors of heat-related impacts. Also, results suggest municipalities with higher unemployment show decreased heat-related impacts. Municipalities with a higher percentage of women also showed decreased effects of extreme heat (Figure 2.3). Municipalities with a higher median age and a greater percentage of residents over 65 years of age are at increased risk of heat-related impacts. Lastly, a higher marginalization seems to be the strongest predictor to explain the greater effects of heat on mortality.

2.5 Discussion

This study used a spatial model with municipality-level data and measures of extreme heat to quantify the effects of extreme heat events on mortality, examining heterogeneity in heat-related health impacts across municipalities and exploring which vulnerability factors are important predictors in the observed variation. The results are three-fold. First, we find that extreme heat increases the risk of mortality in Mexico. Second, the spatial analysis shows considerable spatial heterogeneity in the effects of extreme heat on mortality with some areas of Mexico showing increased risk. Lastly, socio-demographics such as the education, level of marginalization, and median age of municipalities were found to be important predictors of the differences we observed across Mexico indicating that social vulnerability was associated with increased risk of heat-related effects.

Overall, we found that extreme heat drives an ERR of 0.34 [95% credible interval: -0.12, 0.80] mortality on days of extreme heat defined by the 99th percentile of maximum temperature in Mexico overall. The positive association between extreme heat and mortality is consistent with many previous studies demonstrating the pervasive effects of extreme heat on a global scale (Cheng, Xu et al. 2019, Green, Bailey et al. 2019, Ebi, Capon et al. 2021) and previous studies showing the effects of extreme heat in Mexico (Guerrero Compeán 2013, Cohen and Dechezleprêtre 2022). Cohen and Dechezleprêtre (2022) found 2 percent of deaths from 1998-2017 to be induced by hot temperatures on days over 32°C (Cohen and Dechezleprêtre 2022). Our results indicate a 34% increase in the risk of mortality from extreme heat (defined at the 99th

percentile of maximum temperature), although the results are not comparable as we applied a distinct approach. In addition to the methodological approach differing, we used a municipality-specific measure of extreme heat that takes into account the local temperature distribution, while Cohen and Dechezleprêtre (2022) used the same temperature bins to examine these effects in all of Mexico. However, the authors did apply a sensitivity analysis considering relative measures of heat and found similar results to their main analysis (Cohen and Dechezleprêtre 2022). We observe substantial variation in heat-related impacts across Mexico also indicating that one unchanging measure for extreme heat may not be sufficient to fully reveal its effects.

The effects of extreme heat on mortality are not uniform across Mexico and show substantial spatial heterogeneity (Figure 2.2). There is a wide range of impacts across municipalities with some regions showing a negative ERR (although the effects are not precise) and other regions showing an ERR up to 0.76 (for 99^{th} percentile maximum temperature extreme heat events), suggesting a 76% increase in the risk of mortality on extreme heat days. Coastal regions of Mexico indicate higher heat-related effects (Figure 2.2); this is consistent with recent work evaluating city-level effects of extreme temperature on mortality in Latin America which found particularly high effects in coastal cities of the 92 cities included from Mexico (Kephart, Sánchez et al. 2022). The vulnerability of coastal regions to the effect of heat has also been observed in other areas including San Diego County, where lack of adaptation and lower air conditioning are likely drivers of this susceptibility as populations have a lower coping capacity to deal with these hazards since extreme heat is rarer along the coast than inland regions (Guirguis, Basu et al. 2018). Similar drivers may be explaining this heterogeneity in Mexico and future research could consider the role of adaptation and acclimatization in this association.

The results show that unvarying exposure metrics may not be sufficient to capture the full extent of heat-related impacts for a country and highlight the importance of considering spatial variation in the exposure measure and its effects. This is consistent with previous work using a similar methodology to understand the spatial variation in joint effects of heat and ozone pollution on respiratory hospitalizations across California zip codes (Schwarz, Hansen et al. 2021). This adds to the growing literature showing the importance of investigating fine-scale spatial differences in the health effects of heat (Hondula, Davis et al. 2012, Song, Yu et al. 2021, Wang, Solís et al. 2021). Studying these spatial differences and using them to inform policies has been shown to be effective in improving the effectiveness of heat action plans and public health interventions to reduce the burden of extreme heat (Carmona, Linares et al. 2017, Benmarhnia, Schwarz et al. 2019).

Results of the meta-regression showed that the spatial heterogeneity in heat-related effects was not random and that socio-demographics predicted the observed variation. The strongest social factor in predicting municipality-level differences in heat effects across Mexico was the marginalization index, indicating that municipalities with a higher marginalization are at a higher risk of mortality from extreme heat. This is consistent with previous work showing that lower community-level SES may increase heat-related mortality risk (Son, Liu et al. 2019). Similarly to previous studies, the higher the median age of a municipality and the higher percentage of persons above age 65, the higher risk it had for heat-related effects (Son, Liu et al. 2019). This is expected, as older populations are known to be particularly vulnerable to the adverse effects of heat. A systematic review investigating vulnerability to heat-related mortality revealed a ratio of relative risk, or increased risk, of 1.02 (95% CI: 1.01, 1.03) for persons aged

>65 years and 1.04 (95% CI = 1.02, 1.07) for ages >75 years when compared to younger age groups (Benmarhnia, Deguen et al. 2015).

Community-level education was also found to be predictive of heat-related impacts with increased heat effects in municipalities with a higher percentage of the population with no schooling or illiteracy increased while decreased effects in municipalities with higher median schooling. Lower education can decrease risk perception and protective behaviors and is also strongly linked with SES (Son, Liu et al. 2019). Also, populations from a lower SES may be more likely to work outdoor and have more direct exposure to extreme heat. Interestingly, previous work in three cities in Latin America did not identify individual-level education as an effect modifier between heat and mortality in Mexico City (Bell, O'Neill et al. 2008). A systematic review found limited evidence of higher risks of heat from lower education although 16 out of the 26 studies included in the review found a higher risk for those with no or lower education (Son, Liu et al. 2019). Our results add to this evidence indicating that community-level educational indicators can be important in predicting an increased risk of heat in Mexican municipalities. This may suggest that prioritizing municipalities with low education in heat action plans and public health interventions may be beneficial.

Municipalities with a higher percentage of residents with no electricity or more overcrowded households showed increased heat effects. However, the percentage of households without television or refrigerator, a measure of household wealth, was not found to be an important predictor of heat-related impacts, nor was the percentage of households with no amenities. Overcrowding and household wealth were not included as indicators in a systematic review of effect modifiers of temperature-related mortality, but weak evidence was found related to poor housing quality (Son, Liu et al. 2019). Our results suggest that municipalities with overcrowded households may be important to target and prioritize in heat action plans. The population size of a municipality was also not found to be associated with heat effects. This is consistent with previous work that showed similar vulnerability to heat for rural and urban municipalities (Cohen and Dechezleprêtre 2022). Interestingly, municipalities with a higher employment rate showed less heat-related effects, although this result was imprecise (Figure 2.3). This is contrary to previous work showing that unemployment can increase risks of heat-related impacts (Anderson and Bell 2009, Leone, D'Ippoliti et al. 2013), Additionally, municipalities with a higher percentage of women showed lower impacts of extreme heat, which differs from previous research showing that women may be more susceptible to heat impacts (Son, Liu et al. 2019). More work would have to be conducted to confirm these findings. Lastly, average maximum and minimum temperature were also important predictors, indicating that areas that experience higher heat on the absolute scale are at increased risk of heat impacts.

To our knowledge, this is the first study to explore spatial differences in heat-related effects in Mexico and highlight socio-demographics at the municipality level that are predictors in the observed variation. There are several strengths to this study; by applying a multi-stage analysis using a within-community matched design with BHM and meta-regression, we can capitalize on population-weighted temperature measures at the fine spatial scale to understand the differential role of extreme heat across populations. Additionally, by using publicly available satellite imagery and datasets that are available on an online repository, we hope that the analysis can be replicated in other contexts and regions to further understand how heat impacts vary spatially within and across different settings. Nevertheless, there are also limitations to the data sources and approach that should be acknowledged. The mortality data is from the national statistics for Mexico, and previous research using this data has indicated that official records in

Mexico were thought to underestimate deaths by 13.7 % (Silvi 2003, Bell, O'Neill et al. 2008). However, it was later shown that Mexico had 90% or more complete death registration and their certification system follows international standards (Braine 2006). Also, the Bayesian model assumes isotropy, considering the distance to be uniform in all directions, which may not hold as elevation changes and other geographical factors may be violating this assumption. Also, by focusing the analysis on municipalities with more than 500 deaths, we may be excluding rural areas where increased heat effects may be observed; however, the population size of a municipality did not appear to be an important predictor of heat impacts in this context. Lastly, we rely on census data from 2010 as it is in the middle of our study period, but future work could consider the rapidly changing social context in Mexico and account for temporal changes in these socio-demographics. Additionally, although this information was not available in the census data, it would be interesting to explore the role of air conditioning accessibility in understanding heat-related impacts.

Although the adverse effects of extreme heat are well established, there are many regions of the world where the specific epidemiological expressions of these events is not well understood. Countries that contribute the least to anthropogenic climate change will be the most affected by its impacts (Gasparrini, Guo et al. 2017, Bathiany, Dakos et al. 2018); yet there is substantially less evidence coming from many of these regions (Green, Bailey et al. 2019). Understanding the specific impacts of extreme heat at the regional level is important due to the heterogeneity in the impacts of extreme heat. Characterizing differential susceptibility to extreme heat is critical to estimating the epidemiological impacts of these events in understudied regions of the world.

Chapter 2, in part, is currently being prepared for submission for publication of the material. Lara Schwarz, Chen Chen, Kristen Hansen, Gordon McCord, Tarik Benmarhnia. "Socio-geographical variation in the effects of extreme heat on mortality: a spatial analysis of Municipality-level vulnerability across Mexico." The dissertation author was the primary researcher and author of this material.

Table 2.1: Descriptive statistics of mortality, heat events, and socio-demographics across 1740 Mexican municipalities, 1998-2019.

Environmental Information				
Extreme heat event	Threshold (°C)	Extreme heat days	Daily mortality count (mean)	
	mean (IQR)	*Total count*	*Extreme heat days*	*Non-heat days*
99th maximum	35.93 (5.63)	199017	0.92	0.86
95th maximum	34.35 (5.59)	987714	0.89	0.86
99th minimum	19.43 (8.87)	199017	0.97	0.86
95th minimum	18.55 (8.74)	987714	0.93	0.86
Socio-demographics				
	Median	IQR	Min	Max
Population	21275	34714	2458	1815786
Women (%)	51.0	1.7	46.4	55.7
Unemployment (%)	3.9	2.9	0	37.4
Without schooling (%)	10.7	9.9	0.9	56.0
Illiteracy (%)	11.1	11.0	0.6	58.7
Crowding* (%)	4.7	5.0	0.3	37.3
No electricity (%)	2.4	3.5	0	64.9
No refrigerator or tv (%)	19.0	26.5	0.6	64.9
No amenities (%)	3.5	6.8	0.1	57.6
Age 65+ years (%)	7.2	3.3	1.3	20.4
Median age	25.0	4.0	22.0	36.0
Marginalization#	3.0	2.0	1.0	5.0

*Crowding=3+ people per room

1-very low, 2-low, 3- medium, 4-high, 5-very high

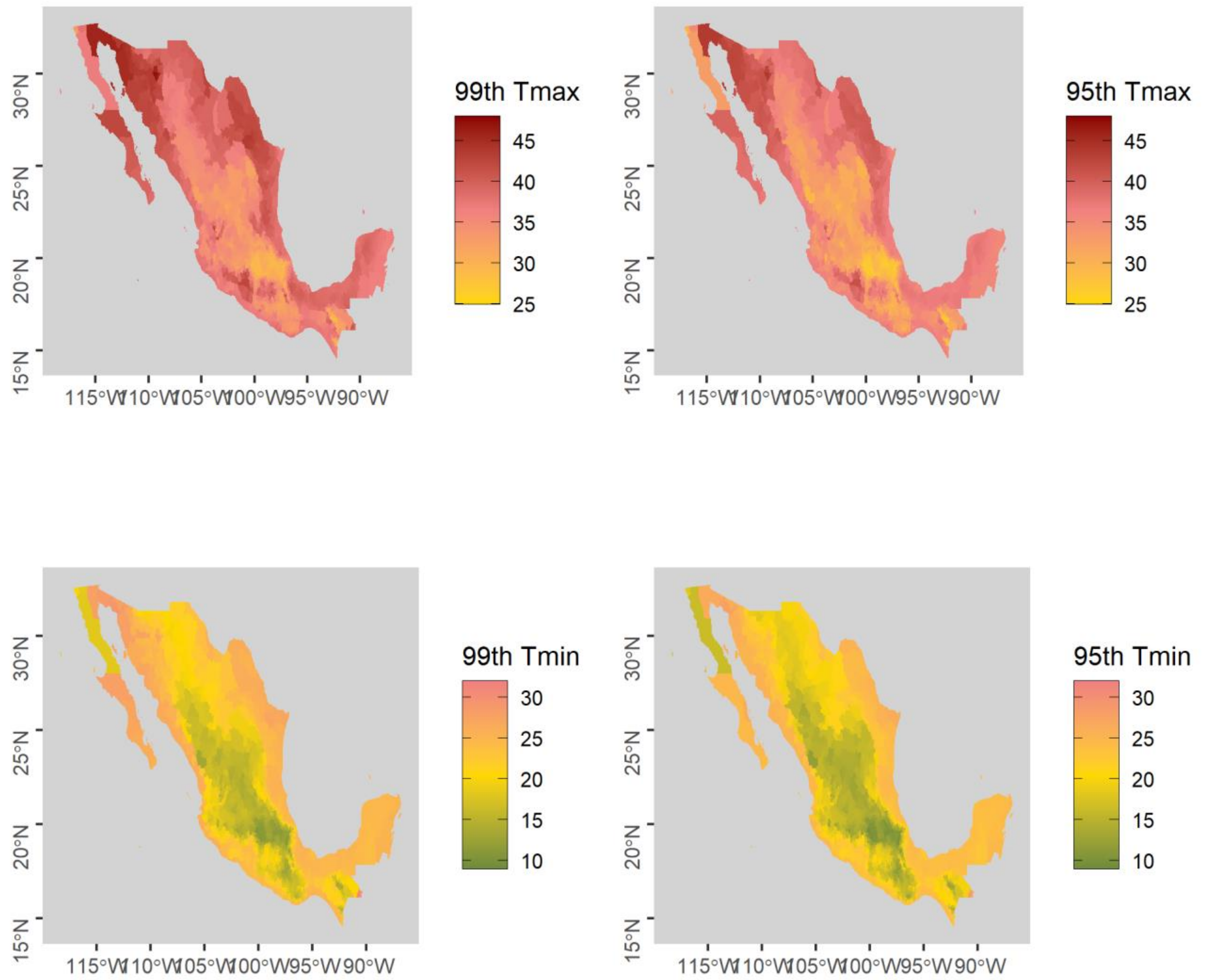


Figure 2.1: Maximum temperature (Tmax) and minimum temperature (Tmin) used for thresholds for four measures of extreme heat (99th maximum, 95th maximum, 99th minimum, 95th minimum) across Mexico, 1998-2019.

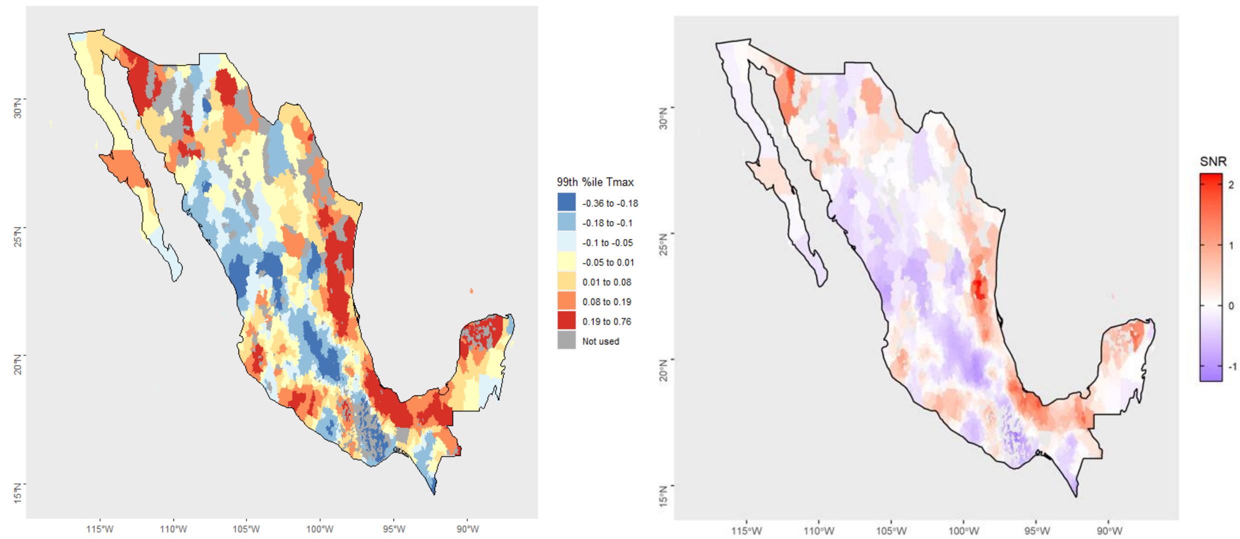


Figure 2.2: Bayesian resolved estimates and signal-to-noise ratio of the effect of daytime extreme heat events (99th percentile maximum temperature) on all-cause mortality across Mexico, 1998-2019.

