Differential Cardiopulmonary Health Impacts of Local and Long-Range Transport of Wildfire Smoke

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Abstract We estimated cardiopulmonary morbidity and mortality associated with wildfire smoke (WFS) fine particulate matter (PM$_{2.5}$) in the Front Range of Colorado from 2010 to 2015. To estimate WFS PM$_{2.5}$, we developed a daily kriged PM$_{2.5}$ surface at a 15 × 15 km resolution based on the Environmental Protection Agency Air Quality System monitors for the western United States; we subtracted out local seasonal-average PM$_{2.5}$ of nonsmoky days, identified using satellite-based smoke plume estimates, from the local daily estimated PM$_{2.5}$ if smoke was identified by National Oceanic and Atmospheric Administration’s Hazard Mapping System. We implemented time-stratified case-crossover analyses to estimate the effect of a 10 µg/m$^3$ increase in WFS PM$_{2.5}$ with cardiopulmonary hospitalizations and deaths using single and distributed lag models for lags 0–5 and distinct annual impacts based on local and long-range smoke during 2012, and long-range transport of smoke in 2015. A 10 µg/m$^3$ increase in WFS was associated with all respiratory, asthma, and chronic obstructive pulmonary disease hospitalizations for lag day 3 and hospitalizations for ischemic heart disease at lag days 2 and 3. Cardiac arrest deaths were associated with WFS PM$_{2.5}$ at lag day 0. For 2012 local wildfires, asthma hospitalizations had an inverse association with WFS PM$_{2.5}$ (OR: 0.716, 95% CI: 0.517–0.993), but a positive association with WFS PM$_{2.5}$ during the 2015 long-range transport event (OR: 1.455, 95% CI: 1.093–1.939). Cardiovascular mortality was associated with the 2012 long-range transport event (OR: 1.478, 95% CI: 1.124–1.944).

1. Introduction

The western United States has experienced increases in wildfire occurrence, total fire area burned, and fire size over the previous four decades, leading to worse summer air quality (Dennison et al., 2014; McClure & Jaffe, 2018; O’Dell et al., 2019; Westerling, 2016). Climate change, natural variability, and a history of wildfire suppression all contribute to varying patterns in wildfire burn areas. Most studies predict significant increases in western U.S. wildfire activity under climate change (Brey et al., 2020; Flannigan et al., 2009; J. C. Liu et al., 2016; Spracklen et al., 2009; Westerling et al., 2011; Yue et al., 2013), at least in the next several decades (Spracklen et al., 2009), though there is a degree of uncertainty associated with these forecasts (Brey et al., 2020). The increase in wildfire activity has both direct effects due to the fire and indirect health effects on downwind communities due to wildfire smoke (WFS) exposure. Although mortality due to direct exposure to wildfires has decreased over the last decade (U.S. Fire Administration, 2019), smoke resulting from wildfire events is predicted to have a considerable impact on morbidity and mortality, especially for this region (Ford et al., 2018). Currently, there is substantial epidemiological evidence on the adverse population health effects of WFS in the western U.S. WFS in the West has been associated specifically with respiratory outcomes, including chronic obstructive pulmonary disease (COPD) hospitalizations (J. C. Liu et al., 2017a, 2017b; C. E. Reid et al., 2016, 2019), asthma hospitalizations (Delfino et al., 2009; Gan et al., 2017; C. E. Reid et al., 2016), asthma emergency department visits (Alman et al., 2018; Hutchinson et al., 2018), asthma inhaler use (Elliott et al., 2013; Tse et al., 2015), respiratory symptoms (Kunzli et al., 2006; Mirabelli et al., 2009; Prunicki et al., 2019), and increased inflammatory response in children (Prunicki et al., 2019). Additional evidence suggests that WFS exposure may induce behavioral changes (i.e., changes in medication use patterns) that result in improved lung function in susceptible populations (Lipner et al., 2019). Evidence on WFS and cardiovascular endpoints has been equivocal: several studies in the western U.S. have found elevated risk of cardiovascular events associated with WFS (Resnick et al., 2015; Wettstein et al., 2018), while others have...
found no effect on cardiovascular outcomes (Alman et al., 2009; Gan et al., 2017). Further, studies have found adverse impacts of WFS on noncardiopulmonary outcomes, such as birthweight (Breton et al., 2011; Holstius et al., 2012). However, the episodic and unpredictable nature of wildfires results in difficulty capturing the full spectrum of endpoints that may be associated with smoke exposure.

There are several approaches to estimate WFS PM$_{2.5}$ in epidemiology studies including use of in situ monitors (O’Dell et al., 2019), chemical transport models (Alman et al., 2015), and blended approaches that combine two or more of these data sources (Ford et al., 2017; Lassman et al., 2017). However, though all of these exposure assessment methods have demonstrated utility in WFS epidemiology, like anthropogenic air pollution, WFS is a complex, evolving mixture of particles and gases (Bertschi et al., 2003). WFS particle toxicity is influenced by a number of factors including fire temperature (Kim et al., 2018, 2019), ecoregion of fire origin (J. C. Liu & Peng, 2018), type of biomass (Kim et al., 2019; J. Reid et al., 2005), and age of particles (Diapouli et al., 2014; J. M. Li et al., 2003). Smoke age may be important because molecules in smoke particles and vapors become more oxidized with time, destroying some toxic emitted species and producing others, which could impact overall smoke toxicity (O’Dell et al., 2019, 2020). To our knowledge, particle age or proxies for particle age have not been incorporated into epidemiological studies. Although determinations of particle age and composition are complex given the nature of wildfire health studies, comparison of health impacts of smoke emanating from local fires compared to smoke from long-range transport may provide some insight into differences found across studies, particularly for disparate findings on cardiovascular disease. The Mountain West region of the U.S. is the ideal setting to evaluate health effects of long-range transport and local smoke. WFS is a critical public health issue for the area; the State of Colorado is uniquely positioned to frequently experience both smoke from local fires as well as long-range transport of smoke from fires in the Pacific Northwest and California (Brey et al., 2018b).

