Hua Lu, Fang Qiu, and Yiling Cheng

Temporal and Spatial Relationship of Ozone and Asthma

Abstract

There is evidence that ozone may cause asthma. However, the effects of asthma on young children are still unclear. This study explores the relationship of daily peak ozone levels and asthma hospital admission rates at the zip code level in California's South Coast Air Basin area during a three-year period (1997 to 1999). The Poisson regression model was used to investigate this relationship. After the adjustments were made for seasonal effect, the results demonstrated that asthma hospital admission rates for children less than 5 years old increases 11% when the daily peak ozone level increases an air quality index of 50.

Introduction

The prevalence of asthma is increasing sharply in the United States and around the world, particularly among children (Woodruff PG, 2001). Between 1980 and 1995, the number of US children with asthma rose from 2.3 million to 5.5 million. Asthma is the most common chronic childhood disease in the U.S. According to the Centers for Disease Control and Prevention (CDC), more than 0.8 million American children under 5 years old have been diagnosed with asthma and more than 0.1 million American children under 5 years had been hospitalized in 1999. It is also reported that the asthma-related death rate for American children increased by 78% between 1980 and 1993. One of the major objectives of the Healthy People 2010 is to reduce the hospitalization rate for asthma.

Potential triggers of asthma include infections, diet, and exposure to indoor allergens or outdoor pollutants. Specific causes of asthma, however, are still unclear. Ozone, an extremely reactive form of oxygen, occurs naturally in the Earth's upper atmosphere—10 to 30 miles above the Earth's surface—where it forms a protective layer that shields us from the sun's harmful ultraviolet rays. In the Earth's lower atmosphere, near ground level, ozone is also formed when hydrocarbon pollutants emitted by cars, power plants, industrial boilers, refineries, chemical plants, and other sources react chemically in the presence of sunlight. However, ozone at ground level is a harmful pollutant if built up to dangerous concentrations. The role of ambient or ground level ozone exposure in the epidemiology of asthma has been explored. There is evidence that ambient ozone levels during summertime are related to the hospital admission rates of children less than 2 years of age (Burnett RT, 2001). Fauroux also demonstrated a significant relationship between emergency room visits for acute asthma in children less than 15 years old and the ozone level one day after such an exposure in Paris (Fauroux B, 2000). Although the effect of other pollutants could not be totally excluded, the strongest association with asthma was observed for ozone in this small sampled (715 cases) study. Inconsistent results have also been reported regarding the association between emergency room visits of acute asthma and air pollution in adults. For example, some studies have actual found a protecting effect of pollution on asthma hospital admission (Bates DV, 1987). Therefore, ozone as one of the risk factors in the increased prevalence of asthma remains debatable (Woodruff PG, 2001).

Epidemiological studies on the health effects of outdoor air pollution have suffered from a number of methodological difficulties. For example, estimating exposure to pollution from an environmental surveillance system, such as monitoring stations, was difficult if not possible. In addition, most epidemiological studies have to rely on aggregated data for large geographic regions, such as counties or state. These studies could only reveal a general relationship between ozone levels and asthma at a global level. Detailed studies of the relationship between asthma risk level and pollution exposure in the patients' immediate neighborhood was always impossible due to the inability to derive data at the local level. Recently, geography information system (GIS) technologies have been employed by epidemiologist to overcome these issues. For example, GIS technologies are able to provide the epidemiologist with some new spatial analysis methods, such as spatial interpolation and zonal statistics functions to obtain better exposure estimation. GIS spatial analysis tools also make it possible to perform causational asthma studies at the local zip code or census tract level. These functions and tools could help substantially reduce the inaccuracy of environmental exposure. As a result, improved insight on the relationship between asthma and environmental exposure could be achieved at a much more detailed level.

This goal of this study is to determine whether variations of the ozone level in California's South Coast Air Basin area were associated with the local hospital admission rate of asthma in children less than 5 years. To this end, the spatial and temporal distributions of the ozone level and asthma hospital admission rates were first derived by using spatial analysis technologies provided by GIS, so that the subsequent statistical analysis can be performed.