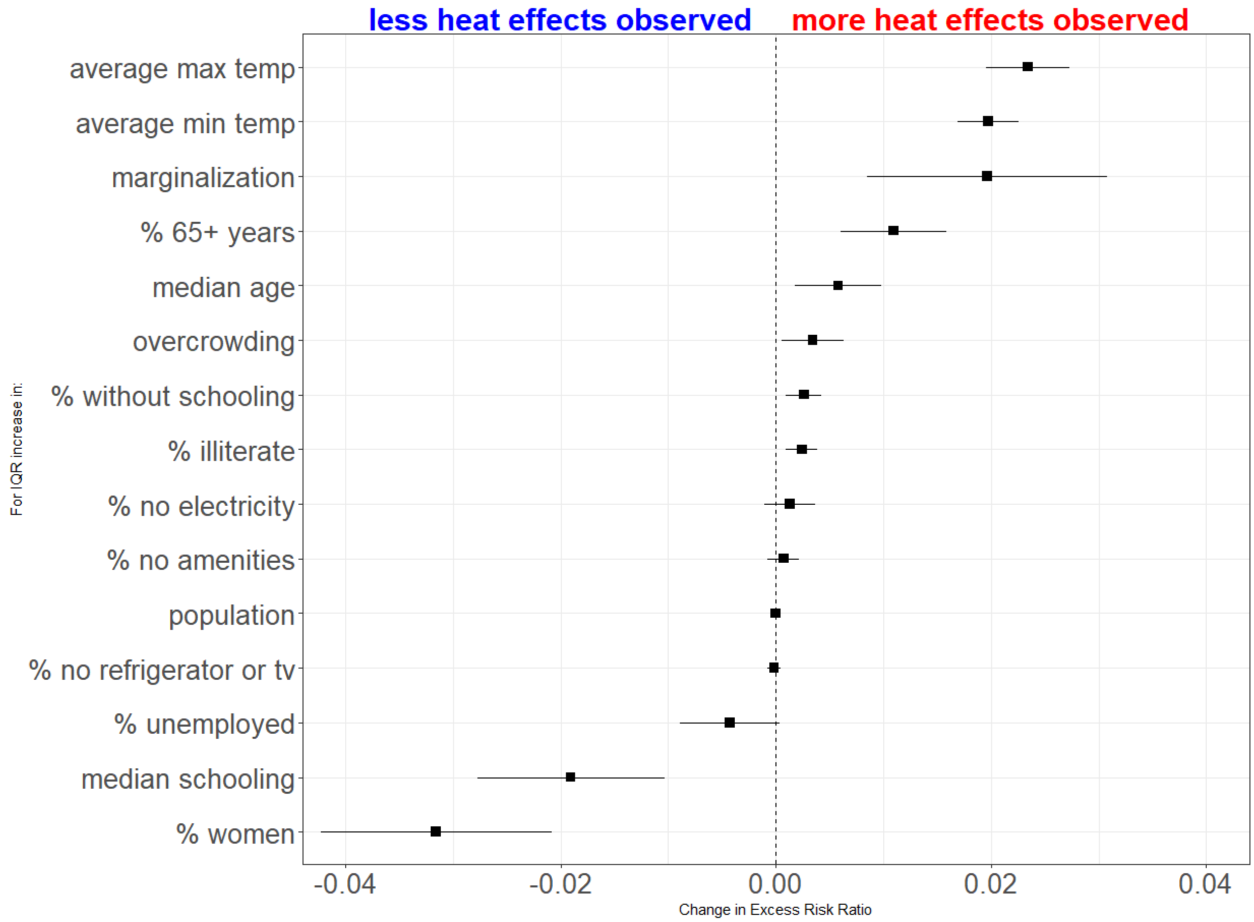


Figure 2.3: Results of meta-regression of the predictors of spatial variation in the effect of daytime extreme heat events (99th percentile maximum temperature) on all-cause mortality across Mexico, 1998-2019.

Supplementary Table 2.1: Age and gender distribution of deaths in Mexico, 1998-2020.

	Number of deaths	% deaths
Age		
<1	695,213	5.18
1-19	47,9640	3.57
20-44	1,770,699	13.19
45-64	3,135,097	23.35
65+	7,279,009	54.21
unspecified	67,273	0.50
Sex		
women	5,891,093	43.88
men	7,528,371	56.07
unspecified	7,467	0.05
Total	13,426,931	100

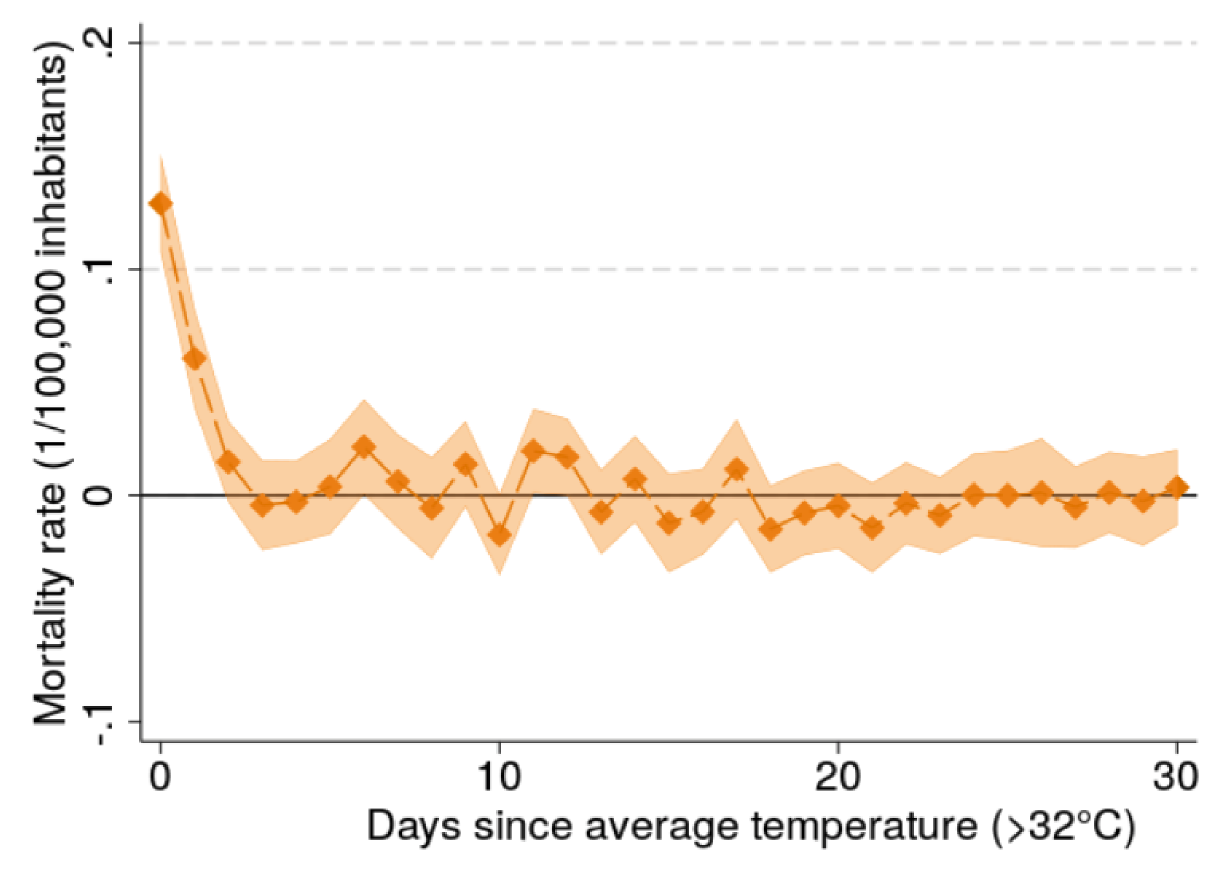
Supplementary Table 2.2: Results of case-crossover analysis of overall effect of extreme heat on mortality for four extreme heat definitions.

Extreme heat	OR	95% CI
99^{th} maximum	1.083	[1.076, 1.09]
95^{th} maximum	1.061	[1.057, 1.064]
99^{th} minimum	1.044	[1.037, 1.05]
95^{th} minimum	1.022	[1.018, 1.025]

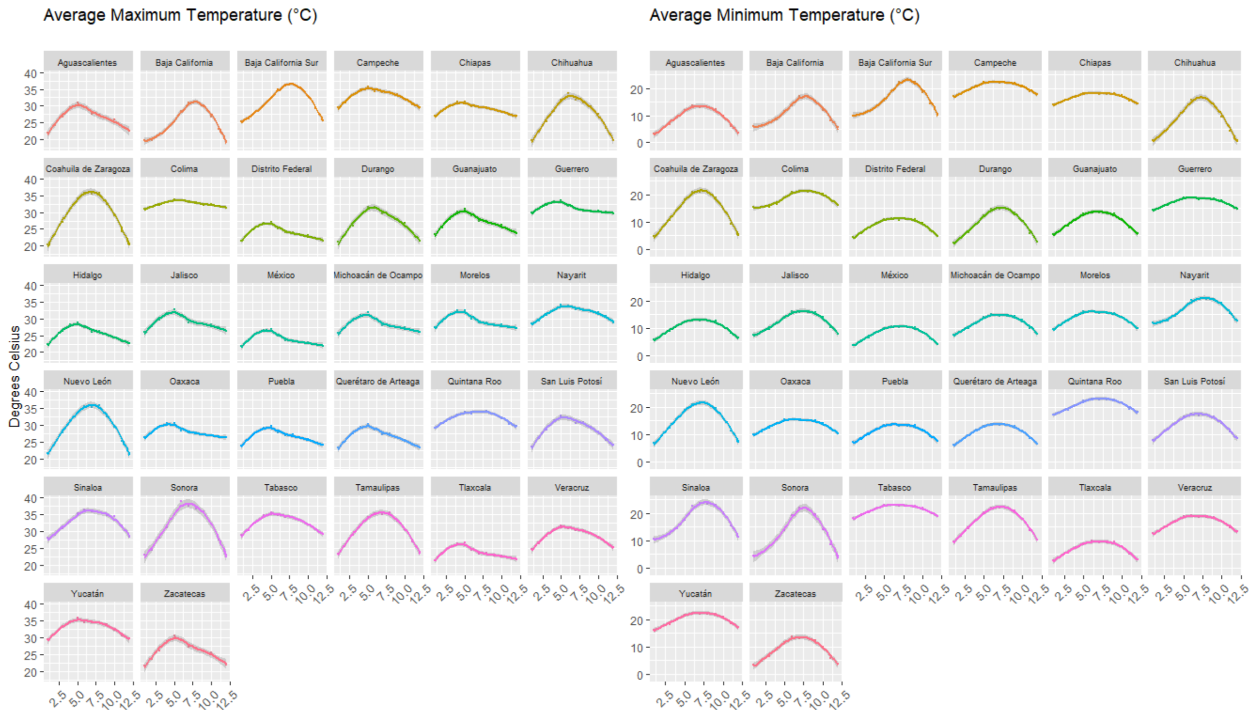
Supplementary Table 2.3: Parameters and results from the Bayesian modeling for various measures of extreme heat in Mexico overall, 1998-2019.

Extreme heat event	Starting parameters			Acceptance rate	ERR (SD)
	phi	Sigma-sq	Tau-sq		
99th maximum	6	0.35	0.42	17.18	0.34 (0.23)
95th maximum	6	0.1	0.14	33.73	0.25 (0.39)
99th minimum	6	0.09	0.14	33.16	0.32 (0.043)
95th minimum	6	0.28	0.5	31.74	0.17 (0.66)

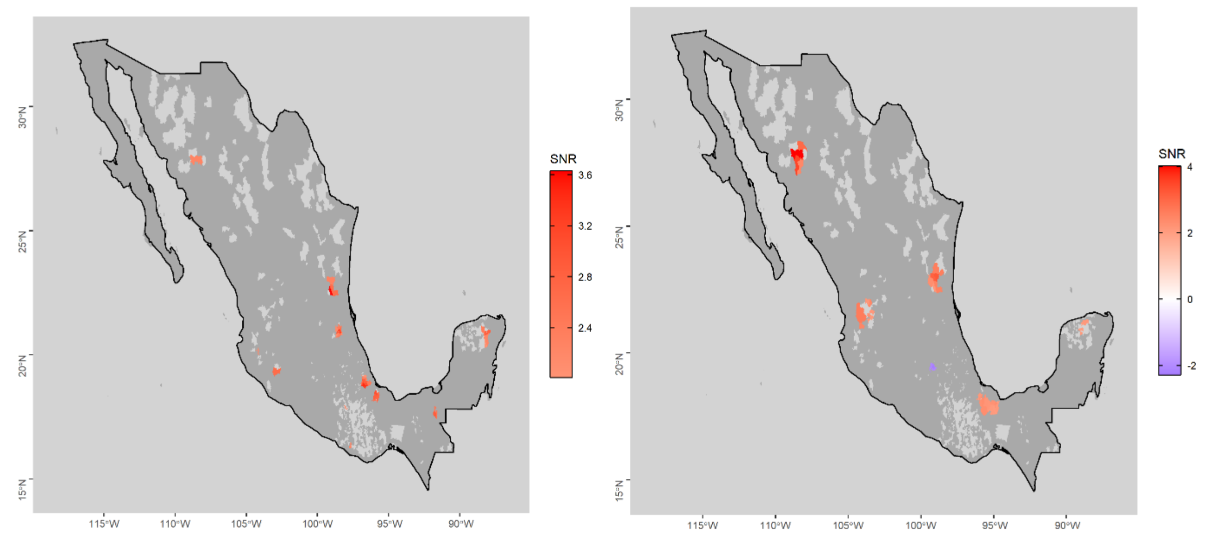
ERR= excess relative risk; SD=standard deviation



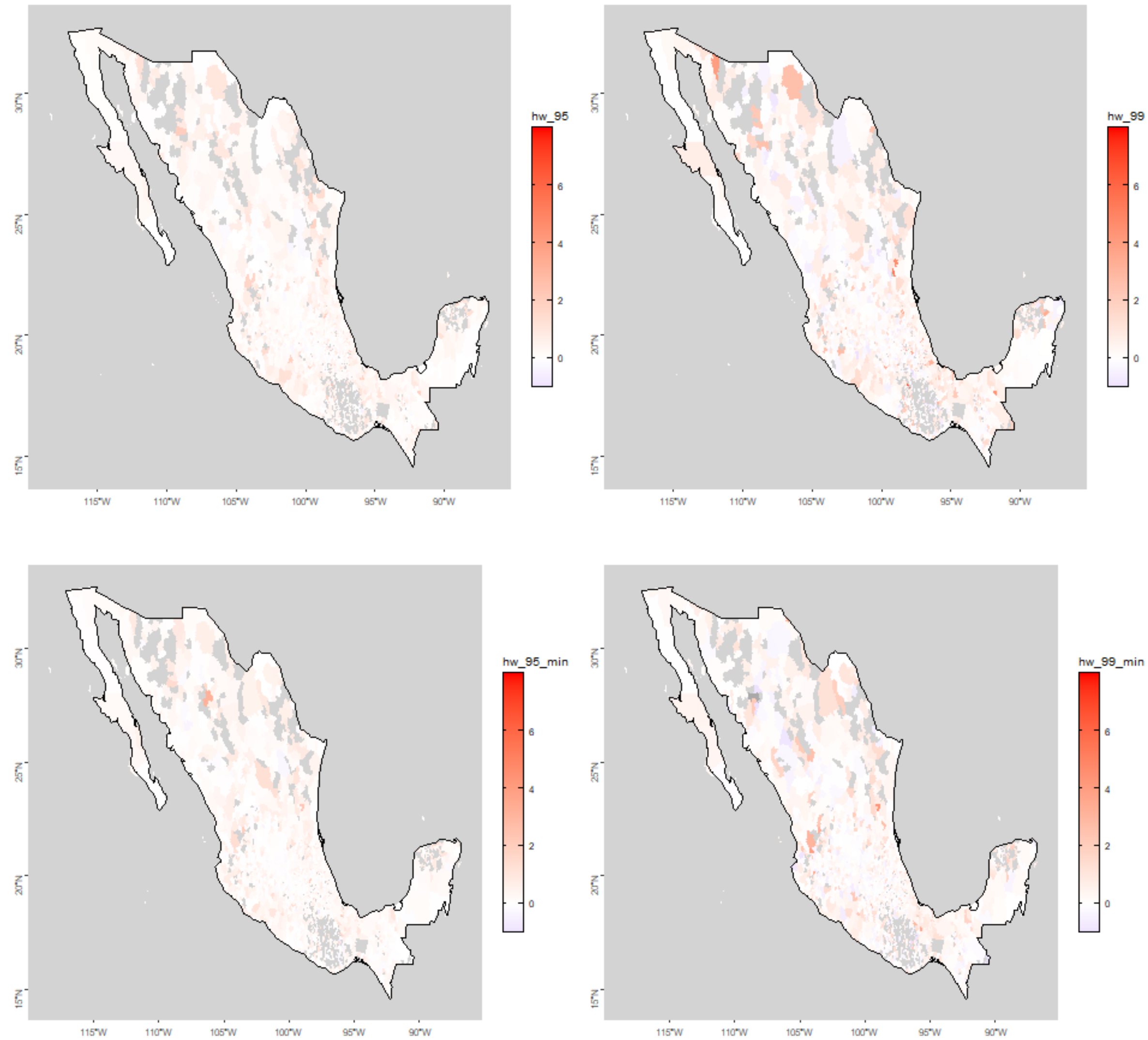
Supplementary Figure 2.1: Lagged effect of hot days (>32°C) on daily mortality rate per 100,000 inhabitants for 31 days estimated for Mexico, 1998-2017 (Cohen and Dechezleprêtre 2022).



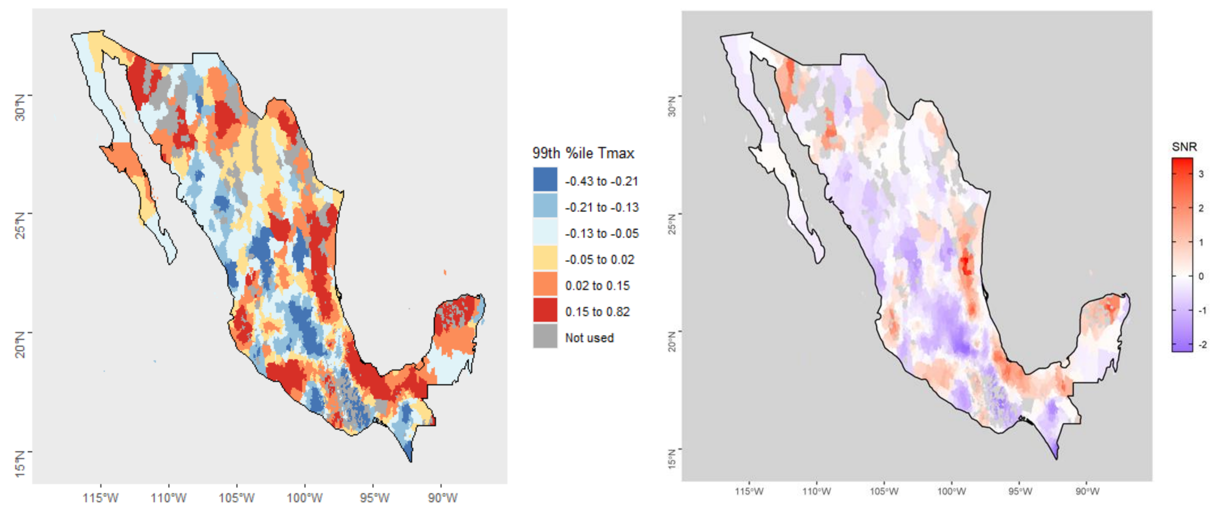
Supplementary Figure 2.2: Average monthly temperature distribution across 32 Mexican states, 1998-2019.



Supplementary Figure 2.3: Results of the municipalities with a precise signal-to-noise (SNR) ratio (|SNR| > 2) of the Bayesian resolved estimates of the effect 99th percentile maximum extreme heat events (left) and 99th percentile minimum extreme heat events (right) on all-cause mortality across Mexico, 1998-2019.



Supplementary Figure 2.4: Results of excess relative risk at municipality level from within community matched design for all four measures of extreme heat (99th max, 95th max, 99th min, 95th min).



Supplementary Figure 2.5: Bayesian resolved estimates for ERR (left) and associated signal-noise ratio (SNR) (right) for sensitivity analysis in Mexico including 2020 in the study period for the 99th percentile maximum temperature measure of extreme heat, 1998-2020.