In addition to differences in particle toxicity or smoke composition, there may be interventions or behavioral changes that result in differential health effects between smoke from local fires and long-range transport. Emergency response to local fires results in evacuation orders (Laumbach, 2019), recommendations for smoke avoidances (e.g., staying indoors) (Fox et al., 2019), distribution of indoor air filtering equipment (Saks, 2018), recommendations to wear personal protective equipment (Laumbach, 2019), and other guidance to protect populations from the direct and indirect effects of wildfires. These directives may explicitly target vulnerable populations, specifically those who have preexisting disease. In contrast, WFS from long-range transport are not associated with acute disaster responses or warnings and may not have concomitant publication action associated with exposure.

Given these gaps in the literature, this analysis has several aims. The first aim is to assess the effect of WFS on cause-specific cardiopulmonary morbidity and mortality in the state of Colorado from 2010 to 2015. The second aim is to determine if there was a differential effect of WFS on cardiopulmonary morbidity and mortality due to WFS from the local June and July 2012 fires that occurred near the cities of Colorado Springs and Fort Collins, CO, to WFS transported to Colorado from the Pacific Northwest in late summer 2012 and 2015.

2. Methods

2.1. Study Domain

Exposure assessment and epidemiologic analyses were conducted for the Front Range Urban Corridor of Colorado, spanning the urban areas of Fort Collins to Colorado Springs (Figure 1). The varied topography in the Rocky Mountain region of the state results in complex atmospheric circulations that are difficult to simulate via chemical transport modeling (O’Dell et al., 2019). Further, evaluation of chemical transport models is limited outside of the Front Range due to the lack of in situ monitors in the mountains and plains area of the state (Gan et al., 2017; Lassman et al., 2017). Though the selected study domain does not allow for estimation of state-level health effects, ~80% (4.55 million) of Coloradans live on the Front Range and over 50% of PM$_{2.5}$ monitors hosted on the EPA AQS site in Colorado are located in this primarily urban corridor.
2.2. Estimation of Gridded Wildfire Smoke PM$_{2.5}$ and Temperature

We estimated total daily average PM$_{2.5}$ ($\mu g/m^3$) from January 1, 2010 to December 30, 2015 for the contiguous U.S. by kriging PM$_{2.5}$ observations from the Environmental Protection Agency (EPA) Air Quality System (AQS) surface monitors across 15 $\times$ 15 km grids as described in O’Dell et al. (2019). In total, there were 2,849 EPA monitors used in the kriging estimates for the U.S. over these years and 49 in Colorado (of these 13 measure every day, 25 measure every 3rd day, and 11 measure every 6th day). Temperature in Fahrenheit and ozone in parts per billion were estimated on the same 15 $\times$ 15 km grid using AQS monitors from the state of Colorado (Martenies et al., 2019). We then subsetted the kriged grids of PM$_{2.5}$ and temperature to the extent of the Colorado Front Range.

Presence of smoke plumes was assessed using the National Environmental Satellite, Data, and Information Services (NESDIS) Hazard Mapping System Fire and Smoke Product (HMS) (Brey et al., 2018a; Rolph et al., 2009; Ruminski et al., 2006). To estimate the concentration of daily WFS PM$_{2.5}$, we subtracted out a seasonal-median PM$_{2.5}$ concentrations on nonsmoky days for each kriged daily PM$_{2.5}$ estimate in a grid cell if a smoke plume was detected by HMS in the atmospheric column for each day as in O’Dell et al. (2019). The seasonal-median PM$_{2.5}$ concentrations on nonsmoky days was calculated from days where no smoke was detected at that location by HMS, calculated independently for each year and grid cell (O’Dell et al., 2019). If a value of the difference in daily WFS PM$_{2.5}$ and seasonal background when smoke was in the column was less than zero, the WFS PM$_{2.5}$ value was set to zero. This method is fully discussed in O’Dell et al. (2019) and the data set has been previously used in Abdo et al. (2019); Burkhardt et al. (2019, 2020); Gan et al. (2020); Lipner et al. (2019).

2.3. Health Outcomes Data

To assess cardiopulmonary morbidity, we used the Colorado Hospital Association (CHA) hospital discharge data set (medical billing records) provided by the Colorado Department of Public Health and the Environment (CDPHE) for inpatient hospitalizations for the time period from January 1, 2010 to September 30, 2015. Each inpatient hospitalization record contained International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM) diagnosis codes, which were used to identify cardiopulmonary events. Based on prior research (Gan et al., 2017; Rappold et al., 2011), we assessed the following reported ICD-9-CM codes across all available diagnosis code fields within the 2010 to 2015 CHA data set: all respiratory (ICD-9-CM: 460–519, inclusive), including specific codes for asthma (ICD-9-CM: 493), COPD (ICD-9-CM: 490–492, 494, and 496), pneumonia (ICD-9-CM: 480–486), acute bronchitis (ICD-9-CM: 466), all cardiovascular disease (ICD-9-CM: 390–459), including specific codes for arrhythmia (ICD-9-CM: 427), cerebrovascular disease (ICD-9-CM: 430–438), heart failure (ICD-9-CM: 428), ischemic heart disease (ICD-9-CM: 410–413), and myocardial infarction (MI) (ICD-9-CM: 410). For all inpatient events, we limited the source of admission to emergency room or urgent care to limit to acute events and to avoid analyzing scheduled hospitalizations (i.e., planned surgery).

