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Air Pollution Related Asthma Inpatient Hospital Admission in the Las Vegas Valley

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AIR POLLUTION RELATED ASTHMA INPATIENT HOSPITAL ADMISSION IN THE LAS VEGAS VALLEY

By

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ABSTRACT

Air Pollution Related Asthma Inpatient Hospital Admission in the Las Vegas Valley

By

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Asthma is a chronic respiratory condition characterized by inflammation in the lungs that causes airflow to be restricted. In Southern Nevada's Las Vegas Valley, the natural basin geography causes air pollutants to accumulate. Research has linked air pollution with worsening asthma symptoms. The goal of this study was to determine the non-linear lagged relationship between Asthma Related Inpatient Hospital Admissions (ARIHA) and the Environmental Protection Agency's (EPA) criteria air pollutants in the Las Vegas Valley using hospital and pollution monitoring station data. Overall, a statistically significant increased RR of ARIHA between 7 and 13 days after exposure to $PM_{2.5}$ 24-hour average levels from 0-35 $\mu g/m^3$, and from 9-10 days after exposure to $PM_{2.5}$ 24-hour average 75 $\mu g/m^3$ was found. Finally, 17 ZIP codes exhibited a statistically significant increased RR of ARIHA after adjusting for all variables, revealing a heterogeneous distribution of ZIP codes at a higher risk of ARIHA.

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BACKGROUND

Asthma is a chronic inflammation and narrowing of the airways, which affects 25 million people in the United States (Xu et al., 2017). Although most episodes of asthma are mild, more extreme episodes, “asthma attacks” may require emergency treatment, and short-term hospitalization (Xu et al., 2017). Asthma is exacerbated by inhaled substances such as air pollutants and breathing becomes difficult as a result. The American Lung Association’s 2017 “State of the Air” report indicated the Las-Vegas Henderson area as being the 10th most polluted in the nation (Mangan, 2017). These high pollution levels cause asthma to be a public health concern in the Las Vegas Valley. Worsened asthma outcomes also represents an economic burden to the Las Vegas Valley, as the 88,570-asthma related inpatient hospital admissions (ARIHA) in this study had an average cost of $55,103.44 each.

The Las Vegas Valley is comprised of the cities of Las Vegas, North Las Vegas, Boulder City, Henderson, and multiple unincorporated. The Las Vegas Valley is in the southwest of the United States, and comprises the majority of Clark County, Nevada. Asthma affects 7.1% of people in Clark County according to the 2007 Clark County Health Status Report (Feng, 2007). The valley is surrounded by mountains, forming a natural bowl where pollutants can pool. The Las Vegas Valley experiences frequent temperature inversions, which are layers of hot air that trap cold air and prevent the dispersal of air pollutants released from the valley (Green et al., 2013). The resulting pollutant buildup can exacerbate asthma symptoms. This study investigated the relationship between pollutants and ARIHA in the Las Vegas Valley in order to determine if pollution worsens asthma outcomes for an extended period after exposure using a Distributed Lag Non-linear Model (DLNM). A secondary analysis was also performed which determined which ZIP codes were at higher risk for ARIHA.

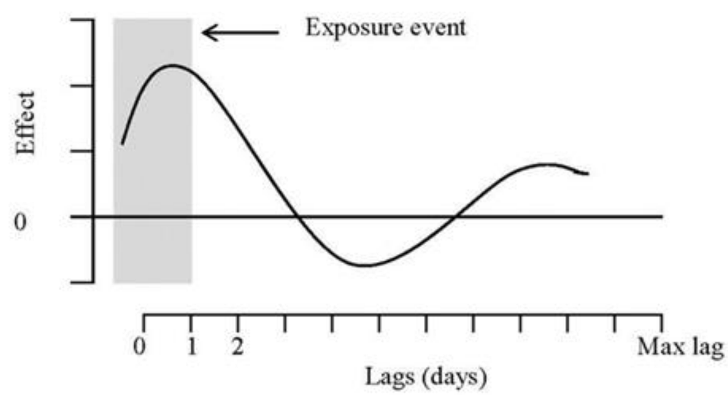
INTRODUCTION

The Environmental Protection Agency (EPA) notes that the six criteria air pollutants are harmful to human health and regulates them using the National Ambient Air Quality Standards (NAAQS) as part of the Clean Air Act, which was last amended in 1990 (NAAQS) (*Criteria Air Pollutants* 2018); (Environmental Protection Agency, 2016a, 2018); *NAAQS Table* 2016). A failure to meet these standards results in the area becoming *designated*, with a State Implementation Plan which details how the state intends to lower pollutant levels to acceptable levels (Environmental Protection Agency, 2016b). There is a growing body of evidence that air pollutants are strongly linked with negative health outcomes. Biologically, the criteria air pollutants negatively impact lung function. For example, particulate matter with a diameter less than 2.5 micrometers ($PM_{2.5}$) can induce alveolar inflammation (Vardoulakis & Osborne, 2018). Nitrogen dioxide (NO_2) and ozone (O_3) cause inflammation through oxidative injury (Vardoulakis & Osborne, 2018). The corollary is also true that reducing pollution levels is linked with better asthma outcomes (Burbank & Peden, 2018).

In relation to asthma, previous research indicates that criteria air pollutants such as particulate matter (PM) are associated with exacerbated asthma symptoms (Bouazza et al., 2018). Moreover, those with asthma are particularly susceptible to the effects of O_3, with some suggestions that long-term O_3 exposure could be related to asthma development (Environmental Protection Agency, 2016a). Therefore, this research sought to investigate the relationship between ARIHA and criteria air pollutants to determine if a lagged relationship exists.

A lagged effect refers to the delayed relationship between an exposure and an outcome. Figure 1 illustrates how a single exposure can affect an outcome 11 days after initial exposure. This research utilized a nonparametric model as some exposures can produce negative outcomes in both extremely high and low values, such as temperature increasing stroke mortality at both high and low values, which requires by a non-linear model (Y. Q. Zhang, Yu, & Bao, 2017). Previous research has determined that lagged relationships exist between air pollutants and several health-related outcomes. In Sweden, NO_2 levels were found to increase primary health care visits for asthma sufferers for a period of up to 15 days (Taj, Jakobsson, Stroh, & Oudin, 2016). Ambient air pollution has also been found to increase relevant medical expenditures for various respiratory diseases for up to a 3-day lag period (H. Zhang et al., 2018). Finally, research in North Carolina has indicated that pollen levels can exacerbate asthma between a lag of 2-3 days (Sun, Waller, Yeatts, & Thie, 2016). Overall, there is little research investigating pollution and asthma at lags of longer than 3 days.

Figure 1. Visual Example of a Distributed Lag Non-Linear Model



Source: (Fraga, Botelho, Sa, Costa, & Quaresma, 2011)

This study also investigated the geographic disparities in the risk of ARIHA based on ZIP code by adding a spatial function to DLNM. The spatial function allowed DLNM to calculate the risk of an outcome based on a geographic unit. The impetus for a spatial analysis was previous research using surveillance data in the Southwestern United States that noted asthma prevalence by county can vary by upwards of 19.9% (Chien & Alamgir, 2014). The goal of the geographic analysis was to determine which areas in the Las Vegas Valley were at a higher risk of ARIHA.