Figure 1. Study area in California's South Coast Air Basin

Study Area and Data Set

The study area is California's South Coast Air Basin, including Orange county, and part of Los Angeles, Riverside and San Bernardino Counties (Figure 1). The total population count under study was 14,287,940 and was distributed in 447 ZIP codes areas. In the study area, 1,132,961 (7.9%) people were less than 5 years old.

Ozone Data

Ozone data was provided by the South Coast Air Quality Management District of California. Ozone level data contains hourly readings from each monitoring station in the study area for all three years. There is a network of 30 monitoring stations in operation within the study area. The daily peak ozone level of each station was used as the representative value for each specific date. During the data analysis stage, the peak ozone level one day before the date of admission was used to predict the risk rate of being hospitalized as an asthma case. The original readings of ozone levels were in unit of parts per million (ppm).

Hospital Admission and Population Data

Hospital admission data from January 1, 1997 to December 31, 1999 was obtained from the Office of Statewide Health Planning and Development of California (OSHPD) in the form of patient discharge records. The OSHPD granted the data after removing the patient identification information, while preserving date of admission, age at admission, disease type diagnosed at discharge, and the zip code of the patient's home address, etc. Although, it was not possible to pinpoint the patient's exact home address, the inclusion of zip code information in the data allows a spatial analysis of the hospital admission rates based on patients' general living environment. It also makes it possible to relate the occurrence of asthma disease with the possible environmental exposure of the patients. For this reason, zip code area was selected as the basic research unit in this study.

In light of the information provided by OSHPD, a 5-digit International Classification of Disease (ICD-9) Code was also facilitated to represent the diagnostic type of the cases. ICD-9 Code started with 493 (in addition to any combination of fourth and fifth digit extension) was defined as of an asthma case and was used to extract diagnosed asthma cases in the hospital admission data. Based on ICD-9 Code and patient home zip code, the number of asthma cases was summarized for each day from January 1, 1997 through December 31, 1999 in each zip code area.

In order to calculate the occurrence rate of the asthma incidents, it is essential to have the knowledge of the population in each study unit. The population data came from the 2000 Census Bureau 2000 Population data and its corresponding geographic boundaries from the Census Bureau's 2000 TIGER spatial data.

Methodology

Point Interpolation and Zonal Statistics

The ozone values obtained from the monitoring stations in California's South Coast Air Basin area were point measurements recorded at the specific location of each monitoring station. In order to relate the ozone readings with hospital admission data at the zip code level, it was necessary to estimate the potential ozone concentration at locations other than the 30 operational monitoring stations in the study area.

Estimating the value of attributes for the surface at all unsampled locations from a set of observed values made at control points within the same area is usually called point-to-area interpolation, or simply point interpolation (O'Sullivan and Unwin 2003). There are three major groups of point interpolation approaches, namely, global deterministic interpolation, local deterministic interpolation, and optimal geostatistical interpolation. Global deterministic interpolation, such as trend surface analysis, uses all control point data to statistically determine a polynomial function to reach the best fit of the underline surface based least-squared error criterion. Global deterministic approaches are objective and let all the data speak for themselves, but lack the embracement the First Law of Geography (Tobler, 1970), i.e. "everything is related to everything else, but near things are more related than distant things". Local deterministic interpolation approaches, such as Inverse Distance Weighted (IDW), estimate the attribute value at an unsampled location as a distance-weight sum of the sample values in some surrounding neighborhood and thus make good use of the First Law of Geography. However, the determination of the distance function and the definition of the neighborhood in IDW is an arbitrary process, without reference to the characteristics of the data being interpolated. Optimal geostatistic interpolation approaches combine the advantages of both deterministic approaches. Theoretically, optimal geostatistic approaches are also distance weighted interpolation, but employ sample data to inform the choice of function, weights and neighborhood (O'Sullivan and Unwin 2003).

For this reason, one of the much-used optimal geostatistic approaches, Kriging, was selected to interpolate the ozone values in the study area. The Kriging procedure involves first generating a semi-variogram and fitting it to a regular continuous mathematic function , which models the semi-variance as a function of separating distance. Then the fitted model will be used to estimate the weights to interpolate the ozone values at unknown locations. Ordinary Kriging with a spherical model was identified to fit very well with typical dataset extracted from each month. Because the interactive process to interpolate the daily ozone data for three years is very tedious and time-consuming, a Visual Basic For Application (VBA) Program utilizing ArcGIS's ArcObjects Developers Toolkit was developed to automate the interpolation of the daily peak ozone values for the 3 years (i.e. 1095 days).