To assess cardiopulmonary mortality, we used vital statistics death records provided by CDPHE from 2010-01-01 to 2015-12-31. International Classification of Diseases, 10th Revision (ICD-10) was used to determine if the underlying cause of death was cardiopulmonary-related. We evaluated the following underlying causes of death: All respiratory (ICD-10: J00–J98, inclusive), asthma (ICD-10: J45–J46), COPD (ICD-10: J44), all cardiovascular (ICD-10: I00–I78), heart failure (ICD-10: I50), cardiac arrest (ICD-10: I46), ischemic heart disease (ICD-10: I20–I25), MI (ICD-10: I21–I22), and cerebrovascular disease (ICD-10: I60–I69).
Events for both cardiopulmonary inpatient hospitalizations and mortality were geocoded by CDPHE to each 15 × 15 km grid cell ID based on the reported residence address of the patient or deceased.

2.4. Statistical Analysis

We evaluated the association between WFS PM$_{2.5}$ and cardiopulmonary inpatient hospitalizations and mortality using a time-stratified case-crossover study design. This study design is a case-only study that compares the likelihood of an event conditioned on exposure and accounts for time-invariant confounders such as sex and age and time-varying confounders such as day of the week (Janes et al., 2005a, 2005b). For both cardiopulmonary inpatient hospitalizations and deaths, we restricted the events to only those occurring in the months of May through October for each year from 2010 to 2015 to coincide with the wildfire season in Colorado. We then created referent observations on the same day of the week in the month for which an event took place. For each event and reference observation we added WFS PM$_{2.5}$ and temperature on that day and the five previous days as the exposures.

The associations between cardiopulmonary hospitalizations and mortality and WFS PM$_{2.5}$ were analyzed using conditional logistic regression to account for between subject variability and assess within subject variability. Single lag models (SLM), and distributed lag models (DLM) were estimated for 6 days (0–5 days post event) of WFS PM$_{2.5}$, 8-h maximum daily average ozone, and temperature exposure. For the SLM, we fit separate models for exposure on each lagged day of exposure. For the DLM, we constrained the lag functions using natural splines and evaluated degrees of freedom using Akaike's information criterion (AIC). These models allowed us to estimate both the cumulative effect and lag-specific effect of 6 days of WFS PM$_{2.5}$ exposure, adjusting for temperature in the same manner. Model odds ratios (OR) and 95% confidence interval (95% CI) were used to interpret the association between WFS PM$_{2.5}$ and cardiopulmonary outcomes. Subsequent stratum-specific DLM were estimated for both inpatient hospitalizations and mortality by sex, and age categories of <15, 15–65, and ≥65. Given the number stratified models possible by outcome, lag period, and SLM and DLM modeling approaches, we implemented cumulative lag models for lags 0–5 days for the age and sex-stratified analyses.

To evaluate if WFS from long-range transport has a differential effect on cardiopulmonary morbidity and mortality compared to WFS from local Colorado fires, we compared health outcomes for 2 years of major WFS events in Colorado, 2012 and 2015. In 2012, Colorado experienced two large local wildfires: the Waldo Canyon fire near Colorado Springs in El Paso County, which occurred from June 23 to July 10, 2012 and the High Park fire near Fort Collins in Larimer County, which occurred from June 9 to June 30, 2012 (Figure 2). We compared cardiopulmonary morbidity estimates using the same time-stratified case-crossover period as described above with a cumulative WFS PM$_{2.5}$ exposure for a 4-day lag period (lag 0–3) for the two counties in which the 2012 fires occurred, for the entire study domain for 2012 in addition to the wildfire season of 2015, in which wildfires in Washington State and British Columbia, Canada in the Pacific Northwest resulted in long-range transport of wildfires smoke to the Colorado Front Range in August and September (Figure 2) (Lindaas et al., 2017). However, the 2012 wildfire season in Colorado included both local fires earlier in the season (May to July) as well as long-term transport later in the season (August to October). To further delineate the impacts of local smoke events and long-range transport for smoke, we also divided the 2012 and 2015 wildfire seasons into an early phase (May to Jul) and a late phase (Aug to Oct) to deter-
mine if there were differences in hospitalization patterns based on timing of the smoke events all using a cumulative 4-day exposure lag. The time-stratified case-crossover approach for the early phase/late phase analysis implemented a shortened referent period (i.e., 3 months) to reflect distinct smoke events for each phase. Mortality estimates were conducted with the same methods as described for the morbidity analysis. However, due to the comparatively small number of mortality events over these 2 years, only all respiratory and all cardiovascular deaths are presented.

All analyses were approved by the Institutional Review Boards at Colorado State University and the Colorado Department of Public Health and Environment. All epidemiological analyses were performed using R (version 3.5.1) specifically, the “tidyverse” package for data carpentry, the “ggplot2” package for mapping and plotting (Wickham & Chang, 2008), the “sf” package for spatial manipulations, analyses, and plotting (Pebesma, 2018), and the “survival” package for conditional logistic regression (Therneau & Lumley, 2014).