The distributed lag model (DLM) is the fundamental model used to assess lagged relationships. DLM examines the delayed effects of a single event on a given outcome, and works by specifying the distribution of effects after the event, referred to as a lag period (Gasparrini, Armstrong, & Kenward, 2010). The DLM allows for an efficient way to investigate lagged events much more efficiently than using individual linear models, but can suffer when predictor variables have collinear values (Gasparrini et al., 2010). This is problematic for environmental exposures, as environmental exposure values for adjacent days are highly collinear, along with the existence of non-linear relationships.

The distributed lag non-linear model (DLNM) is a newer modelling approach that is designed for evaluating the non-linear delayed effects of environmental stressors on an outcome, such as elevated pollution levels (Gasparrini et al., 2010) A DLNM is an improvement on older DLM models because it helps account for the high collinearity of exposure values on adjacent days (Gasparrini et al., 2010). Since the development of the DLNM in 2010, it has become a preferable tool over the DLM to analyze lagged effects (Chien, Guo, Li, & Yu, 2018; Chuang, Chaves, & Chen, 2017; H. Zhang et al., 2018).

The objective of this research was to model the relative risk of ARIHA in the Las Vegas Valley using a retrospective cohort study. The model employed determined which pollutants at what levels lead to a lasting risk of ARIHA.

Research Questions

The aim of this research study was to analyze the lagged relationship between ARIHA and criteria air pollutants by answering the following questions. First, which criteria air pollutants can best predict an elevated relative risk of ARIHA? Second, how long is the lag period between an exposure to a criteria air pollutant and an increased relative risk of ARIHA? Finally, are there any geographic disparities in the relative risk for ARIHA by ZIP code?

Hypotheses

$H^{1}0$: There will be no significant increase in the RR of ARIHA for $PM_{2.5}$.

$H^{1}a$: There will be a significant change in the RR of ARIHA for $PM_{2.5}$.

$H^{2}0$: There will be no increased RR for ARIHA from a lag period of 0-28 days.

$H^{2}a$: There will be an increased RR for ARIHA from a lag period of 0-28 days.

$H^{3}0$: No ZIP codes will have a statistically significant higher RR of ARIHA.

$H^{3}a$: ZIP codes in the Las Vegas Valley will have a statistically higher RR of ARIHA.

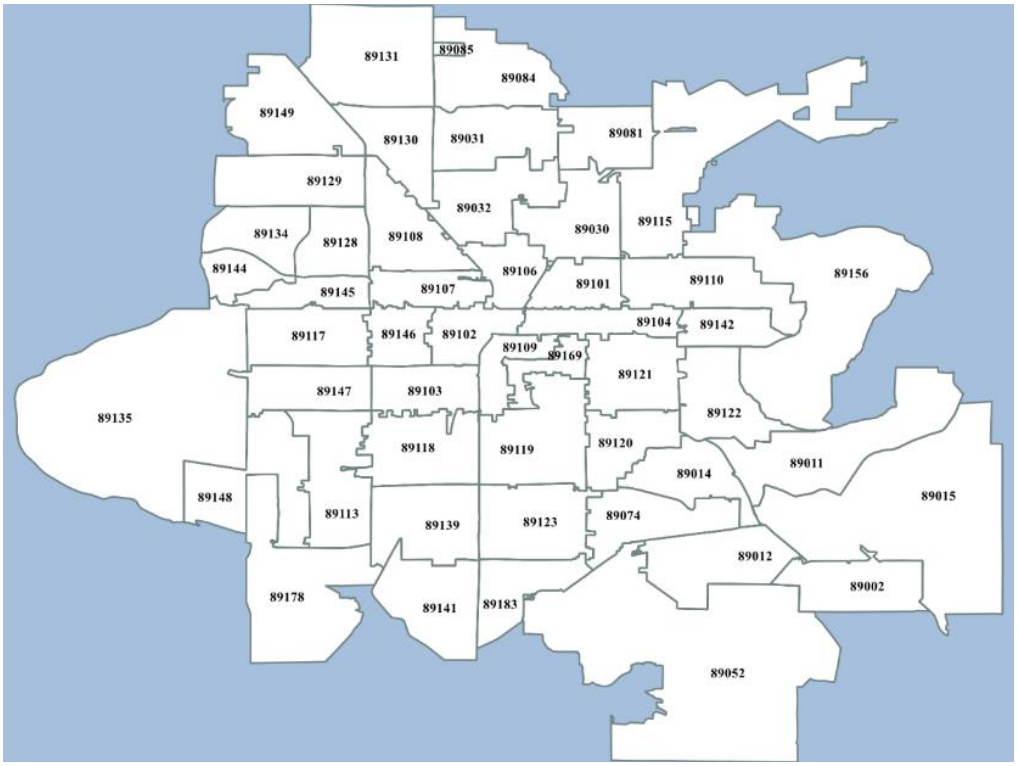
MATERIALS AND METHODS

To conduct this research, Geographic Information System (GIS) data, hospital admission data, pollution data, meteorological data, and socioeconomic status (SES) data for the Las Vegas Valley was obtained. The location of the Las Vegas Valley is illustrated in Figure 2. The geographic unit investigated was ZIP codes. Data for ZIP codes in Clark County were obtained for a total of 73 ZIP Codes. These were narrowed to 50 ZIP Codes because 23 ZIP codes lacked data due to Health Insurance Portability and Accountability Act (HIPAA) rules. The remaining 50 ZIP codes are illustrated in Figure 3. This should not have affected the analysis due to the low population in most of the removed ZIP codes. As 5 ZIP codes with missing data were within inner sections of Las Vegas Valley they were filled with 0's for ARIHA to allow for the spatial calculation, which could have caused an underestimation of the risk of ARIHA. The study examined the period from 2006-2014, for a total of 3287 individual days over the 50 ZIP Codes.

Figure 2. Las Vegas Valley Location in the Continental United States

Shape File Source: https://www.census.gov/geo/maps-data/data/cbf/cbf_state.html

Figure 3. 50 Las Vegas Valley ZIP Codes



The hospital data included ARIHA by ZIP Code, which was designated by a billing code that reflects the inpatient status of the patient. An ARIHA refers to a patient who went to the hospital due to their asthma and required a stay of more than two nights. ARIHA were count data, exhibiting a Poisson distribution – meaning each instance was independent of one another. The remaining 45 Las Vegas Valley ZIP Code hospital data came from the Center for Health Information Analysis for Nevada at the University of Nevada, Las Vegas, which provides healthcare related data and reports to researchers (CHIA, 2018)

Pollution data was sourced from the Clark County Department of Air Quality, which is tasked with ensuring air quality in Clark County meets regulatory standards (Clark County Department of Air Quality, 2015). The EPA requires measurements to be taken for the six criteria air pollutants, including carbon monoxide (CO), nitrogen dioxide (NO_2), sulfur dioxide (SO_2), ozone (O_3), lead (Pb), and particulate matter (PM). Most pollutants are measured in 1-hour averages, with CO being measured using 1-hour and 8-hour averages, and $PM_{2.5}$ being measured using 1-hour and 24-hour averages. To match the ARIHA data, daily pollution data from 2006-2014 was used, which was collected from a variable number of monitoring sites in the valley over the years of the study. For 1-hour average, the highest observed 1-hour average for a given day was recorded. For 8-hour averages, the highest observed 8-hour average for a given day was recorded. A spatio temporal kriging method was used to interpolate the air pollution data by ZIP code – this considers the number of monitoring sites, geographic location, and the distance between each location and monitoring site to estimate values for each ZIP code (Liang & Kumar, 2013). Meteorological data came from weather monitoring stations in Clark County, which varied in number and location over time, and included information such as average temperature, average humidity, and average wind speed. Both pollutant and meteorological data was interpolated by using the spatio temporal kriging procedure to estimate the daily values by ZIP code and simultaneously fill in missing data.