Consequently, an output surface of the daily peak ozone level with a cell size of 100 by 100 meters was produced for each day. Because the hospital admission data was provided and summarized at the zip code level, the average peak ozone level of each specific zip code area needs also to be calculated. It was calculated by adding the ozone peak levels of all the grid cells in each zip code area together and then dividing the sum by the total number of cells in that specific zip code area. In reality, the zonal average statistic analysis function in the ArcGIS Spatial Analyst Extension was employed to conduct the calculation using zip code areas as control zones. Again, a VBA program was also developed to automate the zonal statistic analysis for the 1095 days. The results were then exported into the zip code shape file for subsequent analysis described below.

Air Quality Indexing

The U.S. Environment Protection Agency (EPA) established an Air Quality Index (AQI) to standardize the evaluation of national air quality. This was an effort to better inform the public the harmful health effects of poor air quality. EPA uses the AQI for five major air pollutants regulated by the Clean Air Act: ground-level ozone, particulate matter, carbon monoxide, sulfur dioxide, and nitrogen dioxide. EPA has divided the AQI scale into six categories, ranging from good, moderate, unhealthy for sensitive groups, unhealthy, very unhealthy and hazardous. Each category (usually covering an interval of 50 AQI or more) is assigned a specific color, ranging from green, yellow, orange, red, and purple to maroon (Table 1). The higher the AQI value is, the greater the level of air pollution, and the greater the health danger. For example, an AQI value of less than or equal to 50 represents good air quality (green level) and has little potential to affect public health, while an AQI value over 300 (maroon) represents hazardous air quality. An AQI value of 100 generally corresponds to the national air quality standard for the pollutant. AQI below 100 is generally thought of as satisfactory, above which air quality is considered to be unhealthy.

Because AQI has established a directly link between air pollution and level of health concerns, raw measurements of ozone concentration values in the unit of parts per million (ppm) were converted, or linearly interpolated, into AQI values in this study using the following standard formulas and the breakpoints in table 1 (EPA).

$$I_p = \frac{I_{Hi} - I_{Lo}}{BP_{HI} - BP_{Lo}}(C_p - BP_{Lo}) + I_{Lo}.$$

Where I_p = the index for pollutant $_p$

C_p = the rounded concentration of pollutant $_p$

BP_{Hi} = the breakpoint that is greater than or equal to C_p

BP_{Lo} = the breakpoint that is less than or equal to C_p

I_{Hi} = the AQI value corresponding to BP_{Hi}

I_{Lo} = the AQI value corresponding to BP_{lo}.

Table 1. Air Quality Index for Ozone with definitions of breaking points and colors for each quality category.

Index Values	Parts Per Million	Air Quality
0-50	0.000-0.064	Good (Green)
51-100	0.065-0.084	Moderate (Yellow)
101-150	0.085-0.104	Unhealthy for Sensitive Group (Orange)
151-200	0.105-0.124	Unhealthy (Red)
201-300	0.125-0.374	Very Unhealthy (Purple)
300-500	0.375 -	Hazardous (Maroon)

In most epidemiology studies, 50 AQI was often used as one unit increment of ozone level to analyze its impact on human health concerns.

Areal Interpolation

In order to keep the confidentiality of the population, census data was provided in an aggregated form for each census tract. The hospital admission data, on the other hand, was aggregated across zip code area. To obtain the asthma occurrence rate for each zip code area, it was necessary to transfer the population in the census tracts into that of zip code areas. The process of estimating the population in a set of areas based on the populations of a different set of overlapping areas is called “area-to-area interpolation”, or simply “areal interpolation”. Areal interpolation is based on “areal data”, in contrast to point interpolation mentioned above, which estimates a surface using data collected at sample points.