3. Results

3.1. WFS PM$_{2.5}$ Concentrations

For the study domain, average daily kriged values of PM$_{2.5}$ across the 6 years of the study was 6.62 µg/m$^3$ (range: 0.00–70.00 µg/m$^3$). For the wildfire-season months (May 1 to October 31), average daily PM$_{2.5}$ was 6.54 µg/m$^3$ (range: 0–70.0 µg/m$^3$). Daily average WFS PM$_{2.5}$ of each grid cell in the study domain by county are presented in Figure 3. WFS PM$_{2.5}$ is elevated across all Front Range counties predominantly.

![Figure 3. Average daily WFS PM$_{2.5}$ in µg/m$^3$ for Front Range counties within the exposure grid from January 2010 to September 2015.](image-url)
during the summer months. Specifically, the daily average WFS PM$_{2.5}$ during the wildfire season period was 0.55 µg/m$^3$ (range: 0.00–65.00 µg/m$^3$). An extended period of WFS PM$_{2.5}$ is evident during the warm season of 2012. However, the highest WFS PM$_{2.5}$ days occurred in Summer 2015, with daily values > 60 µg/m$^3$.

### 3.2. Morbidity Analysis

The number of cardiopulmonary inpatient hospitalizations that occurred in the Front Range study domain during the months of May to October from 2010 to 2015 stratified by age and sex are presented in Table 1. Prevalence of respiratory health outcomes differed by age strata, with the youngest age group (<15) having the highest prevalence of acute bronchitis hospitalizations, the middle age group (15–65) with the highest prevalence of asthma hospitalizations, and the oldest age group (>65) with the highest prevalence of COPD and pneumonia. With regard to cardiovascular hospitalizations, the youngest age strata (<15) represented <1% of all outcomes. Cardiovascular hospitalizations were more prevalent in males, with the exception of MI, the most common cause of cardiovascular hospitalization.

| Inpatient hospitalization outcome | Cases (n) | <15 (%) | 15–65 (%) | >65 (%) | Female (%) | Male (%) |
|---------------------------------|-----------|---------|-----------|---------|------------|----------|
| All respiratory                 | 46,585    | 7.9     | 44.9      | 47.2    | 50.8       | 49.2     |
| Asthma                          | 6,816     | 11.5    | 65.8      | 22.6    | 53.0       | 47.0     |
| Chronic obstructive pulmonary disease (COPD) | 6,656     | 0.2     | 37.3      | 62.5    | 53.6       | 46.4     |
| Acute bronchitis                | 1,884     | 65.3    | 20.1      | 14.5    | 41.9       | 58.1     |
| Pneumonia                       | 14,694    | 5.4     | 40.7      | 53.9    | 51.2       | 48.8     |
| All cardiovascular disease      | 68,356    | 0.3     | 40.2      | 59.5    | 47.8       | 52.2     |
| Arrhythmia                      | 9,958     | 0.4     | 31.9      | 67.6    | 48.8       | 51.2     |
| Cerebrovascular disease         | 10,484    | 0.1     | 48.3      | 51.6    | 34.4       | 65.6     |
| Heart failure                   | 10,090    | 0.1     | 48.2      | 51.7    | 33.7       | 66.3     |
| Ischemic heart disease          | 10,930    | 0.4     | 27.5      | 72.1    | 50.2       | 49.8     |
| Myocardial infarction           | 13,660    | 0.3     | 33.7      | 65.9    | 53.6       | 46.4     |
estimates did not contain the null value (Figure 4). However, for IHD, hospitalization risk associated with WFS PM$_{2.5}$ remained positive at lag day 3. Hospitalizations for MI demonstrated a pattern of increasing association for longer lags of WFS PM$_{2.5}$ (Figure 3), though all confidence intervals for MI included the null value (Figure 4).

### 3.2.2. Distributed Lag Models

DLM for a 10 µg/m$^3$ increase in WFS PM$_{2.5}$ exposure for all hospitalization ICD-9 codes are presented in Figure 5. Similar to the SLM, all respiratory hospitalizations, asthma hospitalizations, and COPD hospitalizations demonstrated a linear association with the exposure with increased lag days until lag 3, with day 0 lags inversely related to WFS PM$_{2.5}$ and day 3 lags positively associated with WFS PM$_{2.5}$. With regard to CVD hospitalizations, all individual outcomes had distinct, nonlinear associations with the exposure, with the exception of hospitalizations for heart failure. All confidence bands for CVD hospitalization outcomes in the DLM included the null value, with the exception of IHD at lag 2 (OR: 1.094, 95% CI: 1.036–1.158) and lag 3 (OR: 1.094, 95% CI: 1.036–1.156). Evaluation of the natural spline indicated that two degrees of freedom led two lowest AIC, but led an overly smoothed model; three degrees of freedom had lower AIC compared to four degrees of freedom for all of models. Comparison of DLM with three and four degrees of freedom did not result in demonstrable differences in model interpretation.
3.2.3. Stratified Analyses

Cardiopulmonary hospitalizations for cumulative WFS exposure over lags 0–5 by age and sex are presented in Figures S1 and S2, respectively. For individuals < age 15, a 10 µg/m³ increase in WFS PM$_{2.5}$ on each of the lag days was associated with an OR of 0.526 (95% CI: 0.240–1.156). However, for the largest age strata by population, ages 15–64, WFS PM$_{2.5}$ was associated with an increase in asthma hospitalizations (OR: 1.338, 95% CI: 1.035–1.731). All other stratum-specific age estimates included the null value. Confidence intervals for all sex-specific estimates based on a cumulative WFS exposure over lags 0–5 included the null value.