Finally, SES data were obtained from Decennial Census data, which was aggregated by PolicyMap.com (U.S. Bureau of the Census, 2010). This dataset included information, such as median household income and racial demographics. Due to low variability over time and the centrality of the 2010 Census within the research project's timeframe, 2010 Census data was used for the entire 2006-2014 period. The aggregated data set was used to perform the analysis, allowing for the calculation of RR while considering meteorological and SES data.

A DLNM with a spatial function was used to predict the lagged RR of ARIHA associated with air pollutants and analyzed geographic disparities in the RR of ARIHA by ZIP code in the Las Vegas Valley. The DNLM was an appropriate model for this study because it can measure the lagged effects of air pollution exposure while accounting for the high collinearity of air pollutants on adjacent days using a time function that weighs neighboring values in week-long blocks (Gasparrini et al., 2010). The DLNM was established using a spatiotemporal generalized additive model structure with quasi-Poisson family by:

$$Y_{zt} \sim \text{Poisson}(\mu_{zt})$$

$$\text{Log}\ (\mu_{zt}) = \alpha + f\ (\text{Time}) + f\ (\text{Pollutant 1, lag=l}) + f\ (\text{Pollutant 2, lag=l}) + \beta \times \text{SES} + \eta \times \text{Meteorological} + f_{spac}\ (z) + \text{offset},$$

where Y_{zt} refers to the count of ARIHA at a given ZIP code and time. α is the intercept with the f(Time) being a time smoother using a natural cubic spline to control for temporal autocorrelation. The cross-basis functions f (Pollutant 1, lag=l) and f (Pollutant 2, lag=l) calculated the effect of the pollutant at a specified lag l. Two cross-basis functions were built with equal lag times, to adjust for the effects of two different criteria air pollutants. SES variables (e.g., median household income, insurance coverage), and meteorological variables (e.g., temperature, rainfall) were added to adjust for the effects of SES and meteorological factors, which are both known to worsen the asthma outcomes (Almqvist, Pershagen, & Wickman, 2005; Goodman, Dockery, & Clancy, 2004). The offset was the logarithm of the population by ZIP code from decennial census data from 2010, which was used for the entire period due to the data point's centricity.

After all variables were added to the model, the effects of individual variables were analyzed. This is because DLNM plots are variable specific, with the x-axis representing the lag days, the y-axis representing the value of the specified variable, and the z-axis representing the relative risk for a given variable value and lag. NAAQS values were used for the DLNM reference value, and for variables with data consistently below NAAQS, the average of that pollutant was used. From there, statistical significance was determined by analyzing the 95% confidence interval bands using 2-dimension slice plots. The 2-dimension slice plots can assess the RR across a specified lag day or analyze the RR across a given value of the predictor variable.

DLNM does not inherently allow for the analysis of spatial data, but the addition of a spatial function allows DLNM to jointly consider spatio-temporal data using MRF. The spatial function was added by applying Markov random fields (MRF) (Chien et al., 2018). The MRF smoother accounts for spatial autocorrelations and spatial heterogeneity to determine the RR for ARIHA in each ZIP code due to the specified pollutant (Chien, Guo, & Zhang, 2016). The MRF smoother utilizes a normally conditional autoregressive based upon: whether ZIP codes share a common boundary, the number of adjacent ZIP codes, and an unknown variance to calculate excessive risk of ARIHA by ZIP code compared to the average of all ZIP codes. Overall, the addition of the spatial function allowed for the calculation of RR by geographic (Freni-Sterrantino, Ventrucci, & Rue, 2017). Using maps of Las Vegas Valley ZIP codes, the RR for specific parts of the valley was modeled, which allowed for the identification of spatial risk disparities.

All research was conducted using R Studio version 1.1.442, R version 3.3.3 and QGIS 3.0.0. Statistical significance was set to the 95% confidence level.

RESULTS

Summary statistics are presented in Table 1 for each air pollutant from 2006-2014 for the Las Vegas Valley. The max value recorded for $PM_{2.5}$ 24-hour average was 78.70 μg/m^3 with a total of 26 days that exceeded the NAAQS. For PM_{10} 24-hour average the max recorded value was 267.00 μg/m^3, and the NAAQS value was exceeded on 18 days. No other pollutants exhibited days that exceeded NAAQS. The correlation matrix in Table 2 revealed modest correlations between some pollutants, which allowed for the avoidance of using a model with two pollutants with a correlation coefficient greater than 0.50 to avoid multicollinearity issues. Overall, the statistics revealed relatively low pollution levels in the Las Vegas Valley, except for PM_{10} and $PM_{2.5}$, which both had days which violated NAAQS.

Table 1. Summary Statistics of Air Pollutants

	N	Mean	SD	Min	Q1	Median	Q3	Max
CO 1Hr Avg (ppm)	164,350	0.55	0.29	0.00	0.33	0.48	0.72	3.10
CO 8Hr Avg (ppm)	164,350	0.56	0.30	0.00	0.33	0.47	0.72	3.11
O_3 8Hr Avg (ppb)	164,350	0.03	0.01	0.00	0.02	0.03	0.04	0.08
PM_{10} 24Hr Avg (μg/m^3)	164,350	22.37	2.48	0.00	17.00	21.91	26.84	267.00
$PM_{2.5}$ 1Hr Avg (μg/m^3)	164,350	8.21	2.64	0.00	6.34	7.77	9.58	78.75
$PM_{2.5}$ 24Hr Avg (μg/m^3)	164,350	8.24	8.32	0.00	6.71	7.89	9.34	78.70

Abbreviations: 24Hr Avg, 24-Hour Average; 8Hr Avg, 8-Hour Average; 1Hr Avg, 1-Hour Average

Table 2. Correlation Matrix of Criteria Air Pollutants in the Las Vegas Valley

	(1)	(2)	(3)	(4)	(5)	(6)
(1) CO 1Hr Avg	1.000					
(2) CO 8Hr Avg	0.969	1.000				
(3) O_3 8Hr Avg	-0.747	-0.741	1.000			
(4) PM_{10} 24Hr Avg	0.042	0.035	0.043	1.000		
(5) $PM_{2.5}$ 1Hr Avg	0.213	0.206	-0.106	0.427	1.000	
(6) $PM_{2.5}$ 24Hr Avg	0.260	0.206	-0.119	0.436	0.795	1.000

Abbreviations: 24Hr Avg, 24-Hour Average; 8Hr Avg, 8-Hour Average; 1Hr Avg, 1-Hour Average

Figure 4 contains a map of crude prevalence and total cases of ARIHA for the Las Vegas Valley aggregated from 2006-2014. In total there were 88,570 cases from 2006-2014, with a total economic cost of $4,880,511,647 charges as a result of the inpatient hospitalizations. Northern and central ZIP codes exhibited a slightly higher crude prevalence of ARIH. Eastern ZIP codes tended to have a higher crude prevalence than western ZIP codes. The total case map revealed more cases in the north, northeast, and southeast corners of the valley. The highest concentration of cases was in the northeast, followed by high concentrations in the northwest and southeast.