Chapter 3 : Differential effects of wildfire smoke on cardio-respiratory hospital admissions in the San Diego-Tijuana border region

3.1 Abstract

Exposure to fine particles from wildfire smoke is deleterious for human health and can increase cases of cardio-respiratory illnesses and related hospitalizations. Neighborhood-level risk factors can increase susceptibility to environmental hazards, such as air pollution from smoke, and the same exposure can lead to different health effects across populations. While the San Diego-Tijuana border can be exposed to the same wildfire smoke event, socio-demographic differences may drive differential effects on population health. We used the October 2007 wildfires, one the most devastating wildfire events in Southern California that brought smoke to the entire region, as a natural experiment to understand the differential effect of wildfire smoke on both sides of the border. We applied synthetic control methods to evaluate the effects of wildfire smoke on cardio-respiratory hospitalizations in the Municipality of Tijuana and San Diego County separately. During the study period (October 11th- October 26th, 2007), 2009 hospital admissions for cardio-respiratory diseases occurred in San Diego County while 37 hospital admissions were reported in the Municipality of Tijuana. The number of cases in Tijuana was much lower than in San Diego, and a precise effect of wildfire smoke was detected in San Diego but not in Tijuana. However, social drivers can increase susceptibility to environmental hazards; the poverty rate in Tijuana is more than three times that of San Diego. Socio-demographics are important in modulating the effects of wildfire smoke and can be potentially useful in developing a concerted regional effort to protect populations on both sides of the border from the adverse health effects of wildfire smoke.

3.2 Introduction

The length, intensity, and severity of wildfires have increased under climate change (Goss, Swain et al. 2020) with record-breaking events occurring frequently in recent years. This contributes to high air pollution levels; the worst air quality in decades has been observed in Western North America in recent years due to raging wildfires (EPA 2020). Smoke plumes can extend far beyond the wildfire's perimeter and cause unhealthy air quality for neighboring cities, states, and even countries (Brey, Ruminski et al. 2018). While borders are a physical barrier to human mobility, they provide no obstruction to the transport and flow of fine airborne particles; wildfire smoke can move freely, harming the health of residents on both sides.

The San Diego-Tijuana border (western coast of United States and Mexico) is a unique context to study the health effects of wildfire smoke due to its meteorological and socio-demographic characteristics. The region has been highly affected by climate change; in the Western US, the amount of forest area burned from wildfires was found to be more than 10 times greater from 2003-2012 than it was in 1973-1982 (Westerling 2016). Furthermore, precipitation is expected to decrease by 50% in Southwest California and up to 75% in Baja California (Vaghefi, Abbaspour et al. 2017), increasing the risk of future wildfires in an already water-deprived region. San Diego and Tijuana cities are each located less than 20 miles from the border and less than 25 miles from each other so wildfires starting in either country may produce smoke that reaches both sides of the border. San Diego and Tijuana are two major cities and make up the largest border region shared between the US and Mexico and the fourth-largest in the world (Mendoza and Dupeyron 2020). San Diego County was estimated to have a population of 3 million while the Municipality of Tijuana was home to 1.6 million residents according to the 2010 census in each country (INEGI 2010, Census Bureau 2011). The region's susceptibility to climate impacts and high population density separated by an international border makes it a unique context to explore the differential public health manifestation of wildfire smoke.

Fine particulate matter ($PM_{2.5}$), one of the main components of wildfire smoke (Reid, Brauer et al. 2016), is composed of inhalable particles that produce harmful health effects (Berger, Malig et al. 2018, Yang, Ruan et al. 2019). $PM_{2.5}$ are particles under 2.5 microns in aerodynamic diameter that are small enough to go deep into the lungs and even enter the bloodstream and are consistently associated with increases in cardio-respiratory hospitalizations (Valavanidis, Fiotakis et al. 2008, Liu, Pereira et al. 2015, Chen, Samet et al. 2021). Additionally, in California, wildfires account for 50% of total primary $PM_{2.5}$ emissions, and this percentage is increasing in the context of climate change (Ford, Val Martin et al. 2018). Furthermore, wildfire-specific $PM_{2.5}$ is more harmful to respiratory hospital admissions than non-wildfire $PM_{2.5}$ in Southern California (Aguilera, Corringham et al. 2021). Previous research on the effect of the 2007 San Diego wildfires on Medi-Cal emergency department hospitalizations showed a 34% increase in respiratory visits and 112% in asthma-specific diagnoses during the peak fire period (Hutchinson, Vargo et al. 2018) and a pronounced spatial heterogeneity in health effects was observed across San Diego County (Aguilera, Hansen et al. 2020). Not all populations are equally susceptible to the effects of wildfire smoke, yet there is a scarcity of evidence of these impacts for populations living in low and middle-income contexts (Marlier, Crnosija et al. 2022).

Although Tijuana and San Diego are close in proximity, they have contrasting socio-demographic profiles which may be important in driving differential susceptibility to wildfire smoke effects on health. SES is well documented as an effect modifier in the association between air pollution and various health effects (Cakmak, Hebbern et al. 2016, Chi, Hajat et al. 2016, O'lenick, Winquist et al. 2017). Socio-economic factors may increase susceptibility to air pollution impacts by increasing the risk of other conditions such as asthma and/or affecting development and resistance to other disease threats (Neidell 2004). A study conducted in North Carolina (US) estimated that counties with a higher poverty level had twice the risk of having an emergency department visit following exposure to wildfire smoke than counties with decreased poverty levels (Rappold, Cascio et al. 2012). The same study showed that income inequality is a risk factor for increased emergency department visits due to smoke exposure (Rappold, Cascio et al. 2012).

Neighborhood-level risk factors faced by those living in low-income neighborhoods may increase their susceptibility to environmental hazards (Clougherty and Kubzansky 2009). Stressors, such as crime, noise, and traffic can lead to acute and chronic changes in the functioning of body systems and increase the effect of exposures such as wildfire smoke (Chi, Hajat et al. 2016). Therefore, population-specific estimates of the epidemiological effects of wildfire smoke are critical in understanding its role in exacerbating adverse health outcomes and can contribute to informing preparedness and response to this increasingly prevalent environmental health hazard. We capitalize on a unique natural experiment in which smoke affected the entire San Diego-Tijuana region to assess if the same wildfire event differentially impacted the two socio-economically diverse communities. Although there are many studies estimating the health effects of wildfire smoke in San Diego and Southern California, to our knowledge no research has investigated these effects in Tijuana or Baja California (Mexico).

This study aimed to understand the differential effect of wildfire smoke on cardio-respiratory hospitalizations in San Diego and Tijuana, using the October 2007 wildfires as a case study. The October 2007 wildfires involved about 30 wildfires that began around October 20th in the Southern California coastal region, with the largest area burned concentrated in San Diego County, including areas surrounding the international border (Ruben Grijalva 2009). These extreme wildfire events were mainly driven by severe drought and unusually strong SAWs and, at the time, were considered one the most devastating wildfire events in the history of California. To this day, the largest wildfire during the October 2007 events (Witch Fire) remains the second most destructive fire in Southern California (Sönnichsen 2022). The San Diego-Tijuana region was completely covered by smoke starting October 21st, 2007. As smoke produced from wildfires in the Southern California-Baja California area can affect populations in the entire region, understanding the burden of these events is critical in addressing this global health concern.

3.3 Methods

3.3.1 Study context

The San Diego-Tijuana border region is between a Mediterranean and semi-arid climate (Peel, Finlayson et al. 2007). Most of the annual precipitation occurs in the winter, from November to March, and is subject to high variability, driving increasingly frequent droughts and floods (Wilder, Garfin et al. 2013). The region is affected by Santa Ana winds (SAWs), dry down-sloping winds rooted in cold air masses over the elevated Great Basin, which affect the region primarily between September and May (Guzman-Morales and Gershunov 2015). SAWs are linked to the ignition and spread of wildfires, and spreading the smoke burden during these events (Aguilera, Gershunov et al. 2020). The October 2007 wildfires were a large record-breaking event, which ignited thirteen different wildfires from Los Angeles to Tijuana; this was exacerbated by SAWs (Petersen 2011). This event as well as other more recent wildfires in the region highlight the vulnerability of the region to this climatic threat. The area has experienced many major wildfire events in recent years, and this is projected to continue increasing in the context of climate change.

Numerous studies have been conducted to understand the epidemiological effects of extreme heat and wildfire smoke on California as a whole (Ebi, Exuzides et al. 2004, Ostro, Roth et al. 2009, Guirguis, Gershunov et al. 2014, Aguilera, Corringham et al. 2021) and in San Diego specifically (Guirguis, Basu et al. 2018, Hutchinson, Vargo et al. 2018, Aguilera, Hansen et al. 2020). Contrastingly, little to no research has been conducted in Tijuana or Baja California to understand these impacts. The proximity of these cities and the discrepancy in available evidence on this topic highlights the need to find strategies to adapt research tools and methods to each context; understanding the impacts of extreme weather events in regions with limited epidemiological data will become increasingly important.

In San Diego and California, it has been well established that wildfire smoke drives adverse health outcomes (Kunzli, Avol et al. 2006, Richardson, Champ et al. 2012, Kochi, Champ et al. 2016, Reid, Jerrett et al. 2016, Aguilera, Hansen et al. 2020, Aguilera, Corringham et al. 2021, Heaney, Stowell et al. 2022). An evaluation of the health effects of a major wildfire event that occurred in Southern California in 2003 showed increased eye and respiratory symptoms, medication use, and physician use for children in communities in Southern California (Kunzli, Avol et al. 2006). Recent work in Southern California has shown that PM2.5 from wildfire smoke can drive up to 10 times more respiratory hospitalizations than non-wildfire PM2.5 (Aguilera, Corringham et al. 2021). A study specific to San Diego County found a 30% (95% CI: 26.6% to 33.4%) increase in emergency and urgent care visits at Rady's Children's Hospital network for each 10-unit increase in PM2.5 from wildfire smoke (Aguilera, Corringham et al. 2021). A study evaluating the economic impact of the 2007 wildfires showed that it drove medical costs by over $3.4 million (Kochi, Champ et al. 2016). These are a few of the numerous studies in San Diego and California that demonstrate the health impacts of wildfire smoke and highlight the need to inform policies to limit the harmful effects of this exposure.

The strong health effects of wildfire smoke observed in San Diego County indicate the need to understand and reveal and compare these impacts in Tijuana. Studying these effects in Tijuana is critical to informing early warning systems and addressing this research gap. Ideally, forecasting systems for wildfire smoke will consider environmental risk factors on both sides of the border and inform warning systems and action plans to protect populations in the entire region.

3.3.2 Overview of analytical strategy

To consider the effect of wildfire smoke on cardio-respiratory hospitalizations, synthetic control methods (Bouttell, Craig et al. 2018, Schwarz, Dimitrova et al. 2022) were applied, capitalizing on the timing of the wildfire as a natural experiment. Although these methods were first developed for econometrics, they have recently been applied to study the effects of acute environmental stressors such as wildfire smoke (Schwarz, Dimitrova et al. 2022, Sheridan, McElroy et al. 2022). Synthetic control methods use the trend in the outcome in the "treated" unit or in this case the geographic region exposed to wildfire smoke, to identify and weight control units that can represent a counterfactual trend of what would have happened if the wildfire smoke had not occurred in the region. The benefit of this approach is that it capitalizes on the temporality of the treatment or wildfire event to compare the pre-treatment and post-treatment hospitalization count by estimating what would have occurred if the wildfire smoke had not hit the region through the identification of synthetic controls. The trend in hospitalizations is then followed after the treatment and any difference between the treated unit and its synthetic control can be attributed to the wildfire smoke. The Municipality of Tijuana and the County of San Diego were the two treated units of interest, while all municipalities in Mexico without wildfire smoke during this period were considered as potential controls for Tijuana, and other counties in California without wildfire smoke during this period were considered as potential controls for San Diego. Two analyses were conducted considering San Diego County and the Municipality of Tijuana separately. The pre-treatment period used to identify the control units was 10 days before the wildfire smoke began to give sufficient days to identify a trend in hospitalization counts. The outcome was followed for 6 days from the first day of the wildfire smoke exposure (October 21st, 2007) to consider the full duration of smoke days above the 30th percentile on both sides of the border.

3.3.3 Data sources

The Hazard Mapping Smoke (HMS) product of the National Oceanic and Atmospheric Administration (NOAA) was used to identify smoke plumes for all California counties and Mexican municipalities during the study period (October 11th- October 26th, 2007). This product applied algorithms from visible imagery from various satellites to identify smoke plumes and was revised and modified by trained analysts (NOAA 2020). In our main analysis, any day for which 30% or more of a county or municipality was covered in smoke was considered to be exposed and any potential control with an exposed day during the study period was not eligible; sensitivity analyses were also run considering 20%, 50%, and 70% smoke plume coverage. Visualization of satellite imagery for the border region was obtained from the National Aeronautics and Space Administration Worldview visualization tool (NASA 2021).

Data on cardio-respiratory hospital admissions for California were obtained from the Office of Statewide Health Planning and Development Patient Discharge Data now renamed to the California Department of Health Care Access and Information Patient Discharge Data (OSHPD 2020). For Mexico, data on cardio-respiratory hospital admissions were obtained from the Mexico Secretary of Health (Mexico 2020). Any hospital admission with a primary diagnosis code for diseases of the circulatory system (ICD-9: 390-459, ICD-10: I00-I99) and diseases of the respiratory system (ICD-9: 460-519; ICD-10: J00-J99) based on the International Classification of Diseases, Ninth, and Tenth Revision were considered (DiSantostefano 2009, Control and Prevention 2014). Although the population of the Municipality of Tijuana is much smaller than San Diego County (1.6 million vs. 3 million), the hospitalization rate remains much higher in San Diego with an average daily case of 40.6 per million during the study period and 1.4 cases per million in Tijuana (Table 3.1). The hospitalization rate almost 30 times higher in San Diego is driven by differences in the quality and generalizability of the data sources. While the data from San Diego is comprehensive of all patients admitted to hospitals in the County, the data from Mexico comprises only patients admitted at hospitals administered by the public sector through the Secretary of Health (Dantés, Sesma et al. 2011). This limits the generalizability of our findings in Tijuana, and we are limited by the availability of health data. To our knowledge, this is the only available dataset that included the date of admission, required for this analysis. A daily hospital admission count was estimated for each county and municipality and a two-day rolling average was estimated to increase smoothness in the trend when identifying suitable controls.

3.3.4 Analysis

Hospitalization counts using 2-day rolling averages were used to identify and estimate the synthetic controls using the pre-treatment period (October 11^{th}-20^{th}); synthetic control methods account for population size by identifying municipalities/counties with similar baseline hospitalization counts. All municipalities in Mexico with 0 hospitalizations during the study period were excluded. All municipalities and counties with any level of smoke exposure during the study period were excluded as potential controls. A parametric generalized synthetic control approach was applied which imputes counterfactuals for each San Diego and Tijuana with eligible control groups using a linear interactive fixed effects model with unit-specific intercepts (Xu, Liu et al. 2021, Sheridan, McElroy et al. 2022). Synthetic control methods then follow the trend and compute an average treatment effect in the treated (ATT) by estimating a difference between the treated units and its synthetic controls for 5 days following the start of smoke exposure (October 21st-26th, 2007). Confidence intervals were estimated using bootstrapping with 500 runs and visualized at an alpha=0.05. A percentage increase in hospitalizations attributable to wildfire smoke was estimated by taking the ATT and dividing it by the average hospitalization count for the treated unit in the pre-treatment period; due to differences in the data being used in Tijuana and San Diego, this relative change was thought to be a more suitable comparison. A sensitivity analysis was conducted including mean temperature as a covariate estimated from the Oregon State University PRISM Climate Group for California counties using population-weighted centroids and an average of population-weighted daily minimum and maximum temperature estimated using Daymet V4 product and WorldPop for Mexican municipalities (Tatem 2017, PRISM 2020, Thornton, Shrestha et al. 2022). Another sensitivity analysis was conducted including municipalities that had any day with zero hospitalizations during the study period. All analyses were conducted using R 4.1.0 analytical software (R Core 2022). All shareable data and codes are provided in the following repository: https://github.com/benmarhnia-lab/border_smoke_cardio_resp.

3.4 Results

During the study period (October 11th-October 26th, 2007), there were 2009 hospital admissions in San Diego County, 1215 for circulatory diagnoses and 794 for respiratory diagnoses. In contrast, the Municipality of Tijuana had only 37 hospital admissions, 21 of which were for cardiovascular diagnoses and 16 for respiratory diseases. The hospitalization rate is higher in the after-smoke period than the before-smoke period in both San Diego and Tijuana (Table 3.1). Age and gender distribution of hospitalizations are shown in Supplementary Table 3.1.

Wildfire smoke from the various 2007 Southern California wildfires (including the Witch, Harris, Poomacha, and Rice wildfires in San Diego County) started impacting the San Diego-Tijuana region on October 21st, 2007. Perimeters of the wildfires are shown in Supplementary Figure 3.1. On October 25th, the entire County of San Diego and Municipality of Tijuana were fully covered by smoke exposure according to the HMS smoke plumes (Figure 3.1). In California, 17 counties had no days with 30% smoke coverage during the study period and were eligible as potential controls. In Mexico, 76 municipalities were eligible as potential controls for Tijuana after excluding any municipality with zero hospitalizations for any day during the study period.

The generalized synthetic control estimated a suitable counterfactual trend for both San Diego and Tijuana with an average of less than 9 hospital admissions difference for San Diego and less than 1 case difference for Tijuana during the pre-treatment period (Supplementary Table 3.2). Control units and their weights from the generalized synthetic control approach are provided in Supplementary Table 3.3. An increase in hospitalizations was observed following wildfire smoke exposure in both San Diego and Tijuana, although a precise effect was only observed in San Diego and no effect was observed in Tijuana (Figure 3.2, Supplementary Figure 3.2). Results from sensitivity analyses considering varying percentages of smoke coverage and exposure levels showed similar results (Supplementary Figure 3.3). The ATT and 95% confidence interval on the absolute scale were 19.75 [17.69, 21.81] daily cases in San Diego and 1.08 [-6.87, 9.02] in Tijuana for the six days following the beginning of the wildfire smoke exposure (Table 3.2). When including temperature as a covariate, similar results were observed with a precise effect of smoke in San Diego but no effect was observed in Tijuana (Supplementary Figure 3.4). For the sensitivity analysis in Tijuana including municipalities with zero cases on any day during the study period, similar results were observed (Supplementary Figure 3.5).

3.5 Discussion

While the San Diego-Tijuana border is a delineator for differing economic and social conditions, the October 2007 wildfires that started in California brought damaging smoke exposure to populations residing on both sides. Capitalizing on the random timing of the start of wildfire smoke and its spread to the entire border region, we applied synthetic control methods to explore the role of wildfire smoke in driving adverse cardio-respiratory health effects. We observed a positive ATT for the effect of wildfire smoke on cardio-respiratory hospitalizations in both San Diego and Tijuana (Figure 3.2). The effect, however, differed on each side of the border; while San Diego showed a precise effect of wildfire smoke, we could not confirm an effect of wildfire smoke in Tijuana at the 95% confidence level although results suggest an increase in hospitalizations following smoke exposure (Supplementary Figure 3.2).

These results indicated a differential susceptibility to the effects of wildfire smoke. The social context of San Diego and Tijuana differ- in 2010, the poverty rate was 3 times higher in

Tijuana than in San Diego while the percentage of the population with a high school education was 3 times higher in San Diego according to the 2010 census in both countries (Table 3.1). Socio-demographics including lower education and employment rates have been shown to increase vulnerability to environmental hazards such as air pollution, as people with higher educational attainment may have higher income, improved access to healthcare, and may have improved knowledge to manage health risks (O'Neill, Bell et al. 2008). Furthermore, the GDP of San Diego County was over $170,000 million while it was just over $26,000 million for the entire state of Baja California Norte in 2010 (Mendoza and Dupeyron 2020); this could also play a role in accessibility to economic and healthcare services. Additionally, Tijuana has one of the highest crime rates for cities in Mexico, which may contribute to increased social vulnerability (Arredondo, Orozco et al. 2018). Other harmful environmental exposures such as higher traffic-related pollution can also increase susceptibility to wildfire smoke, which is highly relevant in this region where traffic-related pollution is high due to idling vehicles at the border (Quintana, Khalighi et al. 2018). Although social conditions are hypotheses for which differing effects could be observed, additional research would have to consider the role of social vulnerability to confirm this as a proposed mechanism in the context of wildfire smoke.