3.3. Mortality Analysis

The number of deaths with an underlying cardiopulmonary cause that occurred in the Colorado Front Range counties during the months of May to October from 2010 to 2015 are presented in Table 2. Deaths with an underlying cardiovascular cause were more than twice as common than deaths with an underlying respiratory cause. Individuals aged 65 and older represented the highest proportion of mortality outcomes for all outcomes. Females had a higher percentage of deaths for all respiratory outcomes, though asthma deaths for this time period were relatively rare. With regard to cardiovascular outcomes, females were more likely to die from cerebrovascular disease and heart failure compared to males; males had relatively higher mortality from IHD and MI.
3.3.1. Single Lag Models

Associations of cardiopulmonary deaths and WFS PM$_{2.5}$ using SLM are presented in Figure 2. All point estimates for respiratory causes of death (total and cause-specific) included the null value, with the exception of asthma mortality on lag day 3 (OR: 3.30, 95% CI: 1.03–10.56). Single lags for all CVD mortality codes were positively associated with WFS PM$_{2.5}$, though only the confidence intervals for cardiac arrest on lag day 0 did not include the null value (OR: 2.93, 95% CI: 1.11–7.74). Asthma deaths and cardiac arrest deaths were the two smallest cause-specific mortality categories for the study period (n = 101 and n = 157, respectively, Table 2).

3.3.2. Distributed Lag Models

DLM for all causes of cardiopulmonary death included wide confidence intervals that contained the null value for each daily estimate (Figure S3). Asthma and cardiac arrest deaths were not included in the analysis due to small counts and instability in the DLM estimates.

3.3.3. Stratified Analyses

Associations between mortality risk and cumulative WFS PM$_{2.5}$ for lag days 0–5 stratified by age and sex are presented in Figures S4 and S5, respectively. Age-stratified cardiovascular mortality are presented only for ages 15–64 and 65 and older due to small counts for the age <15 years stratum. All stratum-specific estimates included the null value.

3.4. Effects of Local Versus Long-Range Transport WFS PM$_{2.5}$

3.4.1. Morbidity Analysis

Results evaluating the relation between cardiopulmonary hospitalizations and cumulative lags for WFS PM$_{2.5}$ for the 2012 local Colorado fires (Waldo Canyon Fire [El Paso County] and High Park Fire [Larimer County]), the 2012 wildfire season, and the 2015 wildfire season are presented in Figure 6. For the counties encompassing the two local fires, ORs for all respiratory hospitalizations were close to the null value; risk for asthma and COPD hospitalizations were both <1.0 with wide confidence intervals. However, for the 2012 wildfire season estimate that includes the full study domain, asthma hospitalizations were inversely associated with a 10 µg/m$^3$ increase in WFS PM$_{2.5}$ (OR: 0.716, 95% CI: 0.517–0.993). In contrast, we observed a significant association for the cumulative lag effect of 4 days of 10 µg/m$^3$ increase in WFS PM$_{2.5}$ on asthma inpatient hospitalizations for the 2015 wildfire season estimate (OR: 1.455; 95% CI: 1.093–1.939). All other observations had confidence intervals that included the null value.

### Table 2

| Underlying cause of death | Cases (n) | <15 (%) | 15–65 (%) | >65 (%) | Female (%) | Male (%) |
|---------------------------|-----------|---------|-----------|---------|------------|----------|
| All respiratory           | 7,025     | 0.4     | 14.9      | 84.7    | 50.5       | 49.5     |
| Asthma                    | 101       | 4.0     | 44.6      | 51.5    | 68.3       | 31.7     |
| Chronic obstructive pulmonary disease (COPD) | 4,056     | 0.0     | 12.4      | 87.6    | 51.2       | 48.8     |
| All cardiovascular disease| 18,122    | 0.2     | 20.0      | 79.8    | 49.9       | 50.1     |
| Heart failure             | 1,395     | 0.1     | 6.3       | 93.6    | 59.5       | 40.5     |
| Cardiac arrest            | 157       | –       | 18.5      | 81.5    | 58.0       | 42.0     |
| Ischemic heart disease    | 7,520     | –       | 23.2      | 76.8    | 39.9       | 60.1     |
| Myocardial infarction     | 1,948     | –       | 25.4      | 74.6    | 40.9       | 59.1     |
| Cerebrovascular disease   | 3,443     | 0.3     | 14.6      | 85.1    | 60.1       | 39.9     |

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3.4.2. Early Season and Late Season Morbidity Analysis

Morbidity estimates for the 2012 and 2015 fire seasons early season and late season for the entire study domain is presented in Figure 7. For the early months of the 2012 wildfire season, characterized by local fire activity, confidence intervals for all categories of respiratory and cardiovascular outcomes included the null value. The OR for asthma hospitalizations for this period were below one, but confidence intervals included the null value (OR: 0.721, 95% CI: 0.418–1.246). For the late phase of the 2012 wildfire season, which was characterized by long-range transport of smoke from the Pacific Northwest, point estimates for asthma hospitalizations remained below one, though the confidence included the null value (OR: 0.680, 95% CI: 0.444–1.041). For the early months of the 2015 wildfire season, characterized by a limited number of long-range smoke transport events all point estimates, except for pneumonia, were null or below the null value with wide confidence intervals. However, for the late phase of 2015 wildfire season, hospitalizations followed expected patterns, with increases in odds ratios of asthma hospitalization (OR: 1.568, 95% CI: 1.125–2.185) and IHD (OR: 1.295, 95% CI: 1.020–1.644).