Figure 4. Crude Prevalence and Total Cases of ARIHA in the Las Vegas Valley

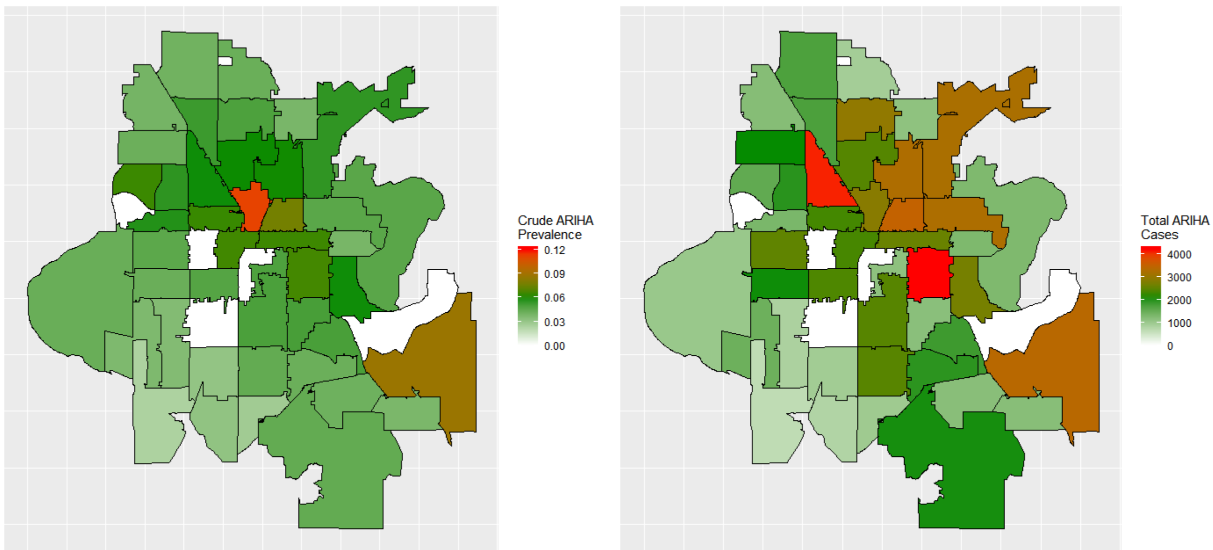


Figure 5 contains maps of the average daily air pollutant values aggregated across the 9-year period for each ZIP code. The main trend was elevated values in the northeast and central parts of the valley, which is apparent in PM_{10} 24-hour average, $PM_{2.5}$ 24-hour average, and $PM_{2.5}$ 1-hour average. The average CO 1-hour average and CO 8-hour average values were highest in ZIP codes 89104, 89101, and 89178. Central ZIP codes exhibited high average values for $PM_{2.5}$ 1-hour average, and PM_{10} 24-hour average. ZIP code 89178, which is in the southwestern corner of the Las Vegas Valley, had high average values across every air pollutant, but did not have a noticeably high crude prevalence of ARIHA or total cases of ARIHA. CO 1-hour average, CO 8-hour average, and PM_{10} 24-hour average never exceeded NAAQS over the nine-year period. There is no $PM_{2.5}$ 1-hour average NAAQS standard, but it did not exceed the $PM_{2.5}$ 24-hour average NAAQS over the nine-year study period.

