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The delayed effect of wildfire season particulate matter on subsequent influenza season in a mountain west region of the USA

Erin L. Landguth[a,*], Zachary A. Holden[b], Jonathan Graham[a,c], Benjamin Stark[c], Elham Bayat Mokhtari[c], Emily Kaleczyc[d], Stacey Anderson[e], Shawn Urbanski[f], Matt Jolly[f], Erin O. Semmens[a], Dyer A. Warren[a], Alan Swanson[a], Emily Stone[c], Curtis Noonan[a]

[a] Center for Population Health Research, School of Public and Community Health Sciences, University of Montana, 32 Campus Drive, Missoula, MT 59812, USA
[b] US Forest Service, Missoula, MT 59807, USA
[c] Mathematical Sciences, University of Montana, 32 Campus Drive, Missoula, MT 59812, USA
[d] Montana Department of Livestock, PO Box 202001, Helena, MT 59620, USA
[e] Communicable Disease Control and Prevention Bureau, Department of Health and Human Services, Helena, MT 59620, USA
[f] Rocky Mountain Research Station, Fire Sciences Laboratory, US Forest Service, Missoula, MT, 59808, USA

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ABSTRACT

Particularly in rural settings, there has been little research regarding the health impacts of fine particulate matter ($PM_{2.5}$) during the wildfire season smoke exposure period on respiratory diseases, such as influenza, and their associated outbreaks months later. We examined the delayed effects of $PM_{2.5}$ concentrations for the short-lag (1–4 weeks prior) and the long-lag (during the prior wildfire season months) on the following winter influenza season in Montana, a mountainous state in the western United States. We created gridded maps of surface $PM_{2.5}$ for the state of Montana from 2009 to 2018 using spatial regression models fit with station observations and Moderate Resolution Imaging Spectroradiometer (MODIS) aerosol optical thickness data. We used a seasonal quasi-Poisson model with generalized estimating equations to estimate weekly, county-specific, influenza counts for Montana, associated with delayed $PM_{2.5}$ concentration periods (short-lag and long-lag effects), adjusted for temperature and seasonal trend. We did not detect an acute, short-lag $PM_{2.5}$ effect nor short-lag temperature effect on influenza in Montana. Higher daily average $PM_{2.5}$ concentrations during the wildfire season was positively associated with increased influenza in the following winter influenza season (expected 16% or 22% increase in influenza rate per 1 $\mu g/m^3$ increase in average daily summer $PM_{2.5}$ based on two analyses, $p = 0.04$ or 0.008). This is one of the first observations of a relationship between $PM_{2.5}$ during wildfire season and influenza months later.

1. Introduction

The last two decades have seen a dramatic increase in wildfire activity across much of the western United States (US), a trend that has been attributed to decreasing summer precipitation and increasing temperatures (Westerling et al., 2006; Abatzoglou and Williams, 2016; Holden et al., 2018). Communities impacted by smoke from nearby and distant wildfires experience high episodic exposures to fine particulate matter (aerodynamic diameter < 2.5 μm; $PM_{2.5}$) with concentrations often exceeding 24-hour ambient air quality standards for extended periods (Liu et al., 2015). While recent studies have shown air quality improving for the contiguous US from the reduction of industrial and vehicular emissions (McClure and Jaffe, 2018; O'Dell et al., 2019), air pollution in wildfire-prone areas, particularly in the mountain west region of the US, has increased and is projected to further worsen due to climate-mediated increases in wildfire activity (Yue et al., 2013; Liu et al., 2016; Ford et al., 2018).

$PM_{2.5}$ is widely known to have significant adverse effects on human health (US EPA 2009; Anderson et al., 2012; Kim and Kabir, 2015), and several studies of $PM_{2.5}$ during wildfires have found similar positive

* Corresponding author.
E-mail addresses: erin.landguth@mso.umt.edu (E.L. Landguth), zachary.holden@usda.gov (Z.A. Holden), benjamin.stark@umontana.edu (J. Graham), jonathan.graham@umontana.edu (B. Stark), elham.bayatmokhtari@umontana.edu (E.B. Mokhtari), EKaleczyc@mt.gov (E. Kaleczyc), SAnderson2@mt.gov (S. Anderson), shawn.p.urbanski@usda.gov (S. Urbanski), matt.jolly@usda.gov (M. Jolly), erin.semmens@umontana.edu (E.O. Semmens), dyer.warren@umontana.edu (D.A. Warren), alan1.swanson@umontana.edu (A. Swanson), emily.stone@umontana.edu (E. Stone), curtis.noonan@umontana.edu (C. Noonan).