3.4.3. Mortality Analysis

Estimates of the relation of cardiopulmonary mortality and WFS PM¿.5 for 2012 local fires, the 2012 wildfire season and the 2015 wildfire season are presented in Figure 8. Respiratory mortality for both 2012 local fires were less than 1.0; for the High Park fire, the odds ratio for respiratory deaths were 0.275 (95% CI: 0.075–1.006). Odds ratios for cardiopulmonary deaths for long-range transport smoke in 2015 were less than
1.0, though confidence intervals contained the null value. In contrast, risk of cardiopulmonary deaths was elevated for the 2012 wildfire season, though point estimates were close to the null value.

3.4.4. Early Season and Late Season Mortality Analysis

Cardiovascular and respiratory mortality estimates associated with a WFS PM$_{2.5}$ cumulative lag 0–3 by early season and late season for the 2012 and 2015 seasons are presented in Figure 9. The 2012 early season, characterized by local fires, resulted in respiratory and cardiovascular mortality results that were null (respiratory: OR: 0.994, 95% CI: 0.631–1.565; cardiovascular: OR: 0.952, 95% CI: 0.722–1.256). However, WFS PM$_{2.5}$ from the 2012 late season, characterized by long-range smoke transport, was associated with an increase in cardiovascular disease deaths (OR: 1.478, 95% CI: 1.124–1.944). Confidence intervals for all 2015 mortality estimates included the null value.

4. Discussion

In our analysis of cardiopulmonary morbidity and mortality over a 6-year period on the Front Range of Colorado, we found that WFS PM$_{2.5}$ exposure was positively associated with hospitalizations for all respiratory outcomes combined, asthma, COPD and acute bronchitis; and cardiovascular morbidity, including hospitalizations for all CVD outcomes, cerebrovascular outcomes, heart failure, and IHD. Further, our analysis demonstrated that deaths from asthma and MI were associated with WFS PM$_{2.5}$. Lastly, these data indicated
that there are differential health effects at the county level from local fires compared to health effects from long-range transport of smoke. To our knowledge, this is the first paper to investigate health effects of both long-range transport and local WFS, as well as the first to demonstrate a WFS-related mortality effect in the U.S.

A number of studies in Colorado and the western U.S. have demonstrated adverse health outcomes associated with WFS exposure (Alman et al., 2019; A. H. Liu et al., 2007; J. C. Liu et al., 2016; C. E. Reid et al., 2016; Stowell et al., 2019; Wettstein et al., 2018). However, direct comparability between our study and other studies is limited by differences in exposure assessment methods, categories of outcomes evaluated, and demographic characteristics of the study population. Two previous studies in Colorado that investigated combined emergency department visits and hospitalizations in Colorado over the 2012 wildfire season (Alman et al., 2019) and over 2011–2014 wildfire seasons (Stowell et al., 2019) both demonstrated increased odds of asthma outcomes for all age groups combined: an increase of 7% per 10 µg/m³ increase, and 8% per 1 µg/m³ increase, respectively. However, the 2012 fire season study implemented a chemical transport model for WFS exposure assessment, and the subsequent study implemented a blended exposure model that included chemical transport models, satellite data, and in situ monitoring, which may have resulted in an effect estimate an order of magnitude higher than found in other studies. Our previous research demonstrated that epidemiologic analyses for WFS morbidity are sensitive to the choice of exposure model, which can result in distinct inference regarding the exposure response relationship (Gan et al., 2017). Further, the combined emergency department and hospitalizations evaluated in these papers are difficult to compare to our morbidity analyses, which only included hospitalizations. Colorado did not have complete state-wide reporting of ED claims during the time period used for this study. Colorado’s ED visit reporting

**Figure 8.** Cumulative effect of same day exposure to lag day 3 of exposure of a daily 10 µg/m³ increase in WFS PM$_{2.5}$ on the risk for a cardiopulmonary mortality for each WFS event.
GeoHealth

began in 2011 but became complete only in 2014. Of note is that ED visits that were subsequently admitted to the hospital would be captured in these hospitalization data. Thus, ED visits generally represent either less serious complications (barring those who may die in the ED), and acknowledge the data used in this study reflect more serious complications/outcomes. A recent Colorado-based analysis included the same exposure assessment methodology as described in this article (Lipner et al., 2019). In contrast to our population-based study, Lipner et al. evaluated pulmonary function in a cohort of patients with moderate to severe asthma. Again, these fundamental differences in study design limit direct comparisons to our findings.

Our morbidity analysis included some novel associations between WFS and respiratory outcomes, specifically for acute bronchitis in children. Our previous work indicated a significant increase in hospitalizations for acute bronchitis for males, but not for children under 15 or any other age strata (Gan et al., 2017). Several studies have investigated general respiratory outcomes, but effect estimates for specific disease classification codes were not available (J. C. Liu et al., 2017a, 2017b). Other studies in the western U.S. have investigated specific claims codes for bronchitis as an outcome associated with WFS (Alman et al., 2019), but no significant findings were detected and age-stratified data were not available. Several studies have identified an association between anthropogenic PM$_{2.5}$ and early life respiratory infections (Darrow et al., 2014; Karr et al., 2009), but the exact mechanisms remain unknown. Several outbreak models have demonstrated that viral and bacterial particles may travel on airborne particles (Hagerman et al., 2018; Schimmer et al., 2010), thus increasing potential infection. However, as acute bronchitis cases may have precipitating factors other than viral exposures, smoke inhalation may be the primary cause of the outcome.