Figure 5. Average Pollutant Values by ZIP Code

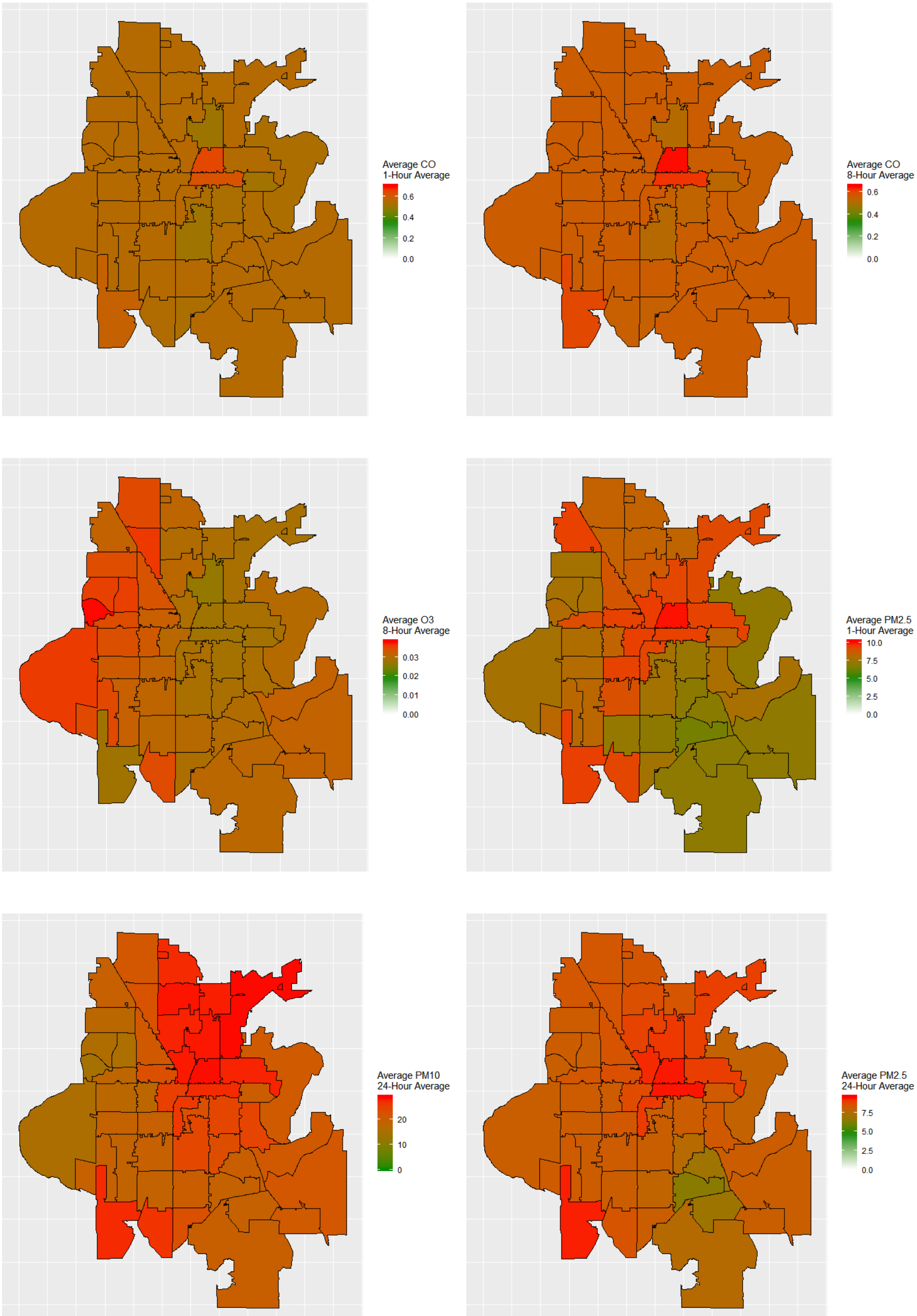


Figure 6. Times Series of Pollutants With Least Sqares Linear Trend Line

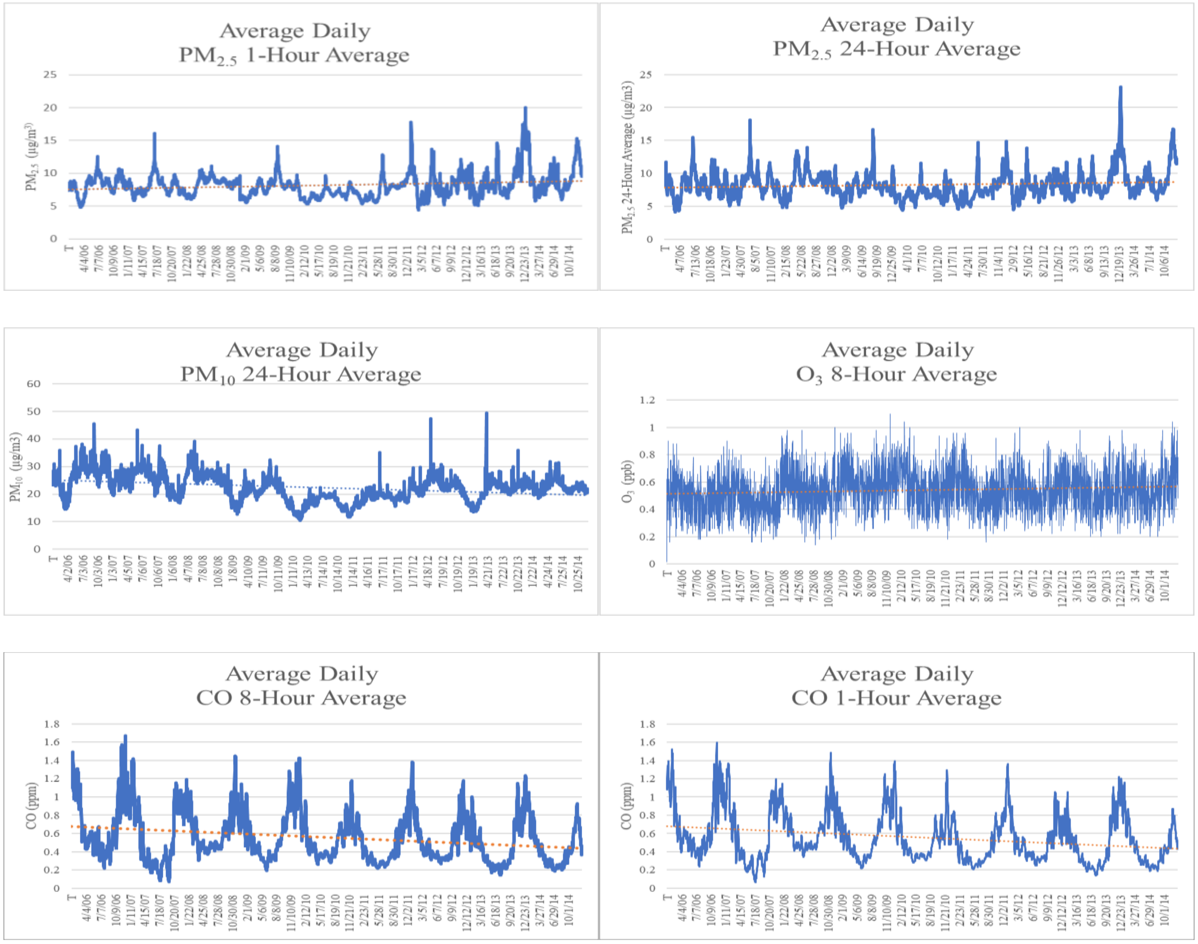


Figure 7. **Daily ARIHA**

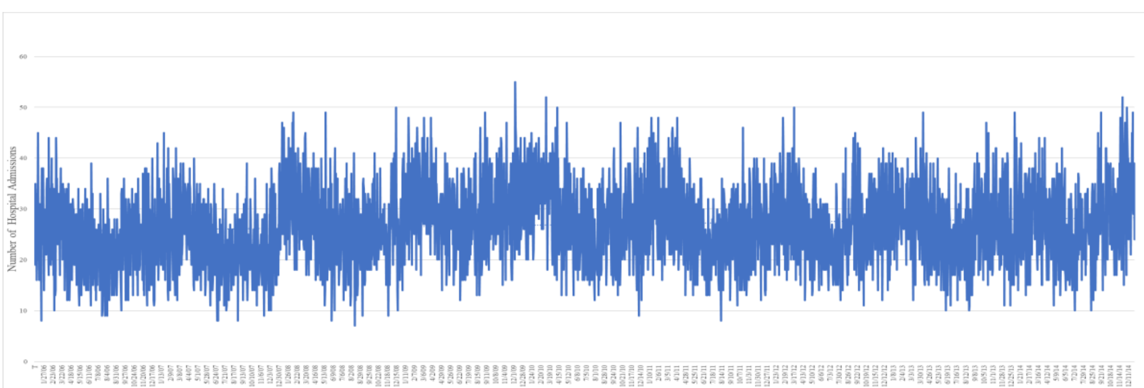


Figure 6 contains time series plots of the aggregate daily average for each pollutant in the Las Vegas Valley. Pollution levels and seasonal trends remained consistent across the nine-year period. None of the pollutants had a meaningful increase or decrease in pollution levels over the nine-year period. Air pollutant measurements exhibited seasonal trends with higher levels in colder parts of the year and lower levels in warmer parts of the year, except for O_3 which exhibited higher values in summer months. Figure 7 is a time plot of the aggregate count of daily ARIHA over the study period. There was a slight upward trend, but otherwise the daily ARIHA counts were consistent. All time series linear trend lines were calculated using the method of least-square regression.

The initial lag period utilized in the model was 30 days. Upon initial examination at 30-day lag periods, only CO 1-hour average, CO 8-hour average, PM_{10} 24-hour average, and $PM_{2.5}$ 24-hour average showed meaningful. These plots were generated using each pollutant as a predictor of ARIHA in a single crossbasis function with a lag period of 30 days, without adjusting for any other pollutants or variables, and are presented in Figure 8. $PM_{2.5}$ 1-hour average, and O_3 8-hour average was excluded for consideration in the model due to the small size of their results at exclusively extremely high or low values. The validity of the findings in CO 1-hour average were questionable as CO 1-hour average levels had consistently low values with a max of 3.1 ppm, far below the EPA NAAQS standard of 35 ppm. The model was narrowed down to a combination of PM_{10} 24-hour average, $PM_{2.5}$ 24-hour average, and CO 8-hour average. Ultimately, $PM_{2.5}$ 24-hour average and PM_{10} 24-Hour average were chosen for the cross-basis functions as that model's low Quasi-Akaike Information Criterion (QAIC) value indicated that it best fit the data, which also resolved the concerns regarding CO 8-hour average's validity. The QAIC values based on model are presented in Table 3. QAIC helped