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associations with respiratory effects, including increased hospitalization and medication use for asthma, increased urgent care visits for cardiopulmonary outcomes and increased mortality (for reviews see Liu et al., 2015; Reid et al., 2016; Adetona et al., 2016). Adverse respiratory outcomes associated with wildfire exposure also include hospitalizations and urgent care visits for respiratory infections, pneumonia and bronchitis (Reid et al., 2016). To date, all studies of wildfires have focused on acute health effects with analyses typically not extending beyond a few days lag period.

Wintertime influenza offers an opportunity to evaluate the potential for longer-lag delayed effects of $PM_{2.5}$ associated with smoke from wildfire events. Traditionally, meteorological factors in temperate countries, such as low temperatures and humidity, have been shown to contribute to the risk of influenza outbreaks (Tamerius et al., 2013) and are well correlated with the seasonal changes in the US (Shaman et al., 2010). Recent studies have begun to investigate the associations of $PM_{2.5}$ and influenza. For example, a study in Beijing, China, reported the association between the delayed impact of short-term exposure of $PM_{2.5}$ and monthly influenza cases (Liang et al. 2014). A follow up study found correlations between $PM_{2.5}$ exposure and daily influenza risk by age group in Beijing, China, suggesting a 1-day optimal lag effect (Feng et al., 2016). A more recent study showed consistently increased odds of healthcare encounters for influenza for elevated $PM_{2.5}$ exposure estimates averaged across several lag periods, 0–28 days (Horne et al., 2018). However, to date and particularly in rural settings, there has been little research regarding the health impacts of $PM_{2.5}$ during the wildfire season smoke exposure period on influenza occurrence months later.

While the burden of influenza can vary from season to season, it is estimated that between 9 and 49 million cases of influenza occur each year in the United States. Of these, an estimated 140,000–960,000 hospitalizations and up to 79,000 deaths due to influenza occur each year (www.cdc.gov/flu/about/burden/index.html). In addition, a 2007 review of the economic burden of influenza determined that direct medical costs average around $10.4 billion (Molinari et. al., 2007). In the western US state of Montana, approximately 10,000 cases of influenza are reported each season (approximately October – May; https://www.cdc.gov/flu/about/season/flu-season.htm), but it is likely that the actual number is higher as not all individuals who are infected will seek medical care (MT DPHHS data). In Montana, influenza is associated with approximately 900 hospitalizations and 60 deaths each year (www.cdc.gov/flu/about/burden/index.htm). Since influenza cases are monitored closely by state and federal agencies and the periods between wildfire activity and influenza transmission are offset by weeks to months, we have the opportunity to investigate the potential of $PM_{2.5}$ exposure from wildfire season months to impart impacts weeks to months after exposure.

Wildfires have been identified as the dominant source of elevated surface $PM_{2.5}$ across the Northern Rocky Mountain region (Idaho, Montana, and Wyoming) during the western US wildfire season (Liu et al., 2016; Brey et al., 2018). Here, we define wildfire season as July 1 -September 30. This time period accounts for greater than 90% of annual wildfire emissions across the region (Urbanski et al., 2017, 2018). Inter-annual differences in wildfire activity and wildfire $PM_{2.5}$ emissions result from variability within this time window. Even in the most active fire years, fire burned area and emissions outside July – September are a minimal fraction of the total in the Northern Rocky Mountain region (Urbanski et al., 2018). In Montana, wildfires are the primary $PM_{2.5}$ emission source during the western US wildfire season (Urbanski et al., 2018). The dominant non-wildfire emissions of primary annual $PM_{2.5}$ within Montana were dust from agriculture and unpaved roadways (53%) and prescribed fires (27%), while residential fuel combustion accounted for ~2%, according to the Environmental Protection Agency (EPA) triennial National Emission Inventories (NEI) of 2011 and 2014 (www.epa.gov/air-emissions-inventories/national-emissions-inventory-nei).

The major contributor to short-lag $PM_{2.5}$ exposures during flu season in Montana is biomass smoke exposure generated from wood stoves used for heating throughout the winter months. $PM_{2.5}$ source apportionment modeling has identified wood smoke contributions to be between 56 and 77% of the ambient wintertime $PM_{2.5}$ in multiple communities throughout western Montana (Ward and Lange 2010). Other contributions include dust (1–4%), ammonium nitrate from heavily fertilized agricultural fields and livestock waste (10–20%), sulfate (0–5%), diesel (0–5%), automobiles (0–4%), and unexplained sources (0–4%) (Ward and Lange 2010).