**Figure 9.** Cumulative effect of same day exposure to lag day 3 of exposure of a daily 10 µg/m$^3$ increase in WFS PM$_{2.5}$ on the risk for a cardiopulmonary mortality for all Front Range Counties, by early season (May 1 to Jul 31) and late season (Aug 1 to Oct 31), 2012 and 2015 wildfire seasons.
Though WFS-morbidity studies routinely evaluate the relation between smoke exposure and cardiovascular outcomes, a limited number of WFS studies have found evidence of cardiovascular health effects associated with smoke in the U.S. (Rappold et al., 2011) and specifically in the Western U.S. (Wettstein et al., 2018). A study conducted throughout eight air basins in California during the 2015 wildfire season using satellite-derived aerosol optical depth data to categorically classify smoke as light, medium, and dense found increases in cardiovascular and cerebrovascular emergency department visits in adults over age 65 (Wettstein et al., 2018). Our data confirmed an association of WFS with cardiovascular outcomes, in which increases in WFS were associated with all CVD outcomes, including hospitalizations for cerebrovascular events, heart failure, and MI. Unlike the California study, our analyses did not result in age-stratified effect estimates that reached statistical significance. However, there were several categories, including MI, where data suggested that adults ages 15–64 were at higher risks of CVD hospitalizations compared to adults ages 65 and older. The lack of significance for age-specific outcomes in this study is mostly likely related to power: over the six seasons of the study, ~68,000 CVD hospitalizations were reported for Colorado; the analysis for the 2012 California fire season included ~361,000 CVD emergency department visits. In contrast to these studies, two larger regional-based studies that evaluate all Medicare beneficiaries in Western U.S. counties over 4 years found WFS to increase the risk for respiratory hospitalizations (J. C. Liu et al., 2017a, 2017b), although no associations were observed with cardiovascular hospitalizations. In addition to differences in study outcomes on CVD hospitalizations, our reports confirm findings that the lags for PM2.5 exposure and hospitalizations tend to be shorter for CVD hospitalizations compared to respiratory hospitalizations (Braga et al., 2001; Dominici et al., 2006).

In addition to morbidity outcomes, our data suggest that there may be some association between WFS exposure and mortality for both asthma and cardiac arrest. Two population-based studies in Australia found an increased risk of mortality following bushfire smoke exposure (Johnston et al., 2011; Morgan et al., 2010); while a metaanalysis conducted with data from 10 southern European cities found suggestion of an increase in cardiovascular, but not respiratory, mortality (Morgan et al., 2010). To date, the relationship between the impact of WFS on cardiopulmonary mortality in the U.S. has not been extensively evaluated. A study that investigated potential increases in mortality in the Metropolitan Denver area following the 2001 Hayman fire, the largest fire (by area) in Colorado history, did not find increased daily mortality counts in the counties impacted by WFS compared to unaffected counties, though extensive exposure assessment was not conducted as part of this analysis (Vedal & Dutton, 2006). Future studies should expand secondary outcomes to include vital statistics data in additional to hospitalization and emergency department data.

The inclusion of multiple fire seasons in this analysis allowed us to differentiate WFS-associated health effects from local fire from effects associated with the long-range transport of smoke. For the 2015 season, where the preponderance of smoke events was from long-term transport, morbidity outcomes followed an expected pattern, with increased respiratory and cardiopulmonary hospitalizations. For 2012 local fires, county-specific and state-wide analyses suggested increased smoke exposure had a protective effect for asthma morbidity and mortality. The 2012 fire season in Colorado was characterized by smoke from both local fires and from fires in the Pacific Northwest and California (Val Martin et al., 2013). However, the CO fires were early in the summer (June), while the long-range transport of smoke occurred later in the summer (August and September). The odds ratios less than one for asthma hospitalizations for the 2012 analyses could be explained by several phenomena. First, these results could suggest that wildfires from local smoke may have a differential effect on behavior. The early summer fires in Colorado were directly upwind of two of the states’ major population areas: The Waldo Canyon fire started four miles northwest of Colorado Springs (2012 population: ~432,000), and the High Park fires started in the Roosevelt National Forest in Larimer County upwind from the county’s largest city, Fort Collins (2012 population: ~149,000). The mountain communities due east of the High Park fire were evacuated for 3 weeks during the event, while 30,000 residents of Colorado Springs were evacuated during the Waldo Canyon fire. These events were well covered through media outlets and state and local health departments, as well as local fire districts. We hypothesize that due to the imminent direct effects of the fire, the combination of media coverage and evacuation orders removed vulnerable populations from the area, thus resulting in odds ratios that appear to be protective. Further, fresh smoke is characterized by a distinct odor due to the compounds guaiacol and o-cresol (McKenzie et al., 1995). These odors may signal avoiding or mitigating activities for downwind communities that are not under immediate fire danger. As long-range smoke events are not associated with immediate
fire danger, publicly issued smoke warnings are less frequent, or may be issued from less utilized sources, such as local air districts. This hypothesis is supported by findings from Lipner et al., who found that lung function measures for a cohort of patients with asthma in Colorado improved one-lag day post local smoke event (Lipner et al., 2019). The authors suggest that awareness of smoke may lead to improved adherence to medication or additional use of rescue medication, which may improve pulmonary function.