Figure 8. Initial Unadjusted DLNM Findings Using a Single Crossbasis Function

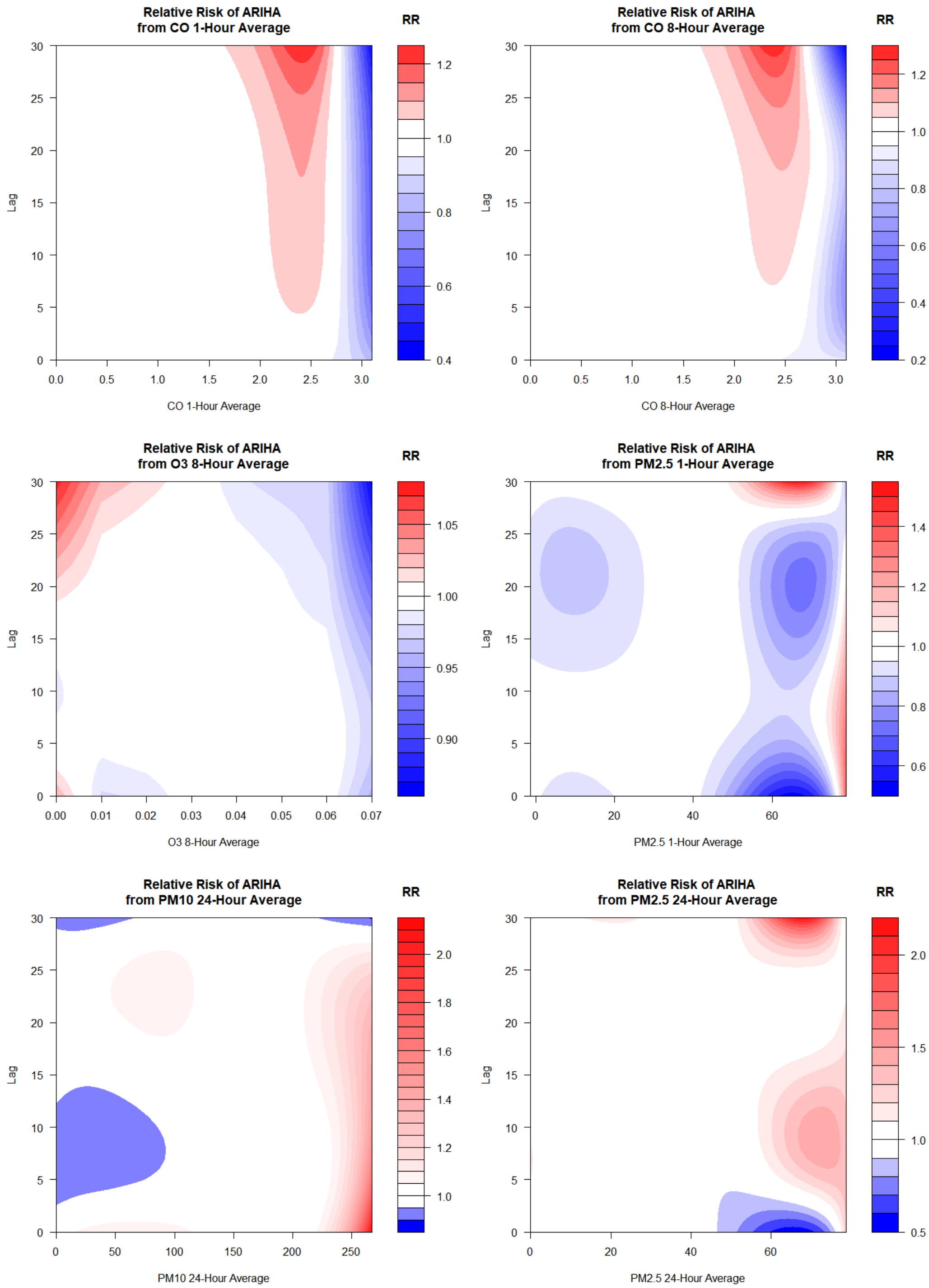


Table 3. QAIC Values for Each Model

Model	QAIC Value
*$PM_{2.5}$ 24Hr Avg & PM_{10} 24Hr Avg	1999207
PM_{10} 24Hr Avg & CO 8Hr Avg	1999228
$PM_{2.5}$ 24Hr & CO 8Hr Avg	1999253
$PM_{2.5}$ 24Hr	2013462
CO 8Hr Avg	2013422
PM10 24Hr Avg	2013274
*Model Selected Based on Lowest QAIC Value	

determine the how well a model fit the data in order to select the best model. EPA NAAQS were used as reference values for PM_{10} 24-hour average, $PM_{2.5}$ 24-hour average, and $PM_{2.5}$ 1-hour average. For O_3 8-hour average, CO 1-hour average, and CO 8-hour average the reference value was the average value of the pollutant in the dataset as the observed pollutant levels were all below NAAQS. This did not affect the final analysis since these variables were not used in the final model.

The model was further refined through the manipulation of the lag period, and the inclusion of meteorological and socio-economic status variables. An initial lag period of 30 days proved to not contain any statistically significant findings, so it was reduced to 21 days, where there were statistically significant findings when investigating $PM_{2.5}$'s effect on ARIHA. Based on their relationship to respiratory outcomes, variables to adjust for mean temperature and median household income were added for metrological and socio-economic factors. The final model focused on $PM_{2.5}$ 24-hour average as a predictor of ARIHA after adjusting for PM_{10} 24-hour average, mean temperature, and median household income.

The null hypothesis that $PM_{2.5}$ would not predict a statistically significant increase in ARIHA was rejected when 35 μg/m^3 was the reference value chosen, which is the EPA's NAAQS. Figure 9 is the contour and 3D plots of the models, which reveal hotspots from $PM_{2.5}$ 24-hour average levels between 0-35 μg/m^3, and at above 60 μg/m^3. Figure 10 presents the slice plots, which reveal a statistically significant RR of ARIHA from 7-13 lag days after adjusting for the effect of PM_{10} 24-hour average, mean temperature, and mean household outcome after exposure to $PM_{2.5}$ 24-hour average levels between 0-35 μg/m^3. Moreover, there was a statistically significant increase in the risk of ARIHA from 9-10 days after exposure to $PM_{2.5}$ 24-hour average levels of approximately 70 μg/m^3, which is double the EPA NAAQS.

Figure 9. Contour and 3D Plots of PM2.5 24-Hour Average as a Predictor of ARIHA

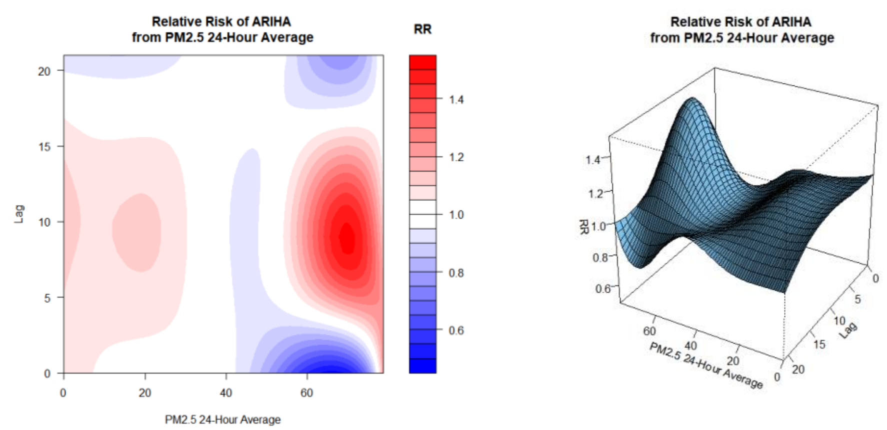
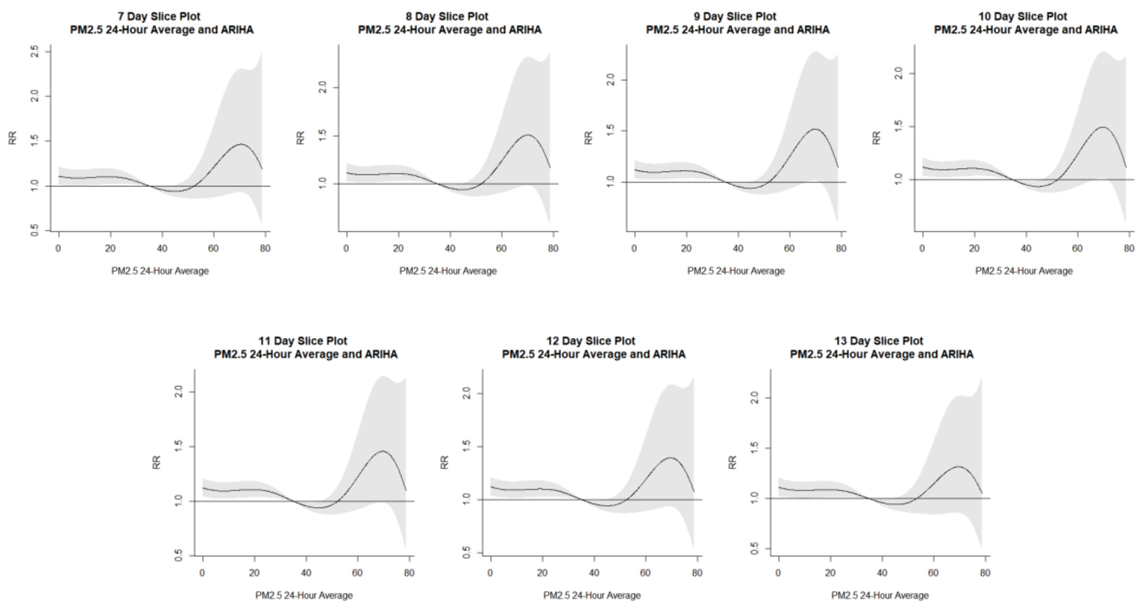