When considering the percentage change in hospitalizations following wildfire smoke exposure, the relative increase in hospitalizations in Tijuana was greater than observed in San Diego, with an increase six times higher although no effect was detected at the 95% confidence level (Table 3.2). Lower SES increases the effect of air pollution on various health outcomes (Cakmak, Hebbern et al. 2016, Chi, Hajat et al. 2016, O'lenick, Winquist et al. 2017), and many socioeconomic factors could be driving an increased susceptibility in Tijuana. The poverty rate of Tijuana is more than three times that of San Diego and less than 25% of the population in

Tijuana have completed a basic education, while this percentage is more than three times higher in San Diego at 88% (Table 3.1). The unemployment rate, however, is higher in San Diego, but this is driven by the strong manufacturing industry in Tijuana that provides employment opportunities for residents of the border region (Mendoza and Dupeyron 2020). Not only do Mexico and the US have differing socio-economic profiles at the national level, but even within each country, inequality intensifies. Out of all cities in Mexico, Tijuana is ranked to have the fourth worst quality of life index based on geographical, environmental, and social factors (Gallardo Del Ángel 2017). In contrast, San Diego is ranked one of the richest cities in the US (Rawes 2015). The socio-economic differences are likely playing an important role in the potential increased susceptibility to wildfire smoke in Tijuana, although the data quality challenged the ability to detect a precise effect of smoke in this analysis.

Interestingly, we observe a drop in the 2-day moving average of cardio-respiratory hospitalizations immediately succeeding the start of the wildfire smoke followed by a steep increase in both San Diego and Tijuana. One possible reason for this could be that there are behavioral changes related to the onset of a high smoke episode that could increase the protection of the population from air pollution and other hazards but which do not last more than one or two days. The implications of this immediate decrease should be further explored to investigate what specific actions and information are the most effective in protecting individuals from wildfire smoke.

There are many actions that can be activated in the context of a wildfire smoke event and may be harmonized in a border region to best protect population health. Warning systems to forecast wildfire smoke exposure have the potential to decrease its burden; smoke-related public health messaging to stay indoors can prioritize at-risk populations (Fish, Peters et al. 2017).

Although there is a need for more research to evaluate the effectiveness of these measures on protecting population health, understanding which characteristics make a neighborhood or area susceptible to the effects of wildfire smoke is critical to the activation of any intervention to maximize public health benefits. Additionally, this could be a factor in explaining the differential impacts observed as residents of San Diego County were likely notified of the wildfire events from evacuation warnings and advisories while Tijuana may have not received information, since fires were burning primarily on the US side of the border. This highlights the need for harmonized warning systems to protect populations from the health effects of this exposure. Although programs for transborder collaboration have been implemented, unfortunately, they usually lack institutionalization and long-term continuity (Ganster and Collins 2017). Mechanisms should be formalized to jointly develop and implement actions between agencies in both San Diego and Tijuana to implement a binational response to environmental health hazards such as wildfire smoke. For example, the California-Baja California 2019-2020 Border 2020 Action Plan includes a Joint Contingency Plan for environmental response to chemical hazardous substances; the mechanisms put in place with this program could be adapted to respond to wildfire smoke events (EPA 2020).

As neither San Diego nor Tijuana has an established early warning system or action plan to protect populations during wildfire smoke events, there are many potential avenues to increase preparedness and response to these events (Cunha 2019). Forecast systems for SAWs have been shown to be accurate for a 6-7 day lead time which can be useful in the prediction of periods of high wildfire risk (Jones, Fujioka et al. 2010). Wildfire and heat wave forecasting systems could be used by policymakers to develop and implement actions to limit the morbidity and mortality attributable to extreme weather in this region. Integrated early warning systems could use local environmental measures and social information to protect public health on both sides of the border by taking into account local vulnerability to these events.

There is a major disparity in evidence that we observe on a global scale with the majority of evidence on the epidemiological effects of wildfire smoke coming from the US and Australia (Liu, Pereira et al. 2015) and very few studies estimating these effects in low and middle-income countries (Marlier, Crnosija et al. 2022). Unfortunately, the limited data accessibility and quality are one of the drivers for the little evidence coming from low and middle-income countries. Poor data quality and availability are often a barrier to health research in these regions; lack of data standards can further contribute to this challenge (Li, Brodsky et al. 2018). Although data from resource-constrained regions may be more limited, studying the effects of wildfire smoke in these settings is critical to understanding and addressing these impacts.

It is important to interpret the findings of this research in light of certain limitations. First, there could be some exposure misclassification as the hazard mapping tool used to identify smoke plumes does not differentiate between smoke at the ground level and smoke higher up in the troposphere. Also, smoke coverage percentages are considered a proxy for the population exposure, therefore exposure misclassification may remain. However, previous studies estimating wildfire-specific $PM_{2.5}$ in San Diego County confirmed high levels of particulate matter from wildfires during this period indicating that exposure misclassification may be minimal during this particular event (Aguilera, Luo et al. 2023). Also, it is important to consider that Tijuana and San Diego have differing population structures and San Diego County has an older population demographic than the Municipality of Tijuana. It is also important to note that there may be cross-border healthcare seeking in a border context that could alter the number of patients on either side of the border; it has been shown that many immigrants return to Mexico to seek out healthcare

(Raudenbush 2021), which could affect our datasets and findings. A study evaluating these health-seeking behaviors on both sides of the border would be valuable to contextualize our findings but this is beyond the scope of this work. Lastly, the hospitalization data in Tijuana is not generalizable, limiting the potential conclusions and comparisons that can be drawn from this analysis. As the hospitalization dataset from Mexico is from the public health system, it may be biased as the population served may be more susceptible. However, we felt this analysis was valuable using the available data even if it is not the ideal comparison.

Although the socio-demographic contexts of San Diego and Tijuana are very different, it is important to consider these two cities as one border region that undergoes similar climate challenges that will continue to be exacerbated under climate change. The importance of developing a concerted effort to protect populations on both sides of the border from these adverse health effects will become increasingly critical. Wildfires will continue to ignite and spread to the region with more frequency and severity (Black, Tesfaigzi et al. 2017). There is a strong need for policy-relevant evidence to inform interventions to protect populations in regions such as the San Diego-Tijuana border that are highly vulnerable to wildfires.

In conclusion, these results can be used to understand how the effects of environmental exposures can differ across a socio-demographically diverse border region. This approach highlights how we can capitalize on binational contexts to explore the differential effects of environmental health risks that spread beyond borders. We hope that this can be applied to other border regions to continue to explore what drivers increase susceptibility to environmental health hazards.

Chapter 3, in full, has been submitted for publication of the material as it may appear in PLOS Global Public Health. Lara Schwarz, Rosana Aguilera, L.C. Aguilar-Dodier, Javier

Emmanuel Castillo Quiñones, María Evarista Arellano García, Tarik Benmarhnia. “Wildfire smoke knows no borders: differential vulnerability to smoke effects on cardio-respiratory health in the San Diego-Tijuana region.” The dissertation author was the primary researcher and author of this paper.

Table 3.1: Descriptive statistics of the study population and hospital admission characteristics for the Municipality of Tijuana and County of San Diego before and after the wildfire smoke event, October 11th-26th, 2007.

	San Diego (SD) County		Municipality of Tijuana (TJ)	
Total population (2010 census)	3,095,313		1,603,955	
Poverty rate (2010 census)	9.5%		32.8%	
Education high school graduate or higher[a]	88%		16.7%	
Unemployment rate (2010 census)	10.8%		2.4%	
Gross Domestic Product (in million dollars)	171,568		26,721[b]	
Hospital admissions	**Before smoke (Oct 11th-20th)**	**After smoke (Oct 21st-26th)**	**Before smoke (Oct 11th-20th)**	**After smoke (Oct 21st-26th)**
Daily average hospitalization count	117.5	143.4	1.5	4.2
Hospitalization rate (per million)	37.9	46.3	0.9	2.6

[a]SD: age 25+, TJ: age 18+
[b]in the entire state of Baja California

Table 3.2: Results of synthetic control method showing the change in the average treatment effect in the treated (ATT) on cardio-respiratory hospitalizations in San Diego and Tijuana from the onset of smoke exposure in October 2007.

	San Diego (SD) County	**Municipality of Tijuana (TJ)**
Relative (%) change in ATT from smoke exposure overall	10	60.1
Absolute change in ATT and 95% confidence interval	19.75 [17.69, 21.81]	1.08 [-6.87, 9.02]
Absolute change in ATT per million	6.38	0.67

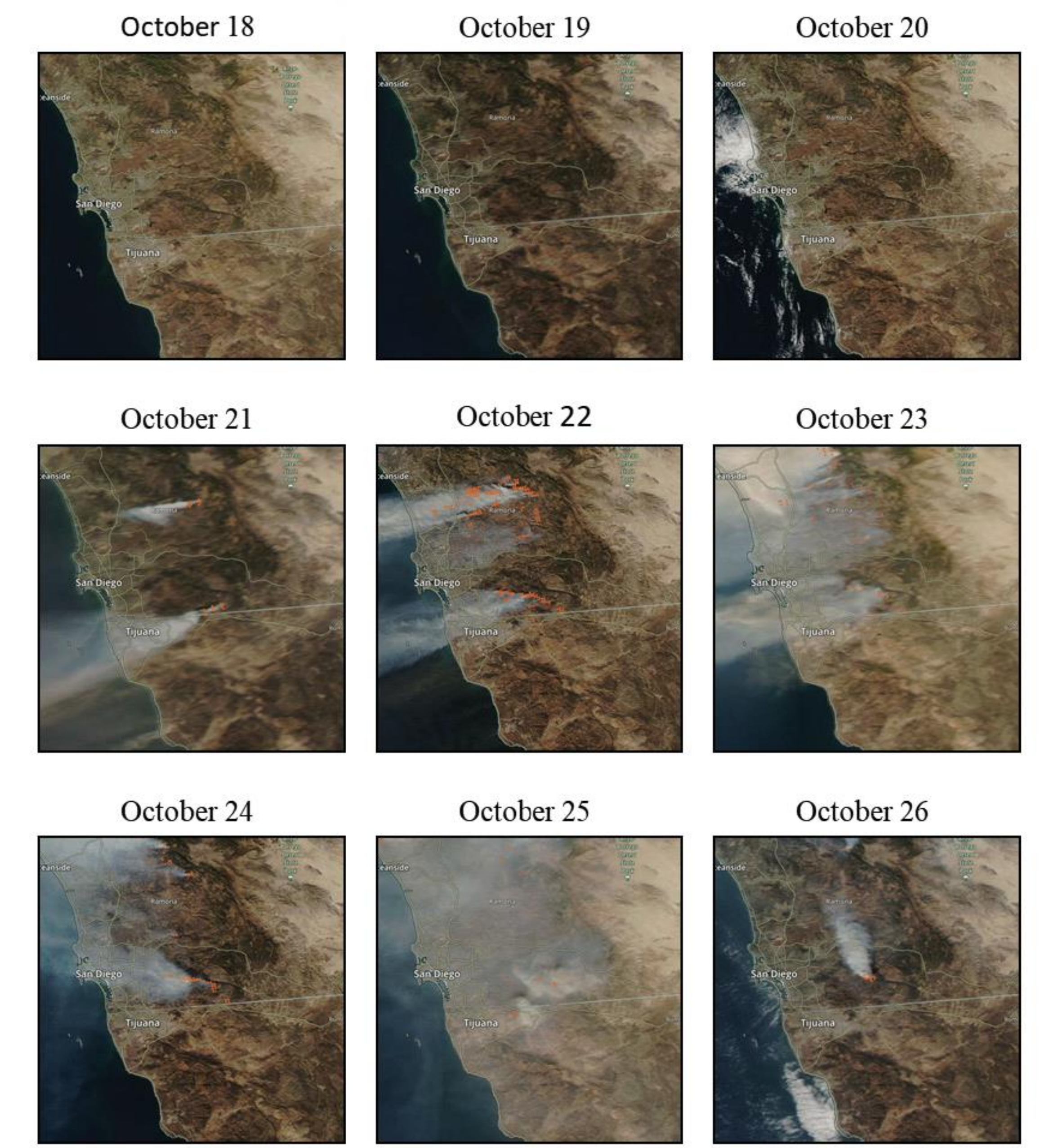


Figure 3.1: Map of San Diego Tijuana border region showing smoke plumes when smoke started covering the region during the study period (October 18th-26th, 2007).

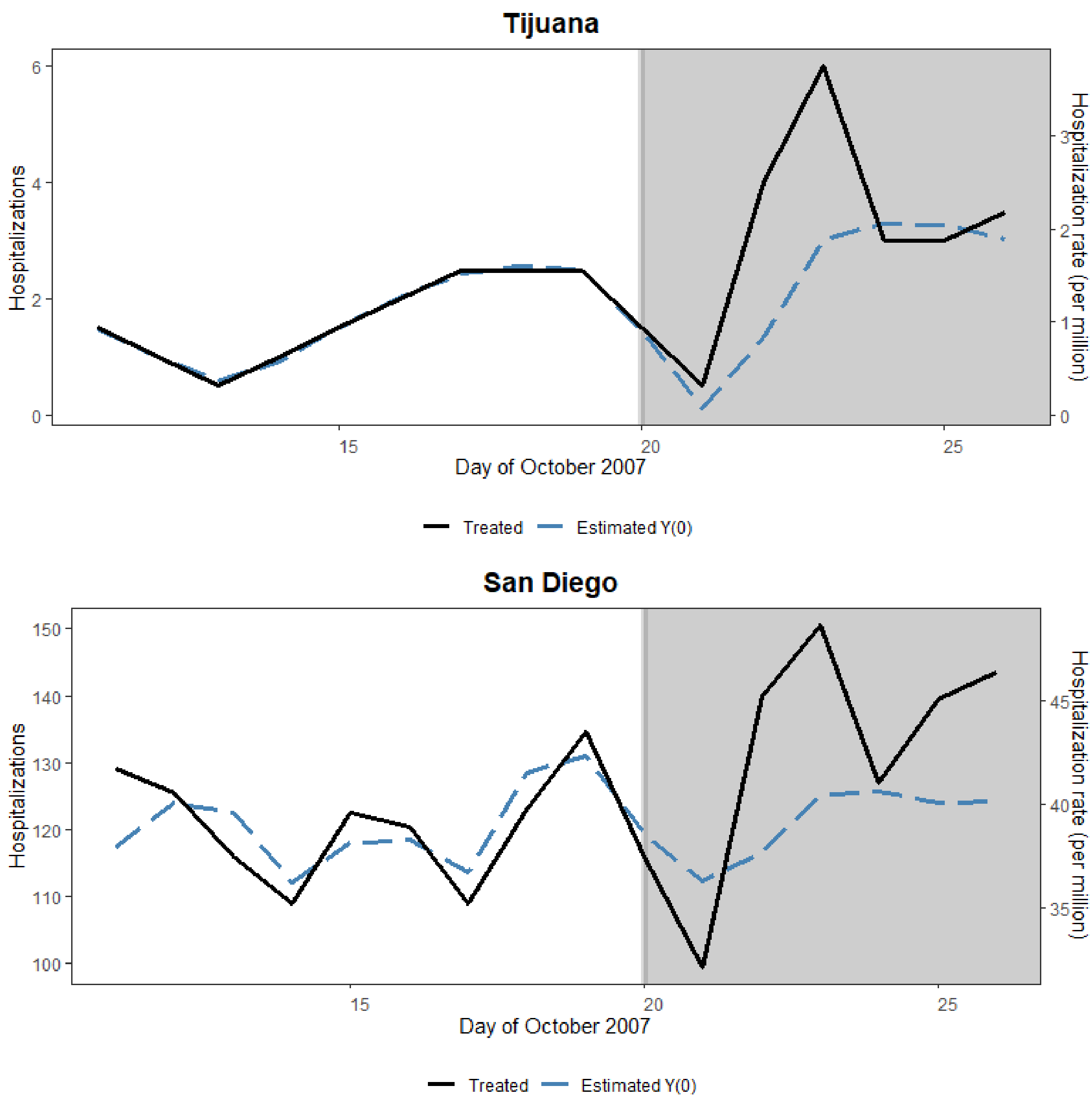
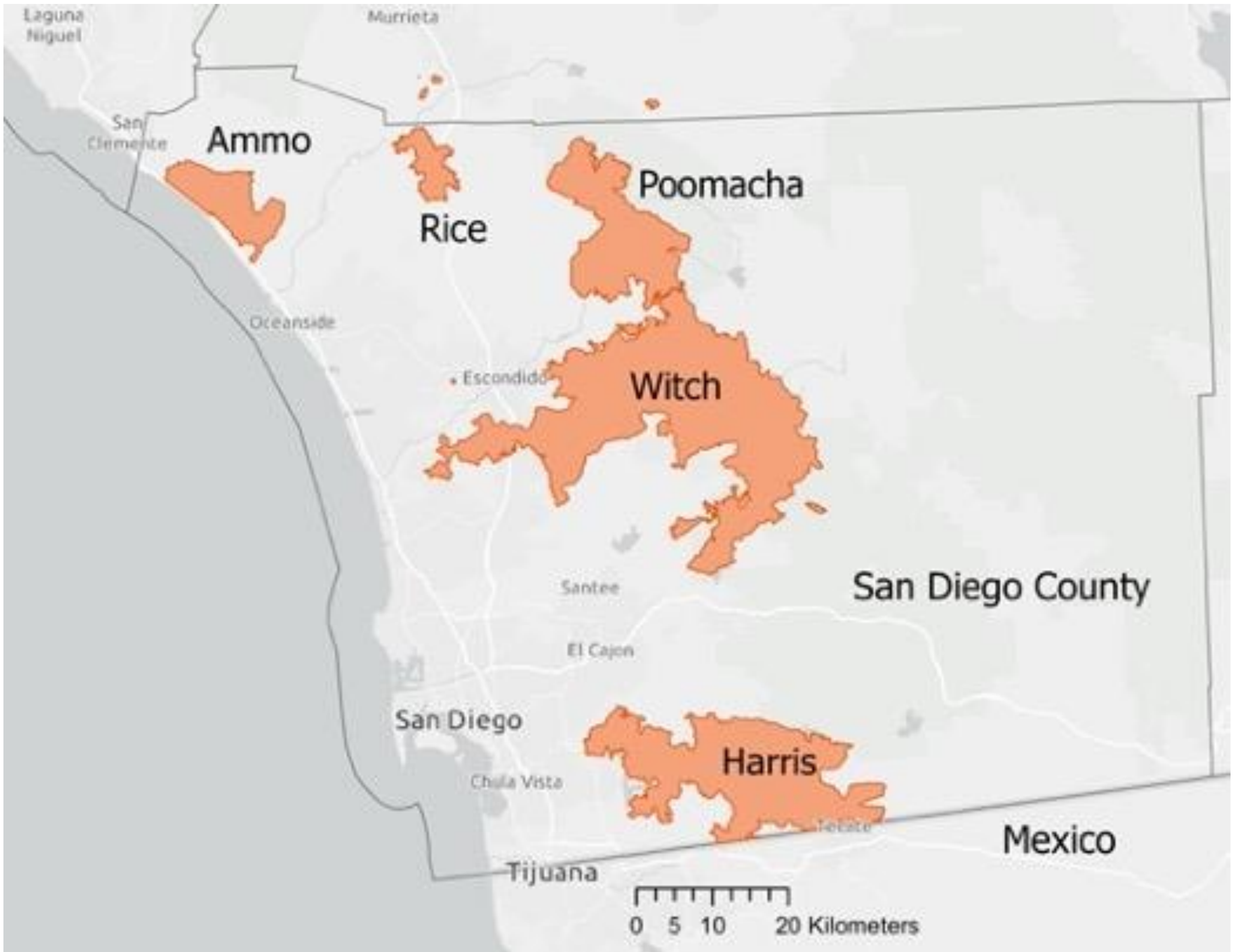
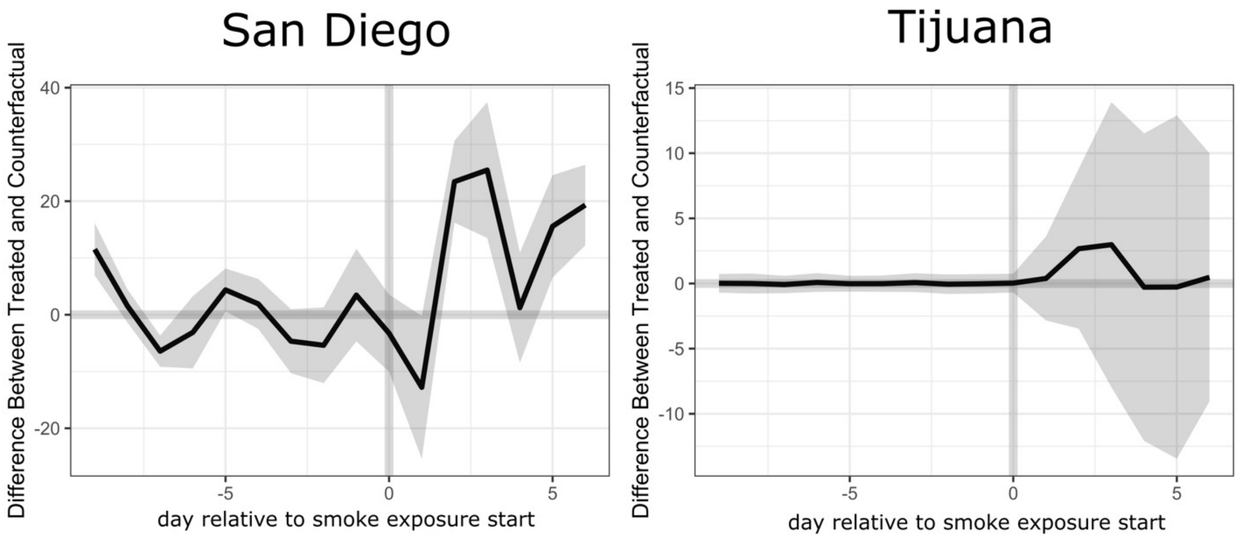