The objective of this study was to evaluate associations between $PM_{2.5}$ and influenza counts at the county level in Montana. Specifically, we developed spatio-temporal $PM_{2.5}$ maps to estimate $PM_{2.5}$ effects for two different time frames: (1) $PM_{2.5}$ exposure 1–4 weeks before influenza cases, hereafter referred to as short-lag $PM_{2.5}$ and (2) $PM_{2.5}$ during the wildfire season 1–10 months before influenza cases, hereafter referred to as long-lag $PM_{2.5}$. We then evaluated associations between the delayed effects of $PM_{2.5}$ for each time frame on influenza counts for counties in Montana for 2010–2018, adjusted for temperature and seasonal trend, in a quasi-Poisson model framework.

2. Methods

2.1. Influenza data

In this time-series analysis, influenza counts in Montana were provided by the Montana Department of Public Health and Human Services. The data used in this study are weekly county-level case counts of positive diagnoses of influenza from all reporting sources, including laboratory confirmations, hospitalizations, and clinical diagnoses. Influenza cases in those of all ages are reported. The Centers for Disease Control do not state the estimated under-reporting of influenza, but do acknowledge that it is largely under-reported (www.cdc.gov/flu/about/burden/how-cdc-estimates.htm). Six small population counties (Musselshell, Petroleum, Judith Basin, Wheatland, Golden Valley, and Fergus) were grouped into what is known as the 'Central Montana Health District' (CMHD). The CMHD and all 50 other Montana counties were included in this study for a total of 51 regions which will be referred to as counties for simplicity. In total, the influenza data for Montana produced 51 counties over 8 years or 408 'clusters' of time series. Mean, minimum, and maximum case counts of each week for all counties are shown in Fig. 1A. Fig. 1B depicts flu incidence per 1,000 in each county for an example flu season period (October 1, 2015 – April 30, 2016) for each county in Montana.

In temperate climates and during the northern latitude summer months (May-August), influenza counts are at their minimum, whereas winter months are the predominant season for infection due to cold temperatures, low humidity, and increased indoor crowding (Finkelman et al. 2007; Cauchemez et al. 2008; Tamerius et al. 2013). We considered two datasets for our modeling purposes. For our first dataset, we excluded flu counts from May 1 – August 30, as these primarily contained either unreported cases or 0 counts. This dataset hereafter referred to as the 'complete' dataset (n = 12,474) had an average flu season length of 31 weeks. Our second dataset accounted for the start and end of each flu season, further reducing the zero counts in the flu data. The second dataset hereafter referred to as the 'reduced' dataset (n = 6,308) was subset into vectors of flu counts with a single leading zero and trailing zero for each flu season within each year and each county. The reduced data set had an average flu season length of 15.5 weeks.

2.2. $PM_{2.5}$ model for Montana

We used daily $PM_{2.5}$ measurements from air quality monitoring stations, combined with satellite retrievals of aerosol optical thickness from the Moderate Resolution Imaging Spectroradiometer (MODIS) to