Figure 10. Slice plots of the Relative Risk of ARIHA from $PM_{2.5}$ 24-Hour Average



The null hypothesis that criteria air pollutants would not predict a statistically significant increase in the risk of ARIHA from a lag period of 0-28 days was rejected. The final model selection revealed that $PM_{2.5}$ 24-hour average was able to predict a statistically significant in the increase in ARIHA from 7-13 days. Previous research has generally looked at shorter lag periods of 0-3, and 0-6 days when examining the effects of pollution on health outcomes. Ultimately, $PM_{2.5}$ 24-hour average predicted a statistically significant increase in ARIHA in the model at a longer lag period than previous studies.

The null hypothesis that there was no statistically significant difference in the risk of ARIHA between ZIP codes was rejected. The model determined the RR of ARIHA in each ZIP code after controlling the effects of all variables in the model. The model revealed the RR of

ARIHA by ZIP code after adjusting for $PM_{2.5}$ 24-hour average, PM_{10} 24-Hour Average, mean temperature, and mean household income. ZIP codes with a higher RR of ARIHA were generally further from the center of the Las Vegas Valley. Statistically significant spatial findings are summarized in Table 4, with Figure 12 being a map of all ZIP codes and their calculated RR.

Figure 11. Map of Relative Risk of ARIHA by ZIP Code

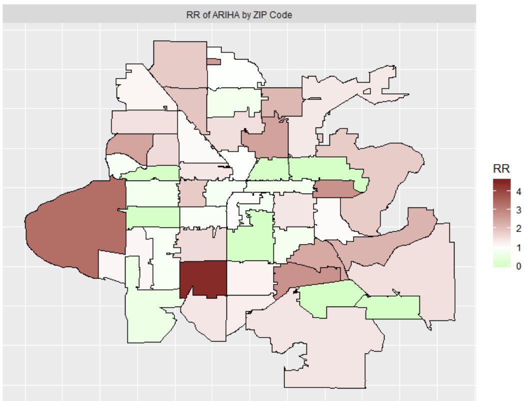


Table 4. ZIP Codes with a Statistically Significant Risk of ARIHA

ZIP Code	RR (95% CI)
89135	**3.31** (1.93, 5.68)
89074	**2.71** (1.14, 6.43)
89085	**2.59** (1.14, 5.83)
89030	**2.45** (1.59, 3.80)
89134	**2.43** (1.10, 5.37)
89014	**2.35** (1.09, 5.06)
89011	**2.17** (1.05, 4.50)
89081	**2.14** (1.15, 3.97)
89130	**1.90** (1.33, 2.72)
89131	**1.82** (1.58, 2.10)
89146	**1.81** (1.39, 2.34)
89156	**1.79** (1.25, 2.56)
89118	**1.55** (1.35, 1.77)
89128	**1.53** (1.40, 1.68)
89032	**1.51** (1.10, 2.08)
89015	**1.48** (1.08, 2.03)
89115	**1.34** (1.21, 1.48)

DISCUSSION

After adjusting for PM_{10} 24-hour average, mean household income, and mean temperature, $PM_{2.5}$ 24-hour average predicted a statistically significant RR of ARIHA from 7-13 days after exposure to $PM_{2.5}$ 24-hour average levels between 0-35 μg/m^3 and 9-10 days after exposure to a $PM_{2.5}$ 24-hour average of 70 μg/m^3. This model demonstrated that criteria air pollutants could successfully predict a statistically significant increase in ARIHA at longer lag periods than previous research, and that $PM_{2.5}$ was associated with a statistically significant RR of ARIHA. The spatial analysis demonstrated that there was a statistically significant increased risk for ARIHA in 17 ZIP codes in the Las Vegas Valley, and a statistically significantly decreased risk of ARIHA in 6 ZIP codes, which we could not explain. All null hypothesis were rejected, and the model successfully utilized criteria air pollutants as a predictor of ARIHA while simultaneously identifying geographic risk disparities based on ZIP code.

Based on the established biological relationship between $PM_{2.5}$ and respiratory health it was predicted that $PM_{2.5}$ would have a statistically significant relationship with ARIHA due to the known biological link between $PM_{2.5}$ and alveolar damage. In this model, $PM_{2.5}$ predicted a statistically significant increase in the risk of ARIHA 7-13 days after exposure. This finding is consistent with previous research that $PM_{2.5}$ increases the risk for respiratory disease in epidemiological studies, which is further supported by research into $PM_{2.5}$'s mechanism of damaging the alveolar wall (Y.-F. Xing, Y.-H. Xu, M.-H. Shi, & Y.-X. Lian, 2016). The findings are also consistent with previous research whereby $PM_{2.5}$ was a strong predictor of asthma and rhinitis related admissions (Tecer, Alagha, Karaca, Tuncel, & Eldes, 2008). These findings continue to build upon the body of evidence suggesting the strong link between PM and respiratory health, while suggesting potential lasting health effects after initial exposure. The public health implication is that $PM_{2.5}$ continues to be associated with negative respiratory health outcomes, creating more impetus for the control of $PM_{2.5}$ levels. Furthermore, reducing PM levels could reduce the economic burden of ARIHA, which from 2006-2014 resulted in nearly $5 billion of hospital charges.