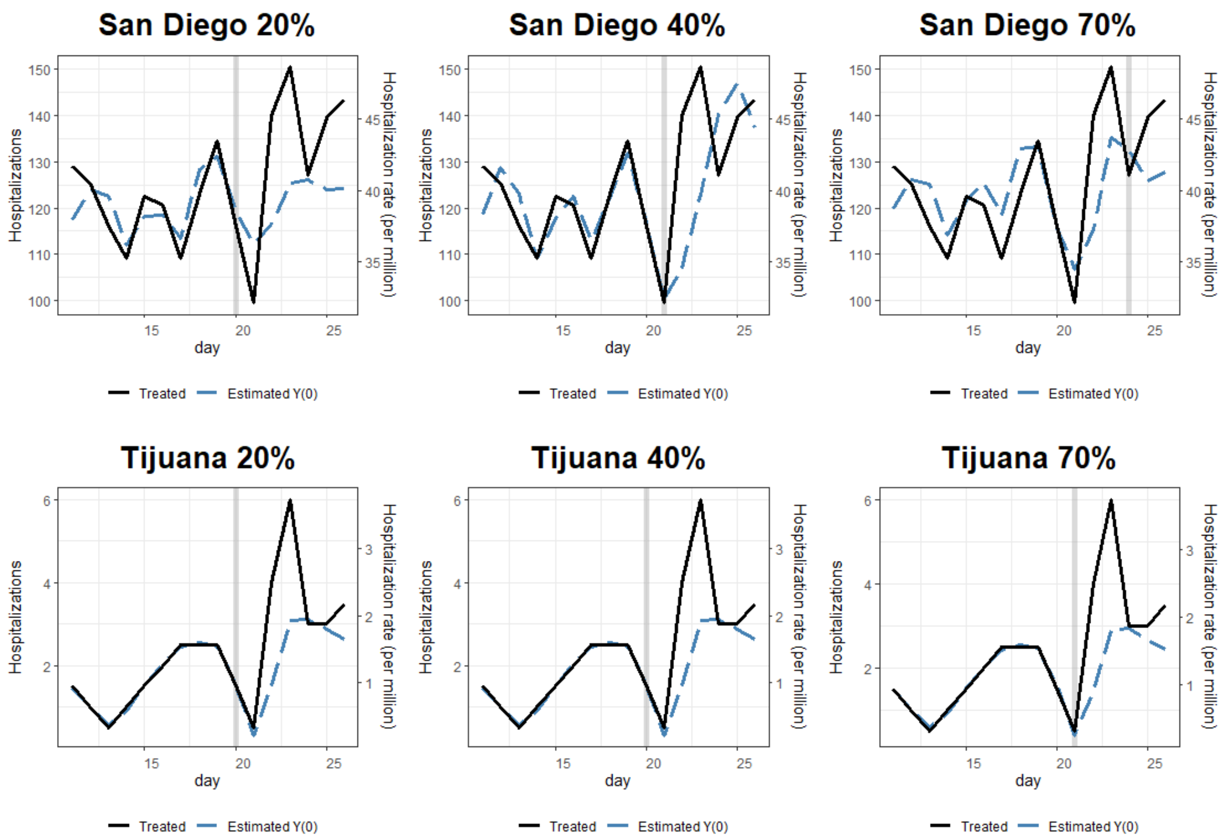
Figure 3.2: Results of the effect of the October 2007 wildfire smoke event on cardio-respiratory hospitalizations in San Diego and Tijuana using synthetic control methods.



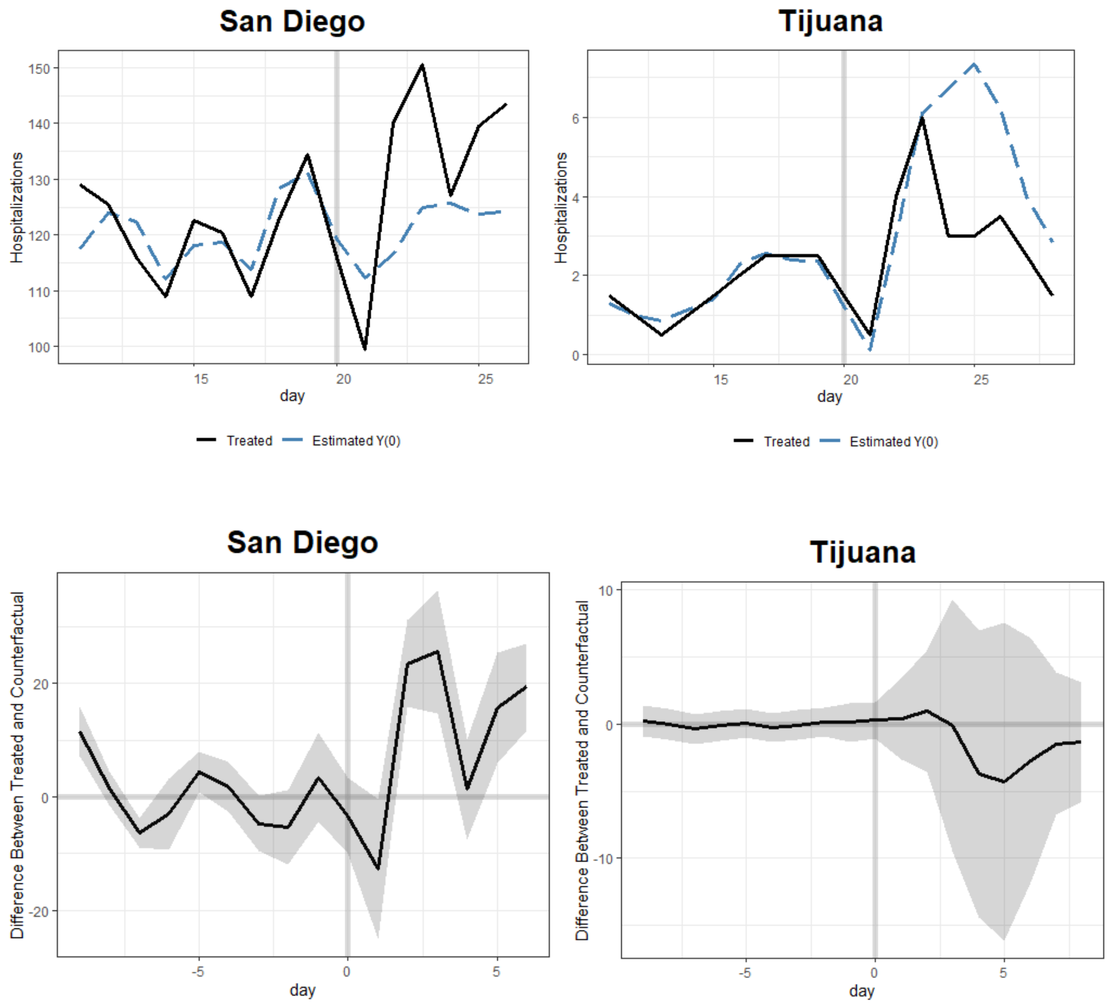
Supplementary Figure 3.1: Map of 2007 wildfires perimeter including the spatial extent of Witch, Harris, Poomacha, and Rice and Ammo wildfires that burned in San Diego County, October 2007.



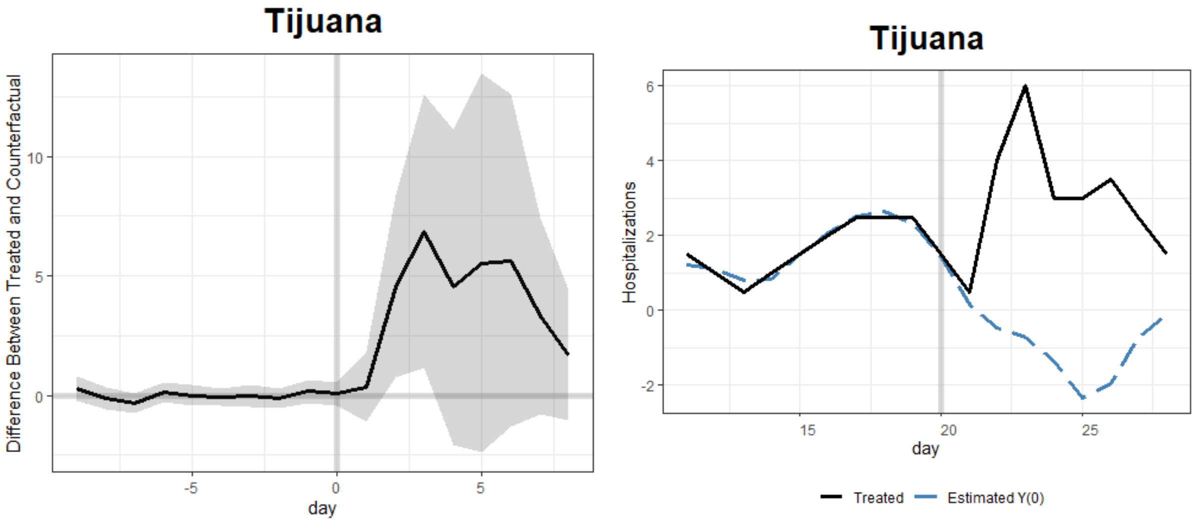
Supplementary Figure 3.2: The effect of October 2007 wildfires on cardio-respiratory hospitalizations in San Diego and Tijuana using generalized synthetic control methods with 95% confidence intervals.



Supplementary Figure 3.3: Sensitivity analyses considering 20%, 40%, and 70% smoke coverage for exposure of October 2007 wildfires in San Diego and Tijuana.



Supplementary Figure 3.4: Results of sensitivity analysis including daily mean temperature as a covariate in evaluating the effect of wildfire smoke from October 2007 wildfires on cardio-respiratory hospitalizations in San Diego County and the Municipality of Tijuana.



Supplementary Figure 3.5: Results of sensitivity analysis including all potential controls (not excluding municipalities that had any day with 0 cases) of the effect of October 2007 wildfire smoke on cardio-respiratory hospitalization in the Municipality of Tijuana.

Supplementary Table 3.1: Gender and age distribution of hospitalizations in San Diego County and the Municipality of Tijuana during study period (October 11th-26th , 2007).

	San Diego	**Tijuana**
	Count (%)	
Age		
0-14	132 (7%)	10 (27%)
15-64	631 (31%)	18 (49%)
65+	1,246 (62%)	9 (24%)
Sex		
Women	1009 (50%)	23 (62%)
Men	1000 (50%)	14 (38%)
Total	2009 (100)	37 (100)

Supplementary Table 3.2: Difference between the daily cases in each treated unit and its counterfactual for the pre-treatment period, October 11th-20th, 2007.

Difference between treated and counterfactual	***San Diego***	***Tijuana***
Oct 11th	11.53	0.016
Oct 12th	1.55	-0.002
Oct 13th	-6.42	-0.079
Oct 14th	-3.10	0.078
Oct 15th	4.37	-0.013
Oct 16th	1.91	0.066
Oct 17th	-4.66	-0.054
Oct 18th	-5.38	-0.024
Oct 19th	3.46	0.030
Oct 20th	-3.26	0.386

Supplementary Table 3.3: Controls and their weights estimated using generalized synthetic control methods for the effect of October 2007 wildfires on cardio-respiratory hospitalizations in San Diego and Tijuana.

San Diego County		Municipality of Tijuana (highest weights)	
County Number	**Synthetic control weight**	**Municipality**	**Synthetic control weight**
103	0.0617	**MX09015**	1.7048
105	-0.0661	**MX14120**	1.1332
11	-0.0394	**MX09005**	1.0402
115	0.0263	**MX28041**	0.9280
15	0.0615	**MX30087**	0.9025
21	0.0325	**MX26030**	0.8488
3	0.0550	**MX11003**	0.7813
33	0.0823	**MX15057**	0.7566
35	0.0142	**MX15033**	0.7565
49	0.0433	**MX09002**	0.7392
51	0.0089	**MX30193**	0.6637
57	0.0929	**MX15039**	0.6473
63	-0.0101	**MX08019**	0.6295
7	0.4499	**MX07019**	0.5427
89	-0.0573	**MX11020**	0.5178
91	0.0040	**MX24028**	0.4991
93	-0.0192	**MX23005**	0.4702
		MX27004	0.4337
		MX16053	0.3971
		MX28038	0.3716
		MX01001	0.3617
		MX09011	0.3323
		MX10005	0.3229
		MX14098	0.3215
		MX28022	0.2896
		MX15104	0.2849
		MX15014	0.2806
		MX10007	0.2666
		MX15106	0.2553
		MX15058	0.2472
		MX07089	0.2364
		MX09003	0.2135
		MX14070	0.2029
		MX19039	0.2022
		MX08037	0.2003
		MX14101	0.1999
		MX07101	0.1758

Chapter 4 : The potential impact of wildfire smoke on COVID-19 cumulative deaths in the San Diego-Tijuana border region

4.1 Abstract

The year 2020 broke records for the most active fire year on the West Coast, resulting in the worst air quality observed in decades. Concurrently, the public health threat of COVID-19 caused over 1 million deaths in the US and Mexico in 2020 and 2021. Due to the effect of air pollution on respiratory diseases, wildfire-specific particulate matter is a hypothesized driver of COVID-19 severity and death. Capitalizing on wildfire smoke that impacted the San Diego-Tijuana border region in September 2020, we applied synthetic control methods (SCM) to explore its differential role in affecting COVID-19 mortality on both sides of the border. Daily data on COVID-19 cumulative deaths for US Counties was obtained from the CDC COVID tracker and data for Mexican Municipalities was obtained from the Mexican Secretary of Health. Counties and municipalities with wildfire smoke exposure were identified using the NOAA Hazard Mapping Smoke product (HMS); a day where 90% of the area covered by smoke was considered exposed for the main analyses. Unexposed counties/municipalities were considered as potential controls. The San Diego-Tijuana border region was covered by dense smoke by September 7th; 707 COVID-19 deaths had occurred in San Diego and 1367 in Tijuana. While a slight increase in cumulative mortality was observed in San Diego, no change was found in Tijuana; neither estimate indicated a strong precise effect of wildfire smoke on COVID-19 mortality. We hope this study will serve as an illustration of how border contexts can be used to investigate differential vulnerability to wildfire smoke for infectious diseases. Examining the interactive effect of COVID-19 and smoke can help in recognizing the implications of these dual health risks which will be increasingly important as wildfires become more frequent and severe in the context of climate change.

4.2 Introduction

Over 1 million deaths from COVID-19 occurred in the US and Mexico in 2020 and 2021 only (Hannah Ritchie 2020). Although biomedical understanding of the disease has drastically improved since the virus emerged in early 2020, many unknowns remain about what individual and environmental factors increase vulnerability to severe disease and death (Fakhroo, Al Thani et al. 2021, Luo 2021). COVID-19 infections can range from being asymptomatic to causing premature death, and the case fatality rate varies with a range from approximately 1% in the general population to up to 37% for those admitted to intensive care units (Alimohamadi, Tola et al. 2021). Understanding the role of environmental health risks in driving severe infection and disease can provide insight into the biological risk factors and help to recognize and understand the implications of these potentially compounded health risks.

The threat of the COVID-19 pandemic was concurrent with raging wildfires and record-high smoke exposure in the summer and fall months of 2020 in the US West Coast (Henderson 2020). Wildfire smoke includes high concentrations of inhalable ambient particulate matter, such as $PM_{2.5}$, particles under 2.5 microns in aerodynamic diameter that are particularly harmful to human health (Valavanidis, Fiotakis et al. 2008). The inhalation of particulate matter can produce oxidative stress and inflammation due to the generation of reactive oxygen species which triggers cellular damage and may increase the risk of cardiopulmonary disease (Valavanidis, Fiotakis et al. 2008). Furthermore, the smallest particles can cross the alveolar membrane to the bloodstream and cause systemic effects on the human biological system (Yang, Ruan et al. 2019). It has been shown that pulmonary response to these stressors can affect airway function and decrease resilience to viral and bacterial infections (Cascio 2018). As wildfire smoke and COVID-19 affect the same biological systems and organs, wildfire-specific particulate matter has been hypothesized and shown to increase the risk of severe infection due to its widespread effect on the respiratory and cardiovascular system (Bourdrel, Annesi-Maesano et al. 2021). There is strong evidence of the adverse health effects of wildfire smoke (Liu, Pereira et al. 2015, Reid, Brauer et al. 2016, Aguilera, Corringham et al. 2021) and emerging evidence of its effects on COVID-19 transmission and severity (Henderson 2020, Hendryx and Luo 2020, Wu, Nethery et al. 2020, Zhou, Josey et al. 2021, Ademu, Gao et al. 2022, Cortes-Ramirez, Michael et al. 2022, Garcia, Marian et al. 2022, Schwarz, Dimitrova et al. 2022). However, the majority of epidemiological studies on wildfire smoke have been conducted in the US, Canada, and Australia, with little evidence from other contexts (Liu, Pereira et al. 2015, Marlier, Crnosija et al. 2022).