There are four major areal interpolation approaches: 1)areal weighting, 2) point-in-polygon, 3) kernel, and 4) intelligent methods (Sadahiro 1999). Both point-in-polygon and kernel approaches requires that the location of representative points in each area are available. Intelligent approach needs to incorporate other supplementary information related to population density, such as land use, in the estimation process. Because no information is available on the distribution of representing points and population density in the census data, the simplest and also the most popular areal interpolation approach, i.e. areal weighting method, was employed. Areal weighing method assumes that population are uniformly distributed in the source area unit. In this study, the areal weighting method was implemented also in ArcGIS Spatial Analyst Extension. The census tract data was first rasterized using a 100 by 100 meters cell size. The total population count of each census tract was then divided by the total number of cells in the tract to obtain the population density per grid cell. Lastly, the zonal sum statistic method was used to aggregate the total population in each zip code area using zip code areas as control zones. The population for children under 5 years old at the zip code level was also derived using the same areal interpolation. The asthma occurrence rate was then obtained by dividing the aggregated asthma case number in each zip code area by its corresponding population count.

Poisson Regression Analysis

A one day lag-time was applied between the ozone level readings and the hospital admission data to perform causational analyses. The number of asthma cases from the hospital admission records was in the form of daily count, suggesting a Poisson model. Therefore, Poisson regression models that accounted for overdispersion were used to estimate the relative risk of being diagnosed as asthma and admitted to hospital after one day exposing to the ozone. In Poisson regression models, the observed number of asthma cases was used as independent variable and the ozone exposure and/or other covariates such as months and years were selected as dependent variable(s) based on whether univariate or multivariate analysis was used. In the univariate analysis, the asthma case number was modeled as a function of a single group of factors, such as the level of ozone exposure, the months, or the years. In the multivariate analysis, the asthma case number was then a function of all these independent variables, where months were included in the model as 11 index variables and January was used as a referent month. There included also two index variables of years and 1997 was used as a referent year.

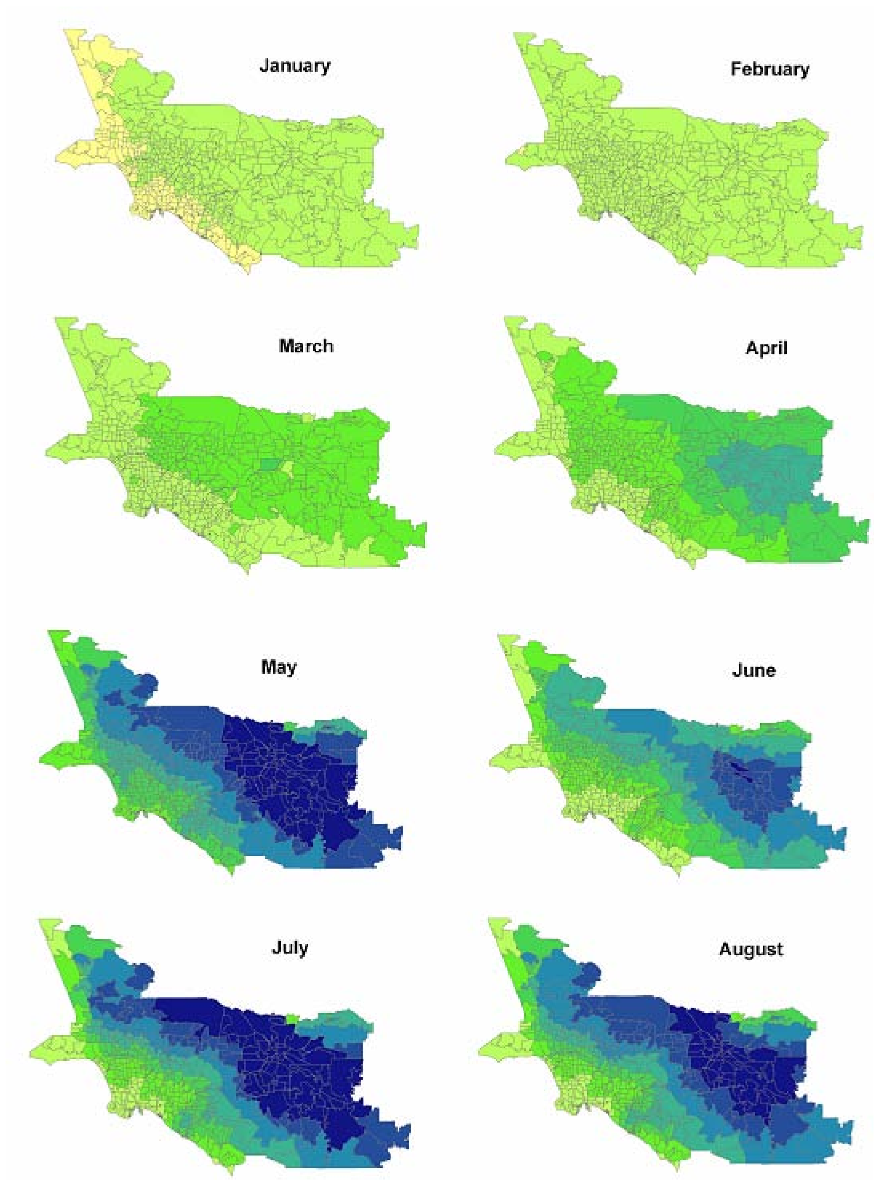
The log-transformed value of the total population (under age of 5) was included in the model as an offset term. In this sense, the Poisson regression analyses are in fact modeling the relationship between asthma occurrence rate and other factors. The Poisson statistical analysis was performed using SAS statistical software, version 8.2 (SAS Institute Inc. Cary, NC) and conducted with GENMOD procedure. Rate ratio (RR) and 95% Confidence interval (95% CI) was used for comparison among groups. Rate ratio compares the risk of disease among those exposed to a factor to those not exposed. All statistical significance decisions were based on two-tailed *P* values or 95% CI.