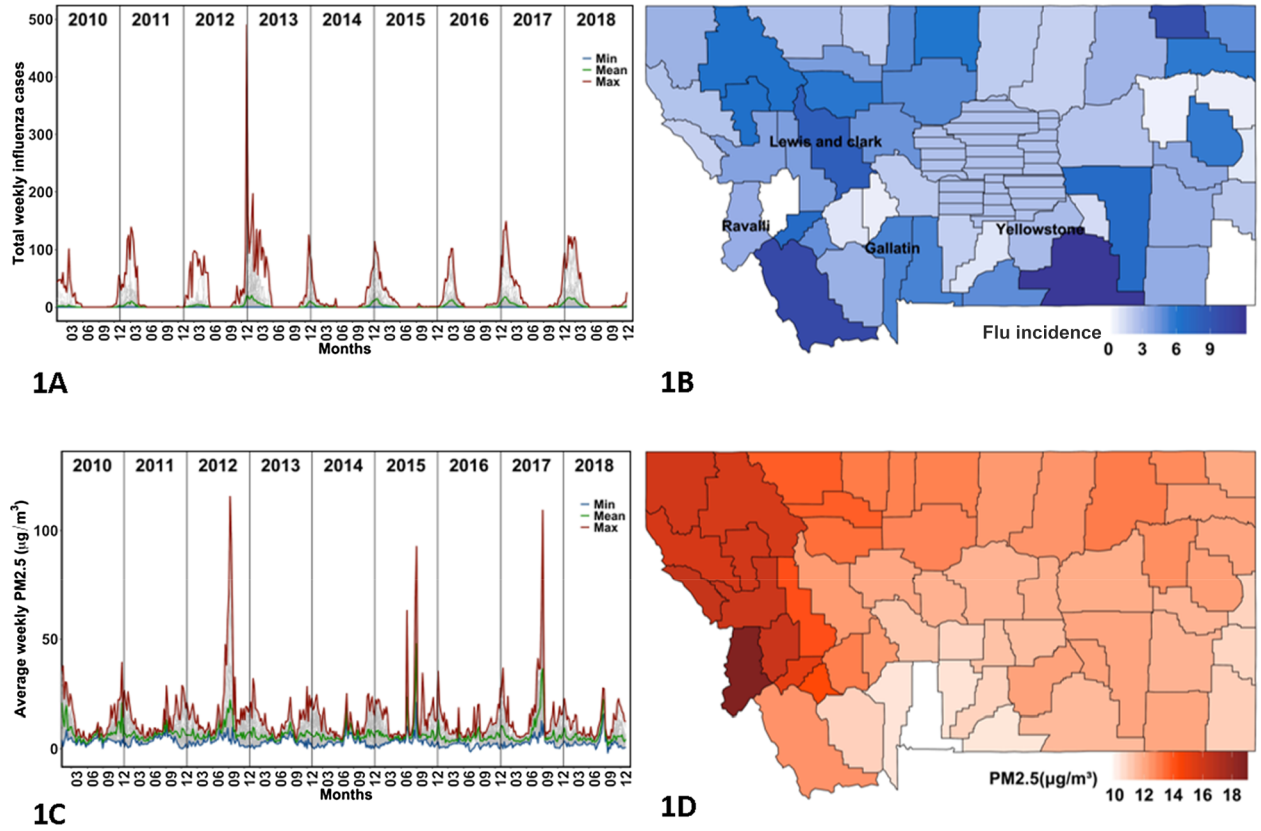

Fig. 1. (A) Total weekly influenza cases plotted for all Montana counties, 2010–2018. (B) Flu season incidence (per 1,000) for each county in Montana, 2015–2016 with the 'Central Montana Health District' (CMHD) shown with dash. (C) Average weekly $PM_{2.5}$ (ug/m^3) plotted for each county in Montana, 2010–2018. (D) Average $PM_{2.5}$ during the wildfire season (July 1 – September 30) for each county in Montana, 2015.

produce gridded maps of daily $PM_{2.5}$ concentrations across the state of Montana from 2009 − 2018. Mean daily $PM_{2.5}$ were retrieved from the EPA (https://www.epa.gov/outdoor-air-quality-data) and used as a response variable in the models. One hundred and seven stations within a domain bounded by −100 to −120 degrees longitude and 42 – 49 degrees latitude were used for model fitting. Counts of daily observations available for each station varied from 1% to 100%, with a mean of 21% and counts of the number of available observations by day ranged from 10 to 57, with a mean of 38. The 1 km MODIS aerosol optical thickness (AOT) product, developed using the MAIAC algorithm (Lyapustrin et al. 2018) was used as predictor. Quality assurance layers provided for each image were used to screen pixels containing snow or clouds, and only the highest quality observations were retained for analysis. Fig. A1 shows the correlation of the AOT data with the $PM_{2.5}$ EPA station data. Use of remotely sensed products is particularly challenging in Montana, due to image contamination by clouds and snow. More than 90% of data were missing during winter months (Fig. A2). Therefore, satellite AOT data were only used in the models from June-October (but see comparison of models for November-May in Appendix). We infilled missing observations in the June-October AOT data using probabilistic Principal Components Analysis (Stacklies et al. 2007).