Generating evidence from regions with differing population demographics and social conditions is important as the effects of wildfire smoke differ based on the study population and it’s specific vulnerability. Socio-economic factors increase susceptibility to air pollution impacts by increasing the risk of other conditions such as asthma and/or affecting development and resistance to other disease threats (Neidell 2004). Also, neighborhood-level risk factors faced by those living in low-income neighborhoods may increase their susceptibility to environmental hazards (Clougherty and Kubzansky 2009). Stressors, such as crime, noise, and traffic can lead to acute and chronic changes in the functioning of body systems and increase the effect of exposures such as wildfire smoke on the biological system (Chi, Hajat et al. 2016). Understanding the role of social factors in driving vulnerability to wildfire smoke is critical to informing and prioritizing efforts to reduce the burden and protect populations that are most at-risk (Fish, Peters et al. 2017).

Border regions, having similar climatic and environmental conditions but different cultural and social contexts, offer a unique opportunity to study the role of social vulnerability in driving health impacts of environmental exposures. The San Diego-Tijuana border is the largest binational urban center shared between the US and Mexico and one of the most densely populated international crossings in the world (Mendoza and Dupeyron 2020). Although both cities are juxtaposed, the socio-economic contexts in San Diego and Tijuana are severely different. The United Nations Development Program ranks the US 17th on the Human Development Index rankings, and Mexico is ranked 74th (UNDP 2020). Furthermore, Tijuana is ranked to have the 4th worst quality of life index out of all Mexican cities based on geographical, environmental, and social factors (Gallardo Del Ángel 2017). In contrast, San Diego is ranked the 5th richest city in the US (Rawes 2015). Such differing social conditions can be used as a natural experiment to better understand how population socio-demographics modify the health risk of environmental stressors.

While international borders are a physical barrier to human mobility that leads to different social contexts, environmental exposures such as wildfires igniting on either side of the border can drive harmful smoke exposure to the entire region. The San Diego-Tijuana border region is particularly affected by extreme weather events. Climatic trends resulting from global warming have increased the likelihood of fire weather, or periods that have a high probability of fire due to high temperature, low humidity, low rainfall, and/or high winds (Jones, Smith et al. 2020). The amount of forest area burned by wildfires was found to be more than 10 times greater in the Western US in recent decades than in previous decades (Westerling 2016). Furthermore, 2020 broke records for the most active fire year in California (Keeley and Syphard 2021), and the smoke emitted by wildfires extended across the border to cities like Tijuana. Changes in economic and transport activity from the COVID-19 pandemic and associated lockdown also played a role in reducing global ambient $PM_{2.5}$ concentrations by 31% in the first months of the pandemic (Venter, Aunan et al. 2020), therefore wildfire smoke may be a greater contributor to harmful air pollution exposure in this pandemic context.

Capitalizing on the timing of the 2020 wildfire smoke event that hit the San Diego-Tijuana border region and using other Counties in the US and Municipalities in Mexico that did not have a smoke event during this period, we applied synthetic control methods to understand the role of wildfire smoke in affecting COVID-19 mortality. This methodology has been previously applied to study the impact of wildfire smoke on COVID-19 case fatality ratios in the San Francisco Bay Area (Schwarz, Dimitrova et al. 2022) and here, it is applied to investigate its role in cumulative COVID-19 deaths in the San Diego-Tijuana border region hypothesizing differential impacts on both sides of the border. Understanding the role of wildfire smoke as a risk factor for severe COVID-19 and differing vulnerability factors can be used to inform measures to prevent protect populations most at risk in the context of recurring wildfires and the ongoing pandemic.

4.3 Methods

4.3.1 Overview of methodology

A synthetic control methodology was applied to study the impact of wildfire smoke on daily COVID-19 cumulative mortality in each San Diego County and the Municipality of Tijuana (Rehkopf and Basu 2018). This approach capitalized on the timing of wildfire smoke as a natural experiment to estimate the short-term changes in COVID-19 cumulative mortality. Using data from areas not affected by the fire (control units), the methodology identifies a synthetic control that best estimates the COVID-19 cumulative mortality before the wildfire smoke starts which then represents the counterfactual of what the trend would have been if the smoke exposure had not occurred. Each county in the US and municipality in Mexico that did not have wildfire smoke exposure was considered to build synthetic controls for San Diego and Tijuana separately. The synthetic controls were identified separately so that San Diego County and Municipality of Tijuana are only compared to other counties/municipalities within the same country since US counties and Mexican municipalities may not be comparable. A counterfactual synthetic control was constructed by weighting control units to most closely match the level and trend of the treated unit before exposure. If an appropriate match was found (i.e. the synthetic control groups and exposed groups have the same trend before the wildfire event), the difference in the counterfactual synthetic control units and the treated unit post-wildfire exposure could be interpreted as the effect of interest. Generalized synthetic control method is an extension of synthetic control approach (Xu 2017) which has more flexibility in controlling for time-varying covariates, it is considered more efficient than traditional synthetic control methods (Xu 2017, Sheridan, McElroy et al. 2022). Lastly, it uses bootstrapping to estimate uncertainty (such as 95% confidence intervals) that are useful in the interpretation of results. A traditional synthetic control was also applied as a sensitivity analysis and presented in supplementary materials.

4.3.2 Data Sources

Daily COVID-19 cases and mortality were obtained from the CDC COVID-19 tracker for counties in the US (CDC 2020) and from the Secretary of Health Epidemiological Surveillance System for Viral Respiratory Diseases for municipalities in Mexico (Paredes 2020) which are counts of COVID-19 deaths based on the patient's residence county or municipality. Daily mobility patterns for each state in both the US and Mexico were extracted from the Google Community Mobility Reports (Google 2021). Differences in movement trends from residential locations were considered a proxy for population dynamics and accounting for potential differences in COVID-19 measures within each country (Aktay, Bavadekar et al. 2020). Smoke imagery was obtained from the National Oceanic and Atmospheric Administration (NOAA) HMS (https://www.ospo.noaa.gov/Products/land/hms.html) for the US and Mexico, which identifies smoke plumes from wildfires applying algorithms from visible imagery from various satellites (NOAA 2020). These estimates were revised and modified by trained analysts to improve accuracy. Aerosol Optical Depth information was collected from the Geostationary Operational Environmental Satellite (GOES) Aerosol and Smoke Products and smoke plumes were categorized by NOAA's Office of Satellite and Product Operations as light, medium, or heavy categories, corresponding to $PM_{2.5}$ concentrations of 0–10, 10–21, and 22+ μg/m3, respectively (Vargo 2020). Satellite imagery for the border region was obtained from the National Aeronautics and Space Administration Worldview visualization tool (NASA 2021).

4.3.3 Analysis

The percentage of a county or municipality covered by heavy smoke was estimated for each day from July through September 2020 using NOAA's HMS product. Smoke exposure was considered to start the first day that over 90% of a county or municipality was exposed to heavy smoke based on this product; sensitivity analyses were conducted using 70% and 100% smoke coverage. The package "gsynth" in R v4.1.0 (Xu, Liu et al. 2021) was utilized to apply a generalized synthetic control, which can be viewed as an extension of the canonical synthetic control approach. A traditional synthetic control was also applied using the "synth" package Stata 16 SE (Abadie, Diamond et al. 2011) as a sensitivity analysis. These approaches identify counties (US) and municipalities (Mexico) that had a similar trend to each unit before the smoke exposure occurred. Any county or municipality with smoke exposure during the entire study period based on the exposure definition was excluded as a potential control so only areas with no wildfire smoke during the study period were eligible for selection for the synthetic control. A weighting procedure was applied to identify the most suitable synthetic control trends in the pre-wildfire smoke period and considered to represent the counterfactual trend to the treated unit for the post-wildfire smoke period. For the generalized synthetic control method, controls are decomposed with calendar time, lagged outcomes (in the pre-exposure period) and time-varying covariates, and an interactive fixed effects model is applied to identify a suitable control based on this time series in the pre-treatment period (Sheridan, McElroy et al. 2022). 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 post-treatment period (Xu 2017, Sheridan, McElroy et al. 2022). Generalized synthetic control has more flexibility in controlling for time-varying covariates, and daily mobility, COVID-19 cases the same day, COVID-19 cases the previous day, and the standard deviation of COVID-19 cases the 4 previous weeks were included as covariates to account for potential differences in the COVID-19 infection rates that vary day to day and could be affected by smoke. The difference in the trend after the wildfire smoke can be considered as the effect of this exposure on COVID-19 cumulative mortality.

The advantage of this methodology is that the analysis itself accounts for any difference between counties/municipalities by finding the best possible fit in trends before the wildfire smoke occurs. By doing so, any difference in socio-demographics, COVID-19 burden, or political action affecting the outcome of interest that is not time-varying is accounted for by design. Other variables included in the model were to account for potential differences in trends related to the progression of the pandemic and related public measures between regions and identify weighted controls that have similar COVID-19 transmission and burden. Missing case and mobility data were interpolated using the "mipolate" command in STATA, which uses linear interpolation using known values before and after the missing values (Cox 2016). Placebo tests were conducted considering the timing of the wildfire smoke exposure to have started on September 20th, four days after wildfire smoke stopped affecting the region. All code and datasets used for this analysis can be found at in the following repository: https://github.com/benmarhnia-lab/border_smoke_covid.

4.4 Results

The study period analyzed was from July 1st to September 30th, 2020. Smoke from wildfires burning throughout California started to cover the San Diego-Tijuana border region in early September 2020. By September 7th the border region was covered by heavy wildfire smoke which continued for 10 days following the start of the smoke (Figure 4.1, Supplementary Table 4.2). From the start of 2020 to the first-day wildfire smoke covered the border region, a total of 707 COVID-19 deaths had occurred in San Diego and 1376 in Tijuana. By September 30th, 2020, at the end of the study period, 783 COVID-19 deaths had occurred in San Diego and 1491 in Tijuana (Table 4.1). However, the number of positive diagnosed COVID-19 cases varied drastically between both sides of the border, with over 55,000 cases in San Diego and less than 8,000 cases in Tijuana during the study period (Table 4.1). This is partially driven by differences in testing, and likely more unreported cases in Tijuana.

For both San Diego and Tijuana, a synthetic control was identified according to the trend of cumulative mortality in each (Figure 4.2). Although the synthetic control prediction was not matched seamlessly for San Diego or Tijuana, it did correspond to the trend in cumulative mortality for the majority of the pre-treatment period. The difference in cumulative mortality for the pre-treatment period is described in Supplementary Table 4.1 and the difference between the trend in San Diego and Tijuana never exceeded 6 deaths, with most of the differences of less than 2 (Supplementary Table 4.1). The counties/municipalities identified with the traditional synthetic control analysis and their weights are included in the supplementary material (Supplementary Table 4.3).

For San Diego, a slight increase in cumulative mortality was observed when compared to the trend in the synthetic control in both the main analysis using generalized synthetic control and the sensitivity analysis (Figure 4.2, Supplementary Figure 4.1). In Tijuana, the cumulative mortality follows approximately the same trend as its synthetic control, showing no change after the wildfire smoke started. Although results suggest a small effect of wildfire smoke on COVID-19 cumulative mortality in San Diego, no effect is observed in Tijuana (Figure 4.2). However, neither estimate shows a strong and precise effect at the 95% confidence level, suggesting that we are not able to confirm a robust effect of wildfire smoke on cumulative COVID-19 mortality in this context. This is consistent across sensitivity analyses using different smoke percentiles as the exposure (Supplementary Figure 4.2). Results of placebo tests using September 20th as the wildfire smoke exposure start date (when wildfire smoke had cleared the region) showed no effect in either San Diego or Tijuana (Supplementary Figure 4.3).

4.5 Discussion

Overall, we did not observe a strong effect of wildfire smoke on COVID-19 cumulative mortality in the San Diego-Tijuana border region. In San Diego, we observed a slight increase in cumulative mortality (Figure 4.2). In Tijuana, no effect was observed as the synthetic control followed a very similar trend to what was observed in the Municipality of Tijuana after the wildfire smoke exposure started affecting the region. Tijuana is socially disadvantaged when compared to San Diego; according to the 2010 census in both countries, the poverty rate was 3 times higher in Tijuana than in San Diego while the percentage of the population with a high school education was 3 times higher in San Diego (INEGI 2010, Census Bureau 2011). It was hypothesized that this could lead to a differential effect of wildfire smoke due to the increased social vulnerability of Tijuana. Although we cannot infer that wildfire smoke drove a change in COVID-19 mortality and that social vulnerability played a role in this context, we hope that these results can highlight the need to continue to study and understand the compounded impact of these joint exposures and associated vulnerability factors. Examining the interactive effect of COVID-19 and extreme weather can help in recognizing the implications of these dual health risks and can be used to inform measures to protect those that are most vulnerable during wildfires.

Several recent studies have identified links between particulate matter air pollution and COVID-19 severity (Hendryx and Luo 2020, Wu, Nethery et al. 2020, Garcia, Marian et al. 2022). A study considering the effect of $PM_{2.5}$ on COVID-19 in Western US Counties during the 2020 wildfires found that short-term exposure to particulate matter drove higher COVID-19 cases and deaths (Zhou, Josey et al. 2021). However, considerable variability was observed with many counties showing no effect and some even indicating a negative association (Zhou, Josey et al. 2021). Similarly, previously published work by coauthors of this work found variability in the effect of wildfire smoke on COVID-19 case fatality ratios in the San Francisco Bay Area with some Counties showing a precise association and others counties showing no effect (Schwarz, Dimitrova et al. 2022). Yu & Hsueh (2023) found the effect of wildfire smoke on COVID-19 mortality in California to be moderated by the availability of hospital and public housing resources at the county level and disproportionally affects counties with higher social vulnerability (Yu and Hsueh 2023). Our results in the context of the existing literature further reinforce the heterogeneity of the role of wildfire smoke on COVID-19 severity. Differences in patterns observed in these studies and our work could be attributed to a range of factors including differences in COVID-19 response measures, population demographics, behavioral risks, and protective factors. Previous research and this current work highlight the need to further disentangle the drivers behind the heterogeneous effects observed thus far.

Wildfire smoke and air pollution may play a role in the COVID-19 pandemic through other pathways. For instance, studies have found that wildfire smoke is not only a driver of disease severity but can also increase incidence, test positivity rates, and case rates (Hendryx and Luo 2020, Ademu, Gao et al. 2022, Cortes-Ramirez, Michael et al. 2022). A study in Reno found that a 10 $\mu g/m^3$ increase in the 7-day average $PM_{2.5}$ concentration increases the SARS-CoV-2 test positivity rate by 6.3% (Kiser, Elhanan et al. 2021). Individual-level studies in Sweden and the US have also shown that short-term exposure to particulate matter is associated with a higher risk of SARS-CoV-2 positive test results and COVID-19 mortality (Kim, Samet et al. 2022, Yu, Bellander et al. 2022). In the constantly evolving COVID-19 pandemic context, more evidence is needed to understand how air pollution or wildfire smoke may interact with or modify the protective effects of vaccines, for example. There are many interesting avenues for future studies to explore the links between extreme weather such as wildfire smoke and various expressions of the COVID-19 pandemic.

We acknowledge our current work has limitations. First, we only consider one county in the US and one municipality in Mexico as case studies, i.e., we were not able to evaluate potential geographic differences between regions or within each country. Also, wildfire smoke is defined based on satellite imagery, therefore exposure misclassification is possible in this context since it may also capture smoke higher in the atmosphere. Nonetheless, validation of the HMS smoke product with ground-level monitors has shown a correlation with $PM_{2.5}$ concentrations (Vargo 2020). Additionally, we only focused on cumulative mortality as the outcome of interest. Many other measures of COVID-19 burden would be worth exploring in future work such as case fatality rates, hospitalization rates, and symptom severity; we chose to focus on cumulative mortality to retain consistency across datasets between both countries. Also, COVID-19 deaths recorded at the county/municipality level based on patient residence were used but there could be regional variations in how the data was recorded and particularly between San Diego and Tijuana. Furthermore, Tijuana experienced more COVID-19 deaths earlier in the pandemic which could decrease the pool of potentially vulnerable people and attenuate the impacts of wildfire smoke. Lastly, many residents of Baja California sought medical care in the US when hospitals exceeded capacity during waves of the COVID-19 pandemic (Gottesdiener 2020); this could play a role in the results we observe. As the first study to consider this research question in a border region, we hope it will motivate further research to broaden this analysis to additional regions of the US-Mexico border region and other border regions around the globe.

In conclusion, we used the San Diego-Tijuana border as a unique setting to explore the potential differences in the effect of wildfire smoke on either side of the border, using it as a natural experiment to explore differential health risks related to socio-economic context. It is critical to continue to study what drives susceptibility to these compounded health risks to best protect populations from these dual public health risks.

Chapter 4, in full, is a reprint of the material as will in appear in Environmental Research: Health. Lara Schwarz, Rosana Aguilera, Javier Emmanuel Castillo Quiñones, L.C. Aguilar-Dodier, María Evarista Arellano García, Tarik Benmarhnia. “The potential impact of wildfire

smoke on COVID-19 cumulative deaths in the San Diego-Tijuana border region." The dissertation author was the primary researcher and author of this paper.

Table 4.1: Descriptive statistics of COVID-19 cases, deaths and mobility patterns in San Diego and Tijuana in pre-treatment period (July 1st-September 6th) and post-treatment period (September 7th-30th).