The following statements are an example of the univariate Poission regression analysis used in the SAS system. In this model, variable *a* represents the number of asthma hospital admissions under age of 5 and variable *o* represent the daily ozone peak level of each zip code area. The variable *ln* stands for *ln(n)* (i.e. log of n), where *n* represents the population count of the less-than-5 age group of a zip code area.

```
PROC GENMOD DATA=OZONE;
MODEL a=o/DISTRIBUTION=POISSION
LINK = LOG  OFFSET = ln;
```

Results

The daily peak ozone level in the unit of AQI of each zip code area was derived using point interpolation and zonal sum statistical approaches for each day of the three study years. An average daily peak ozone level was also summarized for each month in order to conduct exploratory visual analysis. Figure 2 present the average daily peak ozone level for the 12 months in year 1997. It is quite obviously that the ozone level tends to be high during summer hot season and low during winter cold season.



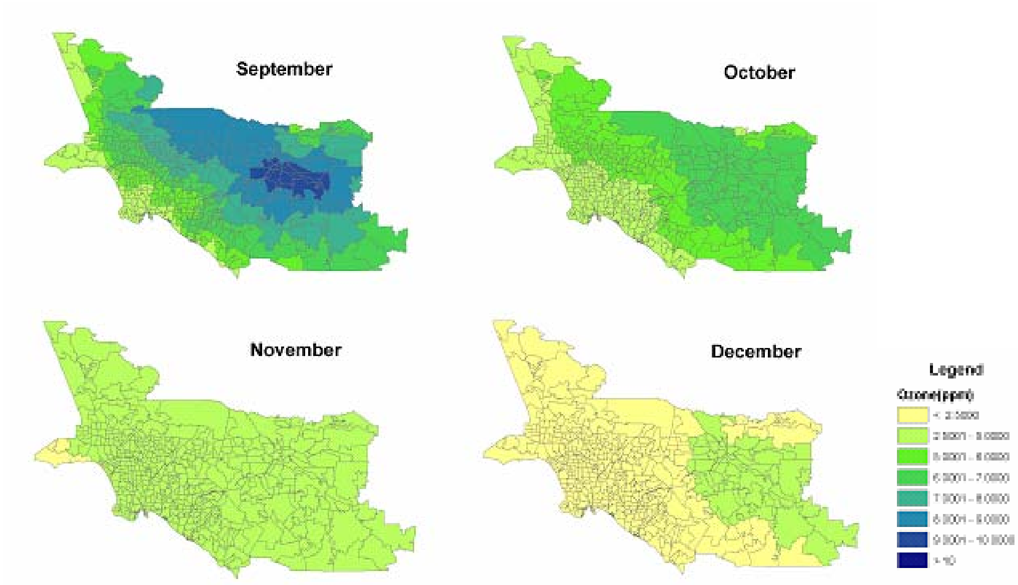
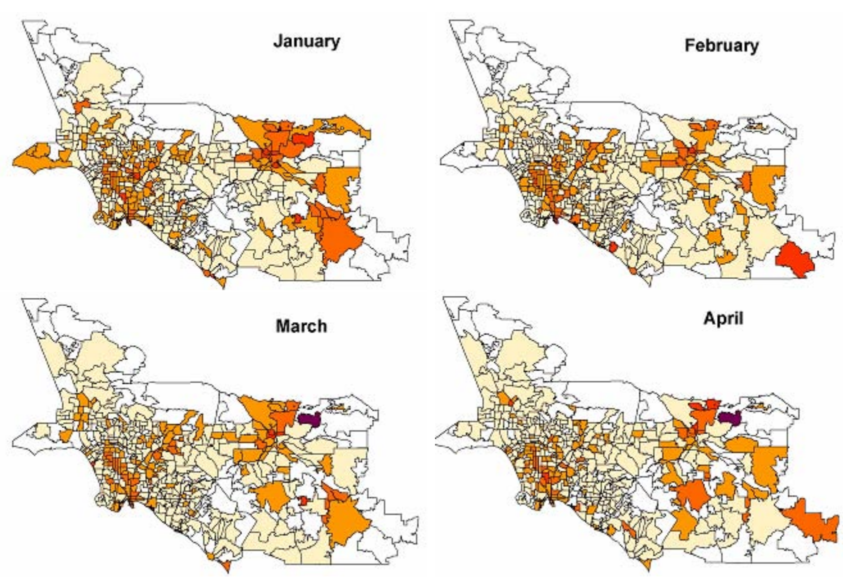