We used Bayesian spatial linear models implemented in the 'spBayes' package (spLM; Finley et al. 2015) in R version 3.5.3 (R Core Team 2019) to estimate daily $PM_{2.5}$ concentrations. We fit a unique model for each day, and predicted the fitted model to a 12 km grid. Aerosol optical thickness was used as a predictor in this model along with an exponential covariance model. Uninformative priors were used for the regression parameters, a uniform prior was used for the spatial decay parameter with support for effective ranges between 5% and 90% of the maximum inter-point distance, and uninformative inverse gamma priors were used for the covariance sill and nugget (σ^2 and τ^2) parameters. For November-May days, we used thin plate spline regression (TPS) in the R package 'fields' (Nychka et al., 2017) to interpolate daily $PM_{2.5}$ observations without any spatial covariates. This decision was made because of the high proportion of missing MODIS data in winter. Here, a spline regression model was fit for each date using the latitude and longitude of each station and predicted the model to a 12 km grid. We evaluated both the spLM and TPS models using a leave-one-out cross validation approach. Here, for every model date each observation was withheld. A model was fit using the remaining observations, and then predicted to the withheld observation. This procedure was repeated for each observation and each date and error statistics were retained for all days. The overall model fit for the summer wildfire season model was reasonably strong, with Mean Absolute Error of 2.79 (µg/m^3) and r^2 = 0.66 (Fig. A3a). The accuracy of the thin plate spline model, fit without the benefit of MODIS AOT data was not as strong as expected, with Mean Absolute Error of 3.11 (µg/m^3) and r^2 = 0.37 (Fig. A3b). Daily gridded $PM_{2.5}$ estimates were combined into weekly grids using the mean, and then extracted for county in Montana also using the mean.

The resulting weekly $PM_{2.5}$ time series for all counties is given in Fig. 1C. For this study, we are primarily interested in evaluating two possible functions of $PM_{2.5}$ in relation to influenza: (1) a long-lag effect experienced primarily from $PM_{2.5}$ during wildfire season, and (2) a short-lag effect experienced primarily from biomass smoke exposure (e.g., Ward and Lange, 2010). We tested multiple such functions to express these different kinds of $PM_{2.5}$ periods and effects as summarized in Table 1. For the long-lag effects, we used the average daily $PM_{2.5}$ concentration for the months July 1 – September 30 preceding the flu-season, when $PM_{2.5}$ density spikes due to wildfires, with the intent of estimating average $PM_{2.5}$ concentrations during wildfire season. An

Table 1
Short-lag and long-lag $PM_{2.5}$ variables considered.

		Variable Name	Description
$PM_{2.5}$ Variables Tested	**Long-lag Effects**	Daily average $PM_{2.5}$ during wildfire season	Total $PM_{2.5}$ from months preceding flu-season (July 1 – September 30) divided by wildfire season total days (91 days)
	Short-lag Effects	(A) *n* week lag (*n = 1,2,3,4)*	Lag $PM_{2.5}$ up to *n* weeks before current week of influenza
		(B) *n* week moving window sum (*n = 2,3,4)*	Total $PM_{2.5}$ up to *n* weeks before current week of influenza divided by *n* weeks
		(C) Daily average $PM_{2.5}$ during flu season	Total $PM_{2.5}$ over entirety of flu-season (October 1 – April 30) divided by flu-season total days

Table 2
Model summary for each variable and dataset.

Complete Dataset (n = 12,474)				Reduced Dataset (n = 6,308)			
Term	Estimate	Robust SE	pval	Term	Estimate	Robust SE	pval
Sine, Cosine	Varies	Varies	$< 10^{-5}$	*Sine, Cosine*	Varies	Varies	$< 10^{-5}$
Temperature Lag	−0.0014	0.0030	0.650	*Temperature Lag*	0.0001	0.0030	0.979
Daily Long-Lag $PM_{2.5}$	0.1995	0.0752	0.008	*Daily Long-Lag $PM_{2.5}$*	0.1470	0.0724	0.042
Daily Short Lag $PM_{2.5}$	−0.0459	0.0464	0.323	*Daily Short Lag $PM_{2.5}$*	−0.0407	0.0483	0.399

example long-lag $PM_{2.5}$ for each Montana county in 2015 is shown in Fig. 1D. Fig. A4 shows how severe the wildfire seasons were each year in Montana using total area burned. For the short-lag effects, we looked at three different $PM_{2.5}$ variables: (A) a lag in $PM_{2.5}$ up to *n* weeks before current week of influenza, (B) a moving window daily average $PM_{2.5}$ up to *n* weeks before current week of influenza, and (C) a daily average $PM_{2.5}$ concentration over the entirety of flu-season.