An alternative explanation for differences in health effects found in our analysis may be the distinct chemistry of transported smoke and fresh or local smoke. WFS contains compounds, including potassium (Lee et al., 2010) and levoglucosan (Sullivan et al., 2008) that can distinguish it from other PM$_{2.5}$ sources. However, the chemical speciation of WFS is difficult to conduct retrospectively over large areas, and easier to characterize in experimental studies or in exposure modeling research. As such, there is a considerable lack of congruence between the toxicological, exposure assessment, epidemiological literature on relative toxicity of WFS. For example, Wegesser et al. found that in an in vivo experiment, mice exposed to WFS had significantly worse histological outcomes compared to mice who were exposed to equal doses of background PM$_{2.5}$ (Wegesser et al., 2009). However, an epidemiological study of cardiopulmonary hospitalizations demonstrated no significant differences in PM$_{2.5}$ mass effects comparing smoke days and nonsmoke days (DeFlorio-Barker et al., 2019). A recent study in the Western U.S. found that the composition of WFS plumes were distinct depending on the ecoregion of origin (J. C. Liu & Peng, 2018). Extending this finding, an experimental study demonstrated that PM from different fuels and combustion phases (e.g., flaming vs. smoldering) have substantial differences in lung toxicity and mutagenic potency (Kim et al., 2018). Further, particle toxicity has been found to differ by age. Specifically, photochemical transformations of primary PM emissions with atmospheric aging enhance the toxicological potential of primary particles in promotion of oxidative stress, which and leading to subsequent damage in cells (Verma et al., 2009). In an experimental study, aged naphthalene- and α-pinene derived secondary organic aerosols (SOA) were more toxic compared to fresh SOA (Chowdhury et al., 2018). The relatively higher levels of peroxide in aged SOA are considered to have adverse inflammatory effects through an oxidative pathway. In addition, aged diesel exhaust PM have been demonstrated to have increased oxidative potential compared to fresh particles (Q. A. Li et al., 2009; Rattanavaraha et al., 2011). However, compositional differences in fresh smoke v. aged smoke were observed in the Western Wildfire Experiment for Cloud Chemistry, Aerosol Absorption, and Nitrogen (WE-CAN) (O’Dell et al., 2020). In highly concentrated fresh plumes with physical ages as young as 20 min, a number of Hazardous Air Pollutants (HAPs, e.g., formaldehyde, acrolein, and benzene) exceeded the California EPA reference exposure levels for no adverse effects. However, in medium and age smoke, no HAPs were found to exceed acute exposure limits (O’Dell et al., 2020). Experimental studies have demonstrated that these HAPs are associated with oxidative stress and dampened immune response (Wen et al., 2016). Thus, relative effects of WFS composition on population health outcomes remains an area of considerable uncertainty.

A third explanation for outcome differences may be exposure misclassification. Local fires have thinner plumes than long-range transport plumes. Local fire plumes, particularly in sparsely monitored areas may not be detected by PM$_{2.5}$ monitors and, as a result, not captured in the kriged surface. Alternatively, a local plume may be detected by a monitor but be thin; kriging may spread the smoke to a larger area than the real plume. As the exposure misclassification is likely to be nondifferential, results may be biased toward the null value. Compared to our previous studies (Ford et al., 2018; Gan et al., 2017, 2020), misclassification of exposure may be greater due to our reliance on kriged models compared to blended estimates with multiple inputs. There are several reasons why we did not implement the blended model in this study. A chemical transport model, WRF-Chem, is highly variable and sensitive to model inputs, and did not perform any better than the kriged estimates only (e.g., Lassman et al., 2017). Satellite overpasses occurred mid-day and do not offer additional information on the 24-h exposure. Additionally, the kriged data set used here has been shown to perform well over broad regions of the U.S. and across multiple seasons (e.g., O’Dell, 2018), and it has now been used in several studies for estimating exposure (e.g., Abdo et al., 2019; Burkhardt et al., 2019, 2020; Lipner et al., 2019).

Common to other WFS studies, our analysis is subject to several limitations. Morbidity and mortality records available from states likely reflect a relatively small fraction of total health effects of PM$_{2.5}$ exposure and limits inference on the true burden of morbidity attributable to smoke. Individual records were not able
to be linked within season or across years, thus limiting the ability to develop inferences on the cumulative effects of multiple wildfire seasons. Lagged effects, particularly for outcomes such as hospitalizations, may be influenced by processes in the health care system, in which a person can be treated in the emergency department, but not admitted to the hospital immediately. In addition to issues with the health data, there are still not consensus methods on how to quantify WFS PM$_{2.5}$. The method used in this paper, which subtracts median seasonal PM from the daily PM estimates by definition results in some exposure misclassification. Lastly, our study did not have sufficient power to detect effect estimates that did not include the null value for DLM, which control for prior and next day effects, unlike single-lag models.

In conclusion, in a 6-year study of health effects of WFS on cardiopulmonary morbidity and mortality in Colorado, we found increases in respiratory and cardiovascular morbidity, increases in respiratory and cardiovascular mortality, and differential effects on health outcomes from local smoke plumes compared to smoke from long-range transport. This analysis has important implications for public health emergency messaging on health effects of WFS, particularly in states affected by local wildfires and downwind of large fires in the western U.S.

**Conflict of Interest**

The authors declare no conflicts of interest relevant to this study.

**Data Availability Statement**

Kriged wildfire smoke PM$_{2.5}$ estimates can be found at: http://dx.doi.org/10.25675/10217/193258.

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