The second hypothesis was that criteria air pollutants could be used to predict ARIHA at a lag period of 0-28 days, which was successfully accomplished using $PM_{2.5}$ 24-hour average and PM_{10} 24-hour average. The main takeaway from the second hypothesis was the successful use of air pollutants as predictors using DLNM across longer lag periods. This is important as DLNM research has largely focused on meteorological factors such as temperature and has usually used pollutants at predictors with short lag periods of 0-3 days. For example, previous research found a 4-day lagged relationship between pollution and asthma related hospital admission cases (Tecer et al., 2008). In comparison to that study, this model found a RR of approximately 1.2 from $PM_{2.5}$ values from 0-35 $\mu g/m^3$ whereas their study found a 1.2 odds ratio during a 10 $\mu g/m^3$ increase in $PM_{2.5}$ (Tecer et al., 2008). A similar study also noted a 4-day significant lag with $PM_{2.5}$ as a predictor of childhood asthma hospital admissions with a 1.2 odds ratio with a 10 $\mu g/m^3$ increase in $PM_{2.5}$ (Lee, Wong, & Lau, 2006). This research was similar to both studies as they examined $PM_{2.5}$ while adjusting for PM_{10}, except this study was able to find significance across a much longer lag period of 7-13 days. One notable difference is that they found statistically significant associations at lower lag times, whereas this study only found statistically significant associations at longer lag periods (Slaughter, Lumley, Sheppard, Koenig, & Shapiro, 2003). Previous research supports the existence of a lagged link between asthma related hospital admissions and $PM_{2.5}$, but the research is notable due to finding a statistically significant effects at lag periods of longer than 0-3 days, which is significant because it means there may be health risks from pollution exposure beyond the initial exposure and a few days after. The public health implication of this study regarding $PM_{2.5}$ is that there may be lasting health effects for up to two weeks after $PM_{2.5}$ exposure.

The final hypothesis was that different ZIP codes would have statistically significant different risks of ARIHA after controlling for all variables in the model. Initially, the total case map revealed a higher number of cases in the northern part of the valley, particularly in the northeast. Furthermore, the spatial maps of $PM_{2.5}$, PM_{10}, and total ARIHA cases also revealed elevated levels in the northeast of the valley. This is likely related to the presence of Nellis Air Force base in the northeast part of the valley as air force bases increase local pollution levels (Naugle, Grems, & Daley, 1978). Overall, the distribution of higher risk ZIP codes was heterogenous, although they seemed to be located further out from the center of the valley, and focused in the northeast, southeast, with a single ZIP code hotspot in the southwest. Conversely, ZIP codes with lower risk were closer to the center of the valley. Previous research has been done regarding the spatial heterogeneity of asthma, but that research done at the county level and it is hard to compare the spatial findings due to the large size difference in the geographic unit used (Chien & Alamgir, 2014). Research conducted in brazil revealed heterogeneity in elderly asthma hospitalizations distributions (Rodrigues, Silva, Ignotti, Rosa, & Hacon, 2011). Overall, there was not much research on the spatial distribution of asthma related healthcare outcomes, and while this model can control for variables within the model, it cannot determine the reason for the spatial distribution with the information obtained. Further research needs to be done to determine the cause of the disparity. The public health implication of this study's spatial analysis is that the cause of the higher risk areas needs to be explored in further research, and from a programmatic standpoint it highlights areas where risk mitigation efforts should take place through health interventions and the reduction of pollution levels.

This study had three major strengths including the size of the data set, and an established biological mechanism between $PM_{2.5}$ and respiratory health, and the consistency of findings from this research and past research. First, the size of the dataset helps emphasize the significance of the findings as it contained 9 years of data from 2006-2014 for a total of 3,287 days of data. The size of the dataset helps ensure these findings were not spurious. Second, the significance of this study is strengthened due to the known biological mechanisms between $PM_{2.5}$ and respiratory health. $PM_{2.5}$ impairs lung function by penetrating deep into the lung, and irritating and corroding the alveolar wall (Xing, Xu, Shi, & Lian, 2016). Having an established biological mechanism between the pollutant and respiratory health outcomes helps support the validity of this study's findings. Finally, these findings are generally consistent with past lagged studies that noted that $PM_{2.5}$ has respiratory health impacts beyond initial exposure. All in all, a large dataset, and established biological mechanisms between $PM_{2.5}$ and respiratory health, and the consistency of the findings with past research all help validate this study's findings.

Despite this study's strength, there were some inherent limitations to this study. One of the limitations is that this study relied on interpolated pollution and meteorological data. The data was collected through monitoring stations, which are not in every, or even most ZIP codes. Interpolation allowed for the study of smaller geographic units despite there not being air pollutant monitoring stations in every ZIP code. Although relying on interpolated data weakened the results, the weakness of the interpolation was offset by using a large data set that included 9 years of daily readings. The second major limitation is that the ZIP code where lives is in may not be the ZIP code one resides in during the day such as their workplace or school, meaning the exposure may have not occurred where the ARIHA case was attributed to. Unfortunately, there is no mechanism to deal with this phenomenon or a way to track this at the population level. Although these limitations must be kept in mind, this study identified a possible broad association between $PM_{2.5}$ and ARIHA at exposure levels below EPA NAAQS.

Overall, this study explored criteria air pollutants in the Las Vegas Valley, their relation to ARIHA, and a spatial analysis of the data. While there were some indications that $PM_{2.5}$ 24-hour average levels below NAAQS may cause an increased risk of ARIHA, there is still more research to be done. For example, this study did not delve deeply into the spatial distribution of pollutants and the risk of ARIHA. Although trends were noted, some phenomenon could not be explained such as why certain ZIP codes had such high pollutant levels. There also needs to be more research done to explore the relationship between $PM_{2.5}$ and other respiratory health outcomes to see if effects exist across a longer lag period such as the one in this study. Regarding DLNM, there needs to be more work focusing on pollutants as predictor variables, rather than as just adjustment variables, as this research demonstrated that criteria air pollutants can be successfully applied to DLNM across longer lag periods. This study also implies that there may need to be more experimental research into lasting damage from air pollutants beyond initial exposure. The most significant practical takeaway of this study is that $PM_{2.5}$ 24-hour average effects need to be further explored at values below current EPA NAAQS. For the Las Vegas Valley, research needs to be done regarding the spatial distribution of pollutants and the risk of ARIHA, especially the high-risk zones identified in the study, which were primarily ZIP codes in the northeast and southeast.

CONCLUSIONS AND RECOMMENDATIONS

Based on these findings the following was concluded: DLNM can successfully utilize pollutants as predictive variables beyond lag periods of less than one week, $PM_{2.5}$ exposure may cause lasting respiratory health effects, and that there may be negative health effects at $PM_{2.5}$ levels below the current NAAQS standard of 35 $\mu g/m^3$.

The significance of this research to other DLNM researchers is that the findings suggest that pollutants can be used to predict health care outcomes at lag periods of longer than a week. Longer lag periods have more practical significance since they can assess negative health impacts well beyond the initial exposure. Previous research using DLNM have utilized environmental exposures such as temperature to establish larger lag periods, but findings using pollutants as predictive variables have been limited to shorter lag periods such as 0-2 or 0-6 lag days (Chen et al., 2017; Zhu et al., 2017). This research suggests statistically significant findings existed up to 13 days. This research demonstrates that longer lag periods can produce significant findings with pollutants as predictive variables for respiratory health outcomes.

The significance of this research for environmental epidemiologists is that it suggests that exposure to $PM_{2.5}$ has negative impacts on respiratory health beyond initial exposure which builds upon existing evidence demonstrating that $PM_{2.5}$'s small size allows is to enter the respiratory system and cause respiratory problems (Y. F. Xing, Y. H. Xu, M. H. Shi, & Y. X. Lian, 2016). Further research should utilize other health outcomes to determine the relationship between other health outcomes and given lag periods.

The significance of these findings for the general public is that $PM_{2.5}$ 24-hour average values below NAAQS could be associated with negative health effects. Although this study cannot prove the NAAQS standard is too high, it suggests the need for further research on the health effects of $PM_{2.5}$ on health outcomes at exposures below the NAAQS standard to determine if exposure below the NAAQS standards has negative health effects. Although this study's risk increase was moderate, it is possible that a larger risk will be seen in less severe health outcomes.

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