2.3. Statistical analysis

The associations between weekly counts of influenza cases and the different $PM_{2.5}$ effects were examined using the following quasi-Poisson regression model weighted by county population for all counties simultaneously:

$$\log(\mu_{t,k}) = \log(Population_{t,k}) + \beta_0 + \sum_{i=1}^{6} \beta_i F_i(t,k) + \beta_7 Temperature_{t-1,k} + \beta_8 LongLagPM2.5_{t,k} + \beta_9 ShortLagPM2.5_{t,k} + \sum_{i=10}^{60} \beta_i County_k \quad (1)$$

where *t* is the week index, $t = 1, 2, \ldots, 435$ weeks from 2010-Jan-03 to 2018-May-31, excluding weeks outside of the flu season, *k* is the county index, $k = 1, 2, \ldots, 51$ counties as earlier defined, $\mu_{t,k}$ is the expected influenza count at time *t* in county *k*, assuming $\mu_{t,k} \sim$ Exponential Family(θ), $Population_{t,k}$ is the population in county *k* in week *t*, entering the model as an offset allowing an influenza rate response, $Temperature_{t-1,k}$ is the maximum daily temperature (in deg. Celsius) extracted using 250 m resolution gridded temperature data (Holden et al., 2018) in county *k* in week *t*-1, $LongLagPM2.5_{t,k}$ is the long-lag $PM_{2.5}$ daily average from the previous wildfire season as described in the previous section for county *k* relative to week *t*, $ShortLagPM2.5_{t,k}$ is the short-lag $PM_{2.5}$ effect as described in Table 1 for county *k* relative to week *t*, $F_i(t,k)$ is the i^{th} Fourier seasonal term ($i = 1,2,3$ for Sine and $i = 4,5,6$ for Cosine) for county *k* in week *t*, and $County_k$ is a county indicator (1 if county *k* and 0 otherwise). Notice that the first seven terms in the model (parameterized by $\beta_1, \beta_2, \ldots, \beta_7$) are all variables regularly associated with influenza dynamics (e.g., Imai et al., 2015).

A generalized estimating equation (GEE) was used to estimate the model parameters for this quasi-Poisson generalized linear model to address any residual temporal autocorrelation and uncertainty in the covariance structure of the flu counts. An autoregressive (AR(1)) covariance structure is assumed for the GEE to account for the weekly dependence in flu counts within each county-year cluster (51 counties × 8 years = 408 county-year clusters). The model for influenza rate (specified as influenza count with population as an offset) given in Eq. (1) was applied simultaneously to all counties in Montana and for the two datasets described in the previous section (complete and reduced), and basic statistical inference performed on the coefficients using Huber-White robust standard error estimates to account for uncertainty in the quasi-Poisson correlation structure. All analyses were performed using the geem and glm function in R (version 3.5.3; R Development Core Team) with a quasi-Poisson family to account for overdispersion, and each case weighted by the county population.

3. Results

3.1. Long-lag $PM_{2.5}$ impacts on influenza

Average daily long-lag $PM_{2.5}$ concentration (averaged over the period July 1 – September 30 during the previous wildfire season) was positively associated with increased influenza rate for both the complete and reduced datasets ($p = 0.008$ and $p = 0.042$, respectively) as shown in the model summary provided in Table 2. The estimated model coefficients are 0.1995 (SE = 0.0752) and 0.1479 (SE = 0.0724) for the complete and reduced datasets, respectively. For the complete dataset, we expect influenza incidence to increase by a factor of exp (0.1995) = 1.22 per 1 μg/m^3 elevation in average daily wildfire season $PM_{2.5}$ exposure (95% CI: (1.05, 1.41)). For the reduced dataset, we expect influenza incidence to increase by a factor of exp (0.1470) = 1.16 per 1 μg/m^3 elevation in average daily wildfire season $PM_{2.5}$ exposure (95% CI: (1.01, 1.33)). We note that these estimated parameters reflect population-based changes in influenza rate taken on average.

3.2. Short-lag $PM_{2.5}$ impacts on influenza

Moving window daily average short-lag $PM_{2.5}$ two weeks prior to the current week showed no association with influenza rate for the complete dataset ($p = 0.323$) and the reduced dataset ($p = 0.399$) (Table 2). Regardless of short-lag method chosen for the model (Table 1), no association was observed. Individual county-specific models indicated a positive association in 13–23 of the 51 counties, depending on which short-lag $PM_{2.5}$ variable was used, but no overall effects were observed (Table A1; Figs. A5–A6).