Figure 2. Average daily peak ozone values for the 12 months in the year 1997.

In total, 1,132,961 hospital visits by asthma patients were recorded from January 1, 1997 to December 31, 1999, among which 2,034 cases were children under age of 5. The total number of asthmas cases for patients under the age of 5 years old was also summarized for each month based on the hospital admissions data. Through areal interpolation, the total population under age of 5 was also obtained for each zip code area. Figure 3 present the asthma occurrence rate for the 12 months of year 1997 at the zip code level. It is observed from this figure that a higher asthma occurrence rate is associated with the winter cold season while a lower asthma occurrence rate is seen mostly during the summer hot season.



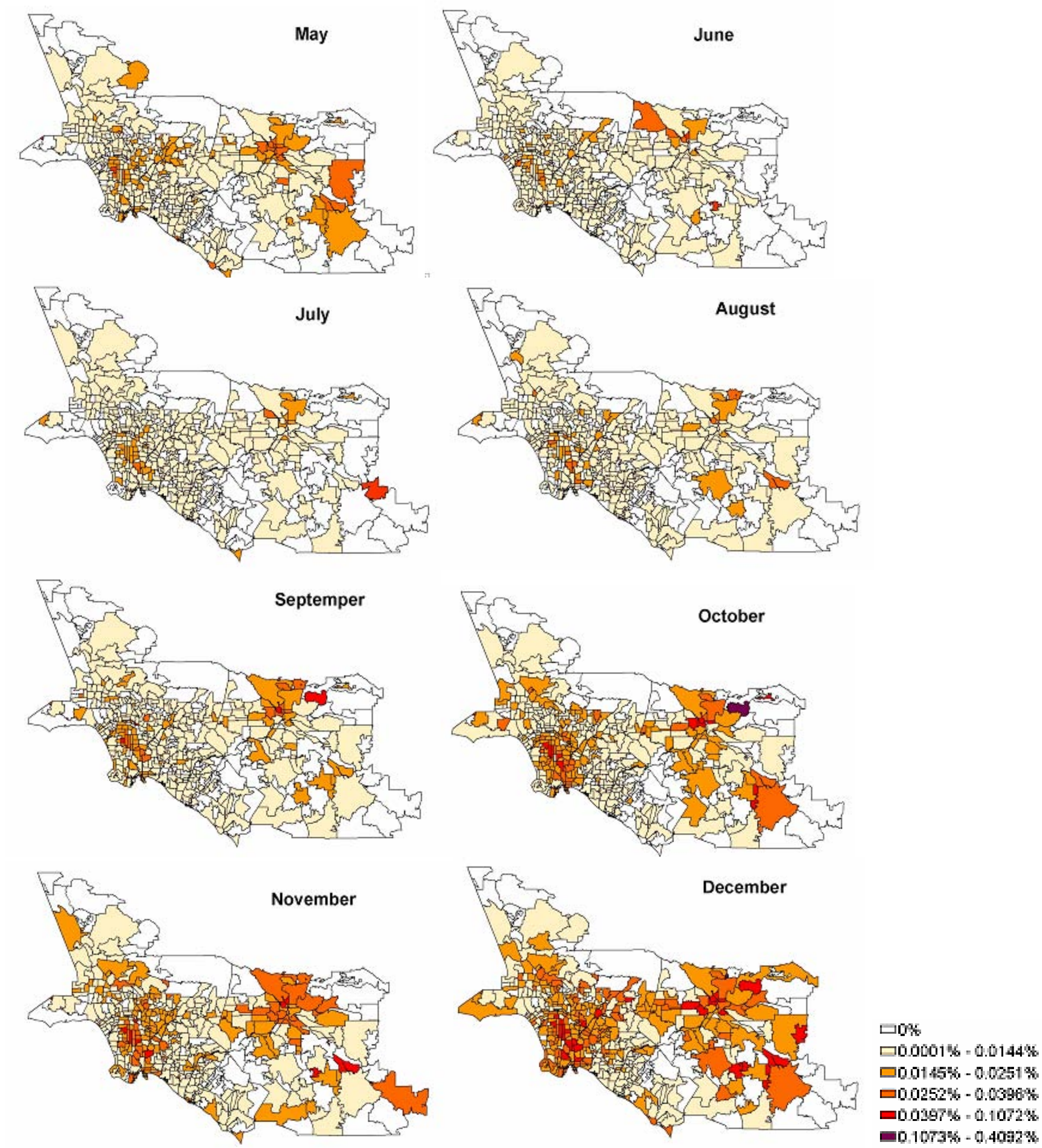


Figure 3. The asthma occurrence rate of each zip code area for the 12 months of year 1997.