COVID-19 measure	***Pre-treatment (July 1-Sep 6)***		***Post-treatment (Sep 7-Sep 30)***	
	San Diego	**Tijuana**	**San Diego**	**Tijuana**
Cumulative COVID-19 deaths (since Jan 2020)	707	1367	783	1491
Total deaths during period	335	409	76	124
Deaths (average)	5.03	6.12	3.17	5.17
Mobility (average)	9.11	10.36	8.79	9.04
Cases (average)	389.72	40.06	272.08	32.79

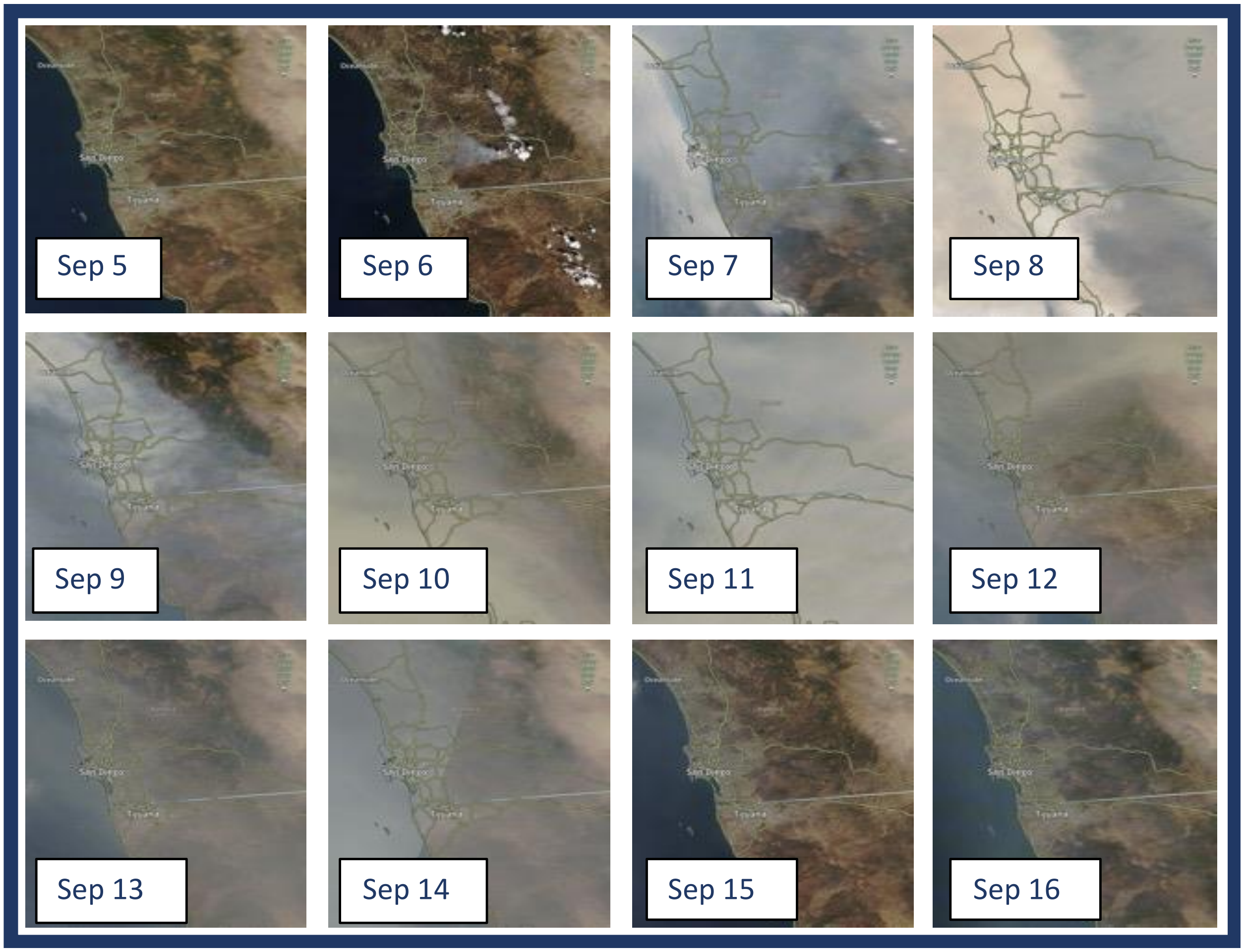


Figure 4.1: Satellite imagery of wildfire smoke covering the San Diego-Tijuana border region in September 2020.

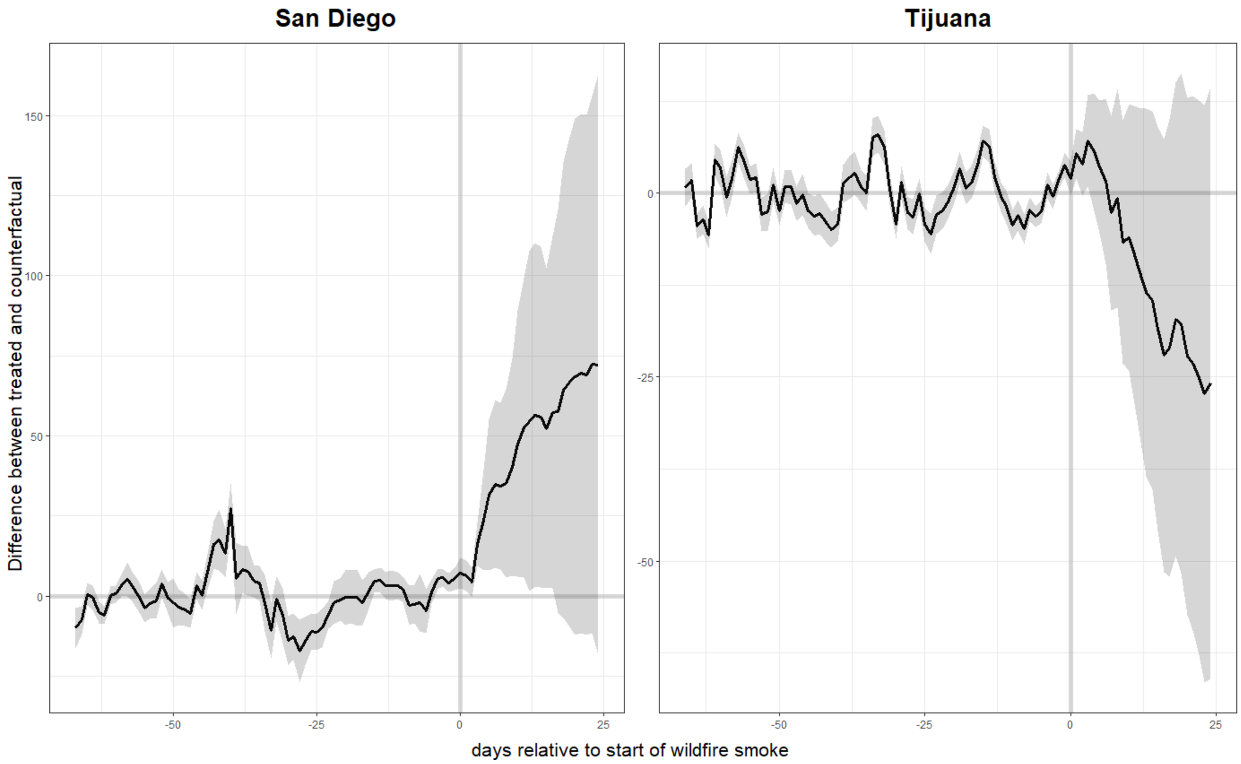
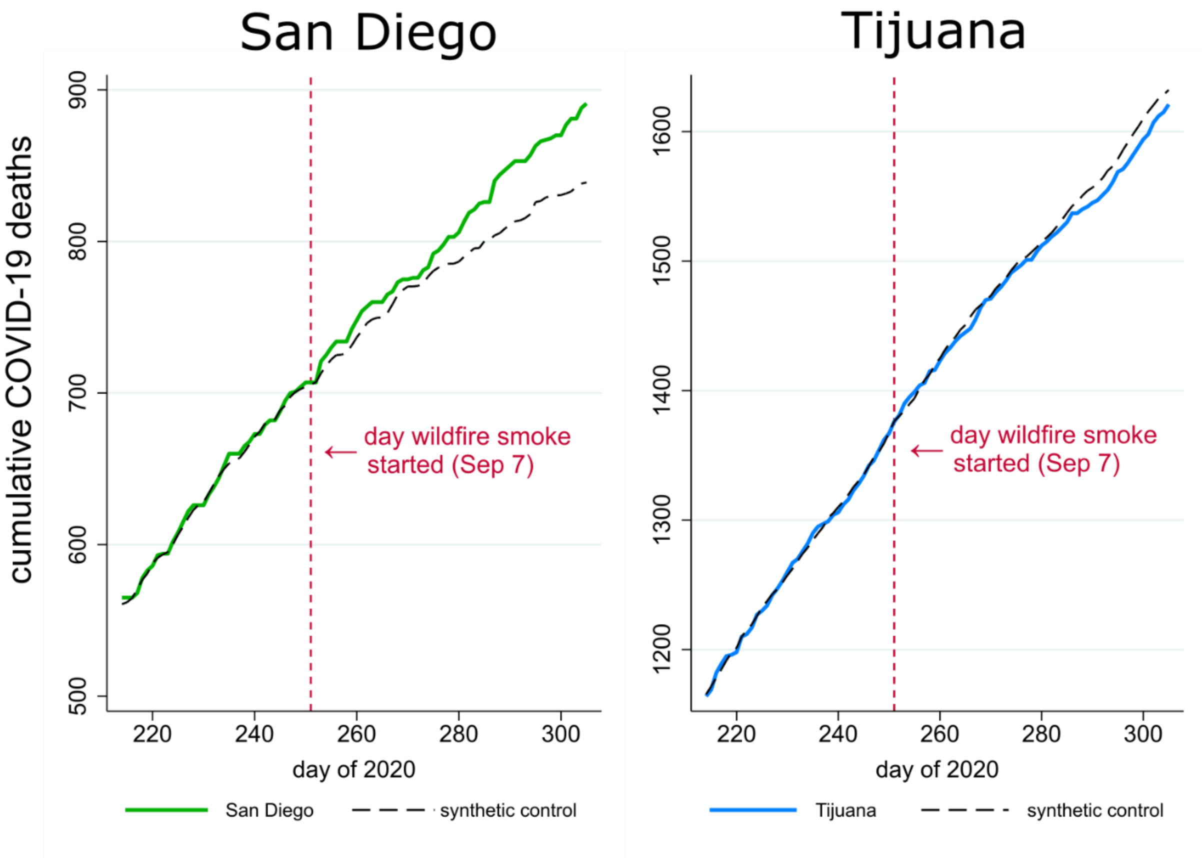
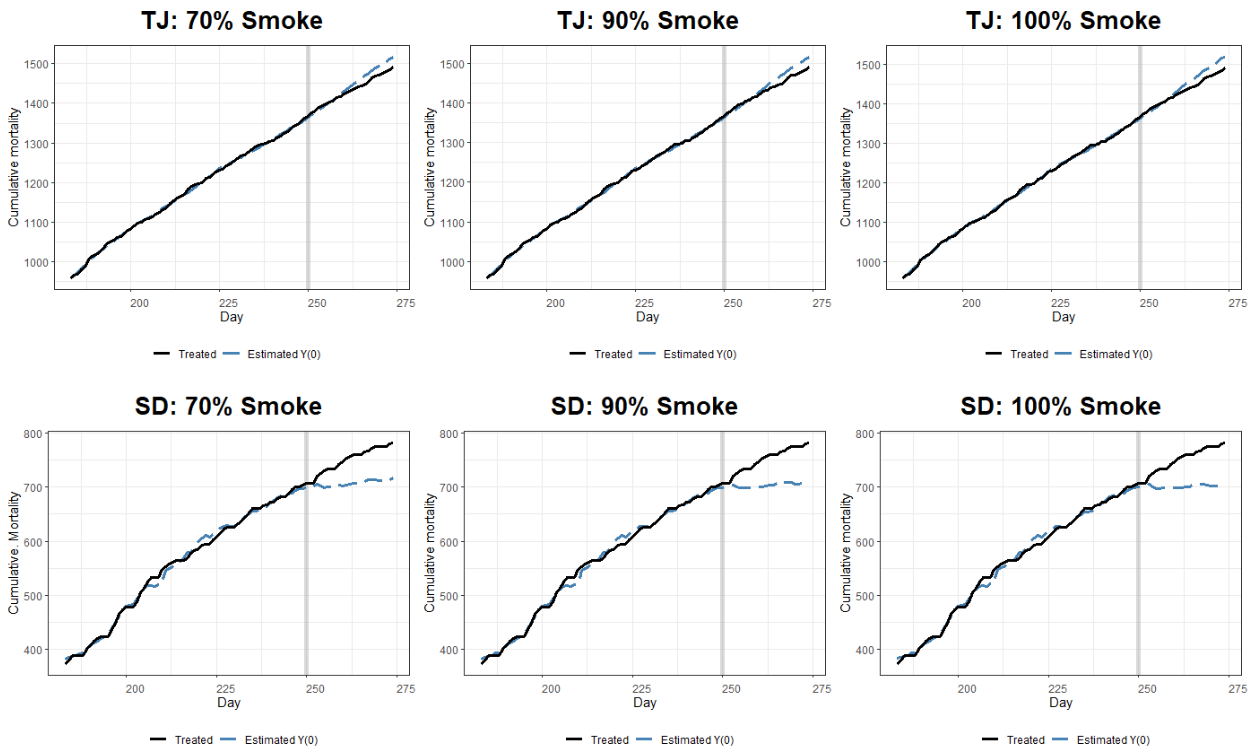


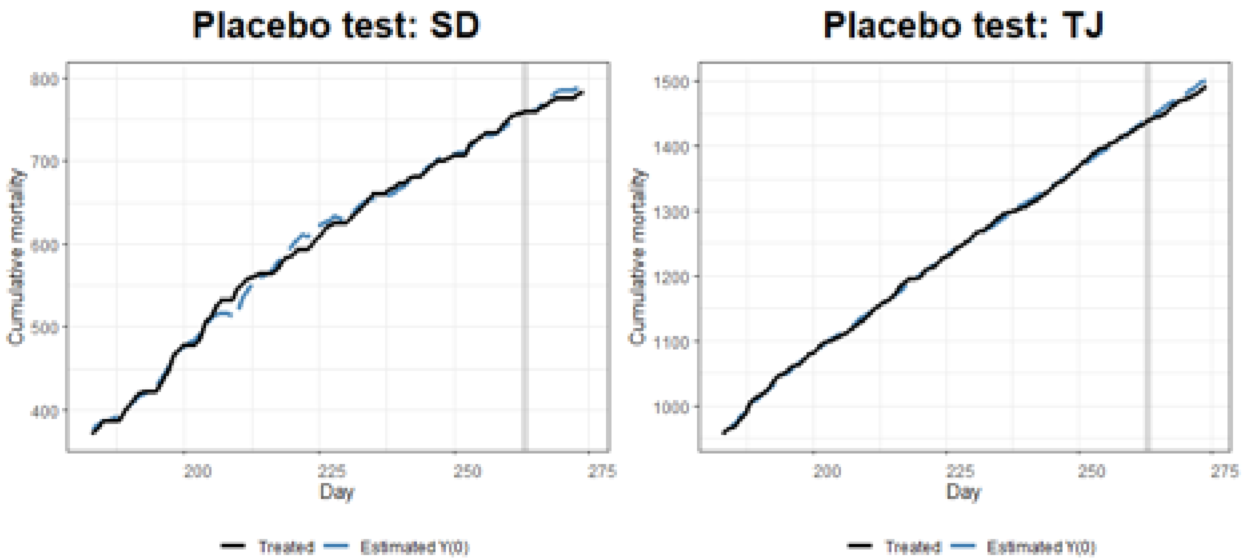
Figure 4.2: Results showing the effect of the 2020 wildfire smoke event on cumulative COVID-19 mortality using a generalized synthetic control approach showing 95% confidence intervals (in grey) for San Diego and Tijuana.



Supplementary Figure 4.1: Results of the traditional synthetic control method of the effect of wildfire smoke on cumulative mortality in the Municipality of Tijuana and the County of San Diego in September 2020.



Supplementary Figure 4.2: Sensitivity analyses of the generalized synthetic control results of the effect of wildfire smoke on cumulative mortality in the Municipality of Tijuana (TJ) and County of San Diego (SD) in September 2020 using 70% and 100% heavy smoke coverage as the exposure metrics and comparison to 90% exposure metric used in main results.



Supplementary Figure 4.3: Placebo test of smoke effects in San Diego (SD) and Tijuana (TJ) as if wildfire smoke event had started on September 20th, 2020 (4 days after wildfire smoke ended in region).

Supplementary Table 4.1: Difference between the San Diego County and Municipality of Tijuana and its respective synthetic control for each time point for the effect of smoke on COVID-19 cumulative mortality, September 2020.

Pre-treatment period			Post-treatment period					
Time point	SD	TJ	**Time point**	SD	TJ	**Time point**	SD	TJ
214	4	-1	**251**	1	0	**288**	39	-10
215	3	-3	**252**	0	0	**289**	39	-12
216	0	4	**253**	8	6	**290**	39	-12
217	-2	4	**254**	7	5	**291**	40	-13
218	1	3	**255**	8	5	**292**	39	-13
219	2	-2	**256**	9	2	**293**	38	-15
220	-2	-3	**257**	9	-2	**294**	39	-12
221	2	0	**258**	7	2	**295**	37	-10
222	1	-3	**259**	11	-4	**296**	39	-15
223	-1	-2	**260**	11	-2	**297**	38	-16
224	2	1	**261**	13	-3	**298**	38	-16
225	1	-3	**262**	11	-4	**299**	40	-16
226	3	-4	**263**	11	-3	**300**	39	-16
227	4	-1	**264**	10	-5	**301**	45	-18
228	3	0	**265**	10	-6	**302**	48	-13
229	0	1	**266**	12	-9	**303**	45	-14
230	-2	3	**267**	8	-8	**304**	50	-13
231	-1	5	**268**	8	-2	**305**	52	-11
232	-2	2	**269**	7	0			
233	-1	2	**270**	5	-2			
234	2	3	**271**	6	-3			
235	6	5	**272**	5	-3			
236	4	5	**273**	9	-2			
237	3	2	**274**	6	-2			
238	4	-3	**275**	11	-4			
239	2	-1	**276**	11	-5			
240	2	-4	**277**	14	-2			
241	-2	-2	**278**	18	-6			
242	-1	-4	**279**	18	-4			
243	1	-3	**280**	19	-3			
244	-1	-2	**281**	23	-3			
245	-1	-1	**282**	26	-3			
246	3	0	**283**	26	-5			
247	2	-3	**284**	29	-6			
248	0	1	**285**	26	-7			
249	1	3	**286**	25	-5			
250	3	-1	**287**	36	-9			

Supplementary Table 4.2: Percentage of San Diego and Tijuana exposed to heavy smoke (22+ $\mu g/m^3$) following the start of smoke exposure in September 2020.

	San Diego	Tijuana
September 7	100	100
September 8	100	100
September 9	100	100
September 10	100	100
September 11	100	100
September 12	100	100
September 13	100	100
September 14	81.5	89.1
September 15	100	100
September 16	92.6	99
September 17	0	0
September 18	0	0
September 19	0	0
September 20	0	0

Supplementary Table 4.3: Weights for estimation of synthetic controls of the effect of wildfire smoke (90% coverage) on COVID-19 cumulative mortality in San Diego and Tijuana, September 2020.

San Diego		**Tijuana**	
County	*Weight*	*Municipality*	*Weight*
Orleans Parish, LA	0.5060	Nezahualcóyotl, México (MX15058)	0.5570
Palm Beach, FL	0.1380	Iztapalapa, Ciudad de México (MX09007)	0.2130
Nueces, TX	0.0910	Gustavo A. Madero, Ciudad de México (MX09005)	0.1470
Lee, FL	0.0760	Puebla, Puebla (MX21114)	0.0570
Jefferson Parish, LA	0.0670	Reynosa, Tamaulipas (MX28032)	0.0260
Jefferson, AL	0.0530		
Miami-Dade, FL	0.0370		
Broward, FL	0.0310		

Chapter 5 : Overall discussion

5.1 Summary of dissertation research

The urgency of generating evidence to quantify the differential impacts of extreme weather events is becoming increasingly imperative in the context of climate change. While there is abundant research demonstrating the harmful impacts of extreme heat events and wildfire smoke, a small proportion of these studies are quantifying the effects beyond high-income settings despite approximately 85% of the global population living in low and middle-income countries (World Bank 2023). Furthermore, those living in lower resource settings are the populations that are contributing the least to greenhouse gas emissions yet will be most affected by climate change impacts (Gasparrini, Guo et al. 2017). A global analysis across 43 countries found that 37% of heat-related deaths in the warm season are driven by anthropogenic climate change (Vicedo-Cabrera, Scovronick et al. 2021). This global injustice is a result of deeply rooted inequity, exploitation, and power relations that transcends all local and global public health issues that are faced by populations today (Friel and Marmot 2011). Unfortunately, the socio-political historical context of these global dynamics is not simple to address and will require cross-border and cross-discipline collaborations and efforts.