3.3. Temperature impacts on influenza

The average maximum temperature (degrees Celsius) in the previous week showed no association with influenza rate for the complete dataset ($p = 0.650$) and the reduced dataset ($p = 0.979$) (Table 2). Individual county-specific models indicated that 39 out of 51 Montana counties show a negative albeit insignificant relationship between temperature and influenza counts (Fig. A7), the direction of which is consistent with all previous literature on this topic (e.g., Tamerius et al. 2013).

3.4. Residual autocorrelation

There was strong evidence of temporal autocorrelation within the county-year clusters in the influenza count model residuals (Breusch-Godfrey test, $p = 0.0004$). To address this residual autocorrelation, robust Huber-White standard errors under an AR(1) covariance structure were used in the GEE modeling framework to assess the significance of model predictors.

4. Discussion

We found that higher average $PM_{2.5}$ concentrations during the wildfire season positively associated with increased influenza in Montana counties in the following winter flu season. Individual county-specific models further support this result, showing long-lag $PM_{2.5}$ positively associating with wintertime influenza in 50 out 51 counties (Table A1; Figs. A5–A7). Although there are studies that report the correlation between short-lag exposure of $PM_{2.5}$ and influenza cases (Liang et al., 2014; Feng et al., 2016; Horne et al., 2018), our study suggests one of the longest lag associations observed for communities impacted by wildfires. Wildfire season for Montana (and much of the intermountain West) occurs between July – September with corresponding peak levels of $PM_{2.5}$. Flu season spans October – April, with peak flu cases typically occurring in January. Thus, average daily $PM_{2.5}$ concentrations during wildfire season months was observed to be positively associated with flu 1–10 months later, even after accounting for seasonal, temperature, and autocorrelative factors.

Past studies modeling the effects of $PM_{2.5}$ during wildfire episodes on respiratory outcomes have typically looked at lagged associations of less than 5 days (Liu et al., 2015; DeFlorio-Bake et al., 2019). However, a recent study showed consistently increased odds of healthcare encounter for influenza for elevated $PM_{2.5}$ exposure estimates averaged across several lag periods, 0–28 days (Horne et al., 2018). We also included a short-lag variable in our model using different methods to account for the effect of $PM_{2.5}$ immediately preceding influenza rates (1–4 weeks; Table 1). Surprisingly, these results were less consistent than the long-lag $PM_{2.5}$ variable, and we found little support for a short-lag $PM_{2.5}$ effect on influenza. Individual county-specific models run with each different short-lag $PM_{2.5}$ variable in Table 1 are compared in the Appendix (Table A1; Figs. A5–A7) and further corroborate this finding. Depending on which $PM_{2.5}$ short-lag variable used, 13–23 of the 51 counties indicated a positive association with short-lag $PM_{2.5}$ and influenza counts with at most 7 counties being significant ($p < 0.05$). The inability to separate out the various contributing factors to short-lag $PM_{2.5}$ in the winter months (i.e., woodsmoke, other industrial pollutants) could be one reason our model was not able to find a short-lag $PM_{2.5}$ association with flu. Several studies have evaluated specific PM components and cardio-respiratory outcomes, but findings have been inconsistent in linking isolated PM factors or sources to specific outcomes (Stanek et al., 2011). To our knowledge no such studies have evaluated PM component or PM source with respect to influenza, and this would be a potential area for further exploration.

Although our modeling was able to partially explain effects of long-lag $PM_{2.5}$ concentrations on Montana's counties, finer scale data could help reveal more spatially resolved details. Our modeling used $PM_{2.5}$ maps produced at relatively coarse (12 km) spatial resolutions and aggregated to the county level. Future research should explore variation at finer resolution. Of particular concern in western rural states is the scarcity of air quality monitoring stations, which provide the data needed to deliver accurate respiratory health warnings and predictions to the public, as well as to provide the data to better understand the role air pollution has on respiratory diseases. In the intermountain west, the sparsity of air quality monitoring stations is further complicated by the region's complex terrain which likely contributes to significant heterogeneity in air pollution levels across communities (Armstrong, 1998). Furthermore, it is likely that during the wildfire season inversions and drainage flows may lead to highly variable smoke exposure. Many areas of Montana and the intermountain west in the wintertime experience an increased risk of poor air quality due to cold-air inversions, trapping air pollutants in mountain valleys where most towns and residents are located (Ward and Lange 2010; Holden et al., 2011). Air quality monitoring stations are often located to represent worst-case exposures for the largest concentration of people or sited to capture background exposure. For example, in 2018 there were 19 sites in the Montana network that monitored $PM_{2.5}$ (13 = Population Exposure, 5 = Background Exposure, and 1 = Source Impact; https://www3.epa.gov/ttnamti1/files/ambient/pm25/qa/vol2sec06.pdf). Regardless, it is unlikely that the single air monitor sites in many Montana communities provide an accurate representation of pollution exposure and could be missing much of the spatial patterning in $PM_{2.5}$, as suggested by other urban area focused studies (Tunno et al. 2016). Thus, improved spatially resolved maps of $PM_{2.5}$ would enhance understanding of particulate matter impacts on public health during both the winter and wildfire season. Such maps would also provide the spatial and topographically resolved data needed to identify fine scale $PM_{2.5}$ effects on specific respiratory diseases, such as influenza.

There are several potential factors that are relevant to influenza risk that were not addressed in our study. For example, previous studies included sociodemographic factors and one study from Australia found that wealthier communities with lower levels of unemployment experienced greater flu activity than those less advantaged areas (Huang et al., 2017). Other studies have found that school calendars may play a role in influenza outbreaks, suggesting that closing schools could be effective in limiting the spread of influenza outbreaks (Chu et al., 2017), also contributing to the hypotheses on indoor crowding and increased person-to-person contact (Cauchemez et al., 2008). Furthermore, our model did not include vaccination rates (e.g., Baselga-Moreno et al., 2019), influenza strain, distance to airports (e.g., Hooten et al., 2010), and possible important determinants influenza in for rural states, such as healthcare access, or any other sociodemographic or economic variables, all of which could influence influenza transmission. Future studies could explore the interactions of virus-specific, climate, sociodemographic, and $PM_{2.5}$ variables. Finally, we note that our models did not explicitly account for uncertainty in the particulate matter model. This uncertainty was higher in winter months, where satellite data were unavailable, and may have contributed to the lack of any relationship between short-lag PM exposure and influenza.

While our study supports a link between long-lag $PM_{2.5}$ during wildfire season and wintertime influenza, the mechanisms underlying this relationship are complex, and beyond the scope of this study. Future work using in vivo and in vitro studies could be conducted to explore these underlying mechanisms for either viral etiology and/or host susceptibility. For example, some animal studies have looked at wood smoke particles' sustained immune suppression effect (Samuelson et al, 2009; Migliaccio et al, 2013), showing this type of PM having a 24 h sustained effect on respiratory bacterial infections. Other animal models suggest that the role of lagged PM exposure on influenza risk could occur via diminished capacity of pulmonary macrophages to secrete IL-6 and IFN-β (Ma et al. 2017). Ma et al. 2017 provide support for a 2-week exposure to outdoor $PM_{2.5}$ from Shanghai, China, leading to decreased resistance to influenza via altered immune responses.

Predicting influenza outbreaks based on climatic and environmental factors, such as $PM_{2.5}$, may be important for both short- and long-term public health planning. In the short-term, models may help predict outbreaks days to weeks in advance, giving public health officials an opportunity to target prevention messages and vaccine efforts. In the long-term, models linking climatic or environmental variables to influenza outbreaks may provide a picture for what populations can expect with ongoing climate change or extreme seasonal conditions. For example, Ford et al. (2018) projected change in $PM_{2.5}$ based on prognostic land-fire models for the continental US with the worst areas in Montana forecasted to have a 5 $\mu g/m^3$ increase in the annual average per decade. Moreover, identifying the predictors of influenza, such as long-lag $PM_{2.5}$ effects, and improving upon the predictive models for influenza, will be important for the population health, as influenza is associated with approximately 900 hospitalizations and 60 deaths in Montana each year (www.cdc.gov/flu/about/burden/index.htm).

CRediT authorship contribution statement

Erin L. Landguth: Conceptualization, Methodology, Writing - original draft, review & editing. **Zachary A. Holden:** Methodology, Writing - review & editing. **Jonathan Graham:** Methodology, Writing - review & editing. **Benjamin Stark:** Formal analysis. **Elham Bayat Mokhtari:** Visualization. **Emily Kaleczyc:** Data curation. **Stacey Anderson:** Data curation, Writing - review & editing. **Shawn Urbanski:** Writing - review & editing. **Matt Jolly:** Writing - review & editing. **Erin Semmens:** Conceptualization, Writing - review & editing. **Dyer A. Warren:** Formal analysis. **Alan Swanson:** Formal analysis. **Emily Stone:** Writine - review & editing. **Curtis Noonan:** Conceptualization, Supervision, Writing - review & editing.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.envint.2020.105668.

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