While it can be deduced from existing evidence in high-income countries that exposure to harmful exposures will drive adverse health outcomes in regions of the world that may not have the data or evidence, the importance of quantifying effect measures to these local contexts is indisputable. First, as the effects of climate change become more severe, it produces unprecedented conditions that will not be evenly distributed across the globe (Pörtner, Roberts et al. 2022). Studying the health effects of extreme weather in understudied regions can also mean revealing the risk of unique exposures that may not be observed in high-income contexts.

Second, even if the populations were to experience the same exposure as what has been observed in a previously studied high-income context, the effects are unlikely to be the same. Vulnerability to environmental hazards is a function of exposure, susceptibility, and adaptive capacity (Huq, Shoeb et al. 2020); as populations in low and middle-income countries by definition live in a different socio-economic context than those from high-income countries, evaluating and understanding these differential effects between and within countries is critical. Lastly, political action and will is motivated and informed by research findings and evidence. Highlighting the specific hazards and quantifying their impacts at the local and regional scale is the most effective approach to persuading policymakers of the importance of addressing these public health concerns and informing them of how to best allocate resources.

The purpose of this dissertation was to bring evidence of the epidemiological impacts of extreme weather events in an understudied region and population in a binational US-Mexico context. This research expands on previous work by 1) applying novel methodologies to study the effects of extreme weather in a region with limited environmental exposure data and evidence, 2) examining differential effects through a social vulnerability approach, and 3) using an international border context to better understand health inequalities in the manifestation of environmental risks. In the first aim of the dissertation, a novel spatial analysis was conducted to evaluate socio-demographic predictors of the differential effects of extreme heat on mortality across municipalities in Mexico. In the second aim, a synthetic control approach was applied to understand the differential effects of wildfire smoke on cardio-respiratory hospitalizations in the San Diego-Tijuana border region. Lastly, the third aim used the same border context to explore the potential role of wildfire smoke in driving COVID-19 mortality.

The first aim expanded on previously published work studying the effects of extreme temperature on mortality in Mexico as a whole (Cohen and Dechezleprêtre 2022) by applying a novel spatial model that can examine fine spatial heterogeneity in the effects of extreme heat. A within-community matched with BHM approach was applied and a meta-regression was used to study what municipality-level characteristics are important predictors in explaining regional differences in heat-related effects across Mexico. There was significant spatial variation in the effects of heat across the country indicating the importance of studying spatial heterogeneity in effects rather than relying on overall measures. Results showed that municipalities with populations with greater social deprivation, lower education, poorer housing conditions, and older age demographics showed stronger heat effects. This highlights specific vulnerability factors that show higher risk of heat impacts in Mexico and can be used to prioritize resources and public health interventions.

The second aim of the dissertation applied a synthetic control methodology, an approach that has recently been adapted from econometrics to consider the effects of extreme weather events (Schwarz, Dimitrova et al. 2022, Sheridan, McElroy et al. 2022). Capitalizing on the social context in San Diego and Tijuana, we explored the differential effects of wildfire smoke on cardio-respiratory hospitalizations in these two distinct populations using the October 2007 wildfires as a case study. Results showed that on the absolute scale, the number of cases driven by wildfire smoke in the Municipality of Tijuana was much lower than in San Diego County, however, when considering the relative increase, Tijuana showed 6 times higher increase in hospitalizations (although the estimates were not precise due to small sample sizes). Although the data were not completely comparable between both sides of the border, these results suggested a higher risk of wildfire smoke on cardio-respiratory hospitalizations in Tijuana, likely driven by the higher poverty level, lower education, and general higher social marginalization.

For the third aim, we explored the potential role of wildfire smoke in driving COVID-19 mortality in the San Diego-Tijuana border region. We also applied synthetic control methods to study the effect of the major 2020 California wildfire smoke event that brought dense smoke to the region concurrently with the COVID-19 pandemic. The results did not show a strong or precise association between wildfire smoke on COVID-19 mortality nor did they show a differential effect across the border. These results add to previous literature showing that the effect of smoke or air pollution on COVID-19 is not consistent across regions (Zhou, Josey et al. 2021, Schwarz, Dimitrova et al. 2022). These results highlight the need to continue to study the compounded impacts of extreme weather events and COVID-19 to understand what makes certain regions susceptible and others resistant to these effects.

This dissertation advances our knowledge of the differential effects of extreme weather across socio-demographically diverse populations. The implications of this work are threefold. First, the results can be used to better understand the public health expressions of extreme weather events and can help inform the hypothesized etiologic mechanism for its effects, particularly in the context of COVID-19 as its underlying risk factors are not well understood. Second, the findings can be used to inform policies to best prioritize at-risk populations at the sub-regional scale and advocate for harmonized cross-border efforts to protect populations from the unequal burden of these exposures. Lastly, we hope the methodological approaches implemented in this work can serve as a model that can be applied to other regions of the world and continue to produce local and regional evidence of the health impacts of extreme weather events in low and middle-income contexts.

5.2 Implications

5.2.1 Epidemiological and etiologic contributions

Results from this dissertation contribute to the epidemiological literature by quantifying the health effects of extreme weather events in a region with few previously published studies and using a unique border context to infer some of the drivers of differential effects. It also explores a hypothesized link between wildfire smoke and COVID-19 mortality for which the causal relationship has not yet been fully established. The results confirm some previously recognized vulnerability factors from existing literature in a new setting and population and differ from some associations observed in other settings and populations. This can strengthen our understanding of some of the epidemiological and etiological relationships between social conditions, climate, and infectious disease.

From an epidemiological perspective, many of the results from the studies in this dissertation are consistent with existing studies from other contexts. Poverty, education, and social conditions are known effect modifiers in the association between climate risks and health outcomes particularly when it comes to extreme heat (Bell, O'Neill et al. 2008, Benmarhnia, Deguen et al. 2015, Gronlund, Berrocal et al. 2015) and also for wildfire smoke (Rappold, Cascio et al. 2012, Rappold, Reyes et al. 2017). Revealing social vulnerability factors that are effect modifiers in these relationships is critical not only to reveal the potential etiological mechanisms and what may drive the observed effects but also to inform efforts prioritizing individuals and communities that are most susceptible to these effects.

The differential vulnerability to extreme heat observed in different regions of Mexico is an important contribution to evidence of climate impacts in environmental epidemiology. By using municipality-level census data, we were able to show that populations living in areas with lower education, older population demographic, higher marginalization, and poorer housing conditions were more vulnerable to heat effects. This is consistent with recent research conducted in various countries including Spain (López-Bueno, Navas-Martín et al. 2022), Scotland (Wan, Feng et al. 2022), the US (Manware, Dubrow et al. 2022), Australia (Adnan, Dewan et al. 2022), Finland (Kollanus, Tiittanen et al. 2021) Germany (Laranjeira, Göttsche et al. 2021), and England (Gasparrini, Masselot et al. 2022). Across all these studies, social deprivation and poverty are associated with higher heat-related effects. However, a study conducted for cities in nine Latin American countries found unexpected patterns with higher poverty levels indicating decreased vulnerability to the impacts of temperature on mortality (Bakhtsiyarava, Schinasi et al. 2023). The etiological mechanism for differential vulnerability is related to a combination of factors including that social deprivation often is accompanied by a higher rate of pre-existing health conditions, reduced risk perception of the detrimental impacts of heat, and diminished capacity to respond to the threat. Our results confirm that social deprivation is an important predictor for heat-mortality effects in Mexico which highlights the need to continue to prioritize these populations. Although the majority of findings from this analysis were consistent with previous literature from other areas, we did not find that higher unemployment rates were associated with increased heat effects, and even suggested a lower effects. Several previous studies included unemployment in the development of a social deprivation index along with other measures (López-Bueno, Navas-Martín et al. 2022, Manware, Dubrow et al. 2022). Our results from Mexico indicate that unemployment could be considered a separate measure; there may be other factors such as occupational-related heat effects that may also explain this result and would need to be further explored in future work.

One of the reasons for the lower quantity of evidence from low and middle-income countries is that there is not always high-quality data available to study some environmental epidemiological questions. With the surge in the availability of satellite data in recent years, there are numerous options to substitute direct measurements with remote sensing products for environmental data. However, when conducting epidemiological analyses, we are often limited by the health data available and its spatial and temporal consistency and quality. I came across this challenge in the analysis investigating the effects of smoke on cardio-respiratory hospitalizations in the border region. Although the paper is limited by the generalizability and quality of data used in Tijuana which is only from one healthcare system and not available at a fine spatial resolution, we hope it will serve as a contribution to demonstrate how epidemiological datasets that may have some biases or data quality issues can still be utilized to answer some study questions. By focusing on one acute wildfire event that affected the entire border region transiently, we capitalized on the day-to-day change in cardio-respiratory hospitalizations over a short time frame and focused on the relative change to limit the potential drawbacks of this dataset. Although many regions of the world may not have access to high-quality epidemiological datasets, we must use what is available to best estimate these impacts with existing data.

When studying the novel question of the association between wildfire smoke and COVID-19 mortality, no major effects were observed in either San Diego or Tijuana. This is not consistent with previous work that has shown air pollution and wildfire smoke to exacerbate COVID-19 incidence and severity (Bourdrel, Annesi-Maesano et al. 2021, Bowe, Xie et al. 2021, Cortes-Ramirez, Michael et al. 2022, Kim, Samet et al. 2022). The proposed etiologic mechanisms for which particulate matter can drive increased COVID-19 mortality by producing oxidative stress, inflammation, and increasing ACE2 receptors (Woodby, Arnold et al. 2021). Recent work has shown a positive effect of $PM_{2.5}$ during wildfires on COVID-19 deaths but only when its interaction between hospital and public resources was considered and greater impacts were observed in areas with high social vulnerability (Yu and Hsueh 2023). Although we did not observe a strong and precise effect of wildfire smoke on mortality in San Diego or Tijuana, our results contribute to the body of evidence showing that there is substantial variation in this relationship. From an etiological perspective, this seems to suggest that certain demographic, environmental, and/or social factors make some populations at risk to these effects and others not. There also could be publication bias in that the articles that are published are those finding positive effects, further clouding the true association. This work will contribute to the body of evidence on this topic and we hope it will motivate future research to further clarify the etiological mechanism and identify what factors are important in explaining the differential result from studies investigating this association.

5.2.2 Policy implications

To decrease the impacts of extreme heat and wildfire smoke on health, many cities and regions implement action plans to provide a framework for response activities during extreme weather events. Heat action plans are effective in reducing mortality during heat waves, particularly in vulnerable populations such as the elderly and those with a low SES (Benmarhnia, Bailey et al. 2016, Benmarhnia, Schwarz et al. 2019). Actions such as opening cooling centers during extreme heat can be critical in protecting those that are most vulnerable in our society (Bedi, Adams et al. 2022). Wildfire smoke forecasting systems have also been shown to be valuable; the BlueSky smoke plume forecast has been used in British Columbia and demonstrated to be effective in the prediction of respiratory health outcomes during a wildfire (Yao, Brauer et al. 2013).

Various measures to decrease the associated impacts are in place in California and the US. The Department of Public Health and California Environmental Protection Agency has established a Heat Adaption Workgroup which includes the development of emergency response guidelines for heat waves (Brown 2013). Additionally, the National Weather Service issues a warning when a Heat Index (combination of heat and humidity) is expected to be 105 degrees Fahrenheit or greater for two or more days (NWS 2018). Heat alert systems are based on this national heat index threshold developed from the temperature-mortality relationship revealed in a few major cities in the US (Guirguis, Gershunov et al. 2014). By using a defined threshold for an entire region, some "hotter" areas may frequently surpass it, and others may never reach the threshold, but this may not correspond to a threshold with the greatest potential to reduce health impacts. Since it has been shown that people living in coastal areas of California are more vulnerable to extreme heat because of their decreased capacity to acclimatize to these extreme weather events, either physiologically or technologically (having air conditioning), the activation threshold may need to be lower in this region when compared to the desert or inland California area (Guirguis, Gershunov et al. 2014). Our results of heat-related effects in Mexico highlight the importance of implementing a heat action plan that accounts for specific social vulnerability factors to protect most at-risk populations.

As for wildfire smoke, to our knowledge, neither San Diego nor Tijuana has an established early warning system or action plan to protect populations during these events (Cunha 2019). The Air Quality Index can be used to evaluate local air and regional air quality conditions during a wildfire event, but no specific communication or intervention is activated based on these exposure levels (Cunha 2019). Strengthening the network of environmental health research in Baja California and San Diego can help increase the preparedness of the region in the context of climate change. Forecast systems for SAWs have been shown to be accurate for a 6-7 day lead time (Jones, Fujioka et al. 2010), which can be useful in the prediction of periods of high wildfire risk. Wildfire and heat wave forecasting systems could be used by policymakers to develop and implement actions to limit the morbidity and mortality attributable to extreme weather in this region. Ideally, integrated early warning systems that account for local environmental measures and predict population exposure to extreme heat and wildfire smoke will be implemented to protect public health on both sides of the border by taking into account local epidemiologic information.

5.2.3 Methodological advances

The methodological approaches applied in this dissertation have not been traditionally used in environmental epidemiology and are novel in their development and application. The within-community matched design with BHM used in Aim 1 was recently applied to study the impacts of extreme weather events and compounded effects of dual environmental exposures (Aguilera, Hansen et al. 2020, Schwarz, Hansen et al. 2021). Until now, this analytical strategy had only been employed for studies in California. In Aim 2 and 3, synthetic control methods are employed that have been recently adapted from econometrics to study the health effects of acute environmental exposures such as wildfire smoke (Schwarz, Dimitrova et al. 2022, Sheridan, McElroy et al. 2022). The application of this approach to an international border region is a novel context to employ these methods. Both of these methodologies have major advantages over traditional approaches to studying these types of events and we hope this dissertation can serve as an illustration of the potential widespread utility of these methods. All datasets and codes that have no restrictions regarding confidentiality have been made available on online repositories (links included at the end of the methods section for each paper) to promote reproducibility and the continued application of these methods.

The benefit of the within-community matched design approach is that it can be used to explore fine-scale spatial differences over a wide area while considering and accounting for spatial patterns in the data. The BHM allows the estimation of localized precision and accounts for spatial autocorrelation. This methodology improves on previously established approaches to study the acute effects of extreme weather events such as the case-crossover (Whitaker, Hocine et al. 2007) and time series analysis (Lu and Zeger 2007) by allowing the investigation of spatial differences across small geographic areas. The within-community matched design can be applied to small geographic units with small samples and the Bayesian modeling extension will allow for increased flexibility and precision. Studying the fine spatial differences in effects was found to be extremely valuable as relying on overall measures is not sufficient to understand the magnitude and significance of the effect. Additionally, this can allow the exploration of what vulnerability factors play a role in the observed spatial differences. We hope this methodology can be applied to other regions and datasets to continue to reveal spatial differences in effect measures and what are the specific drivers of variation.

Synthetic control methods have also shown huge potential to study the effects of acute environmental events (Sheridan, McElroy et al. 2022). By capitalizing on the temporality and location of the affected region and identifying and weighting unaffected regions with similar trends before the event occurs, a counterfactual scenario is estimated. The benefit of this approach is that by using the acute temporality of the event, detailed exposure data is not as essential since it instead relies on the timing of the event of interest to identify a counterfactual. Also, any potential confounding in the association of interest will be accounted for by design. This is very advantageous in contexts such as Tijuana where we do not have comprehensive data on wildfire smoke exposure levels or detailed data on potential confounders. This dissertation was the first application of synthetic control methods to study the effects of wildfire smoke in an international border region. Due to the described benefits, it is a unique approach to studying the effects of wildfire smoke in this setting and we hope it can be used as an example of the value of this method and be applied to other international contexts.

5.3 Future directions

This dissertation illustrates the application of novel methods to study the health effects of extreme weather events and associated vulnerability factors in a binational context. We hope it will serve as an example to inform future work and research directions to understand and highlight the association between socioeconomic vulnerability and climate impacts. Extensions of this work can include applying similar methods to other countries and border regions, utilizing novel datasets and measures to increase our understanding of the effects, and developing new methodologies that can further address issues of data availability and quality.

A natural extension of this dissertation could be to expand the border study for wildfire smoke beyond the San Diego-Tijuana border to consider the entire US-Mexico border region. A review of 90 studies on wildfire risk and fuel treatment along the US-Mexico border found that 10% of studies were conducted in California and 1% in Mexico and the remaining studies were spread across the Mexico border with Arizona, New Mexico, and Texas, indicating that wildfire risk in the border region extends far beyond Southern California-Baja California region (Laushman, Munson et al. 2020). By focusing on key wildfire smoke events that affect each portion of the US-Mexico border region, we could expand this work to not only understand cross-border differences but to study variations in effects within and between counties/municipalities in the greater border region.

Data useful in environmental epidemiology has become increasingly available and accessible through the use of remote sensing technologies and satellite products. Novel datasets are now publicly available such as products estimating the absolute and relative wealth for 2.4-km microregions across low and income countries (Chi, Fang et al. 2022). Using these measures as indicators of socio-economic vulnerability to further understand the differential effects of extreme heat and wildfire smoke would be an interesting avenue for future research. The benefits of using this product as compared to the census data are that it has a finer spatial resolution and accounts for different measures of wealth. Additionally, this product can be used to study these effects beyond Mexico in other low and middle-income contexts for which census data may not be available. Furthermore, temperature variability is an important modifier of the heat-mortality association (Wu, Wen et al. 2022). Future work could consider climate extremes and their variation as a potential driver of the differences observed across Mexico.

Lastly, there is a continued need to develop novel methods to address the gaps in evidence on climate and health in low and middle-income regions (Green, Bailey et al. 2019). Transportability has been proposed as a causal inference method to extrapolate effect measures from one environment to another (Hernán and VanderWeele 2011). These methods have been mostly applied in epidemiology to transport experimental results from randomized trials to a target population and increase the external validity of research findings (Cole and Stuart 2010). However, the purpose of the approach is to reuse causal information in a different environment by accounting for observational differences between populations. Therefore, the potential application of transportability methods to advance research in data-limited settings is remarkable. Future research could involve methodological development in this area such as applying transportability methods to a border context.

5.4 Concluding remarks

In conclusion, the adverse health effects of extreme weather events are pervasive through continents and geographies yet they are not equally harmful across populations and settings. Until the 1800s, what we now know as the US did not have borders and North America was one region with diverse geographical characteristics and populations. To best address the health and environmental inequities that persist in our societies and countries, we must recognize the implications of this physical boundary that generates a power dynamic and produces disparities while advocating for politicians, policy-makers, and the public to recognize that we are one region separated by historic exploitation and persistent inequities. We must acknowledge the historic context while working together to protect the populations that are the most vulnerable to the effects of climate change within and between our communities and countries.

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