This observation implies an inverse relationship between asthma occurrence rate and ozone concentration at the local spatial level. A similar relationship is also observed at the global level in Figure 4, where both monthly ozone level and numbers of hospital admission for asthma in the whole study area demonstrated a seasonal fluctuation. Higher ozone levels are associated with lower asthma cases numbers in the summer hot season, while lower ozone levels are related to higher number of hospital admissions is in winter cold season.

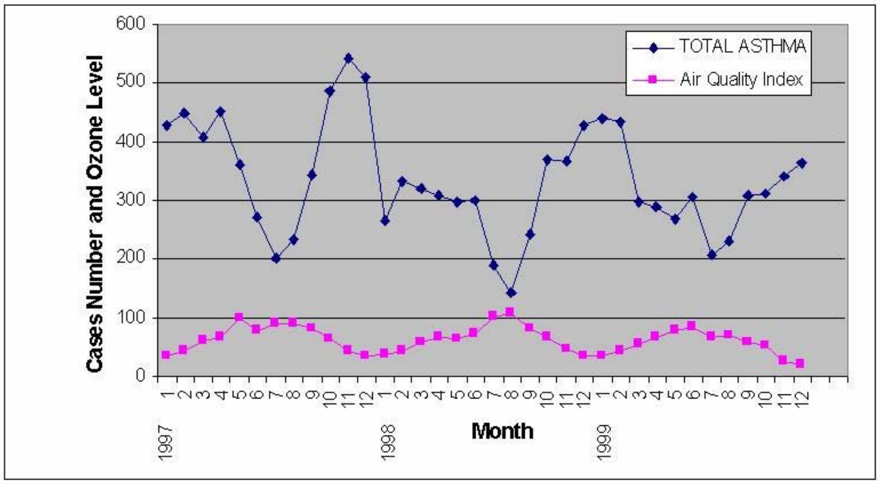


Figure 4. Monthly distribution of asthma cases number for children under 5 and ozone level for the whole study area.

The results for univariate analysis were presents in Figure 5, which also confirmed our earlier observation. Winter months such as January, February, October, November, and December had the higher risk rate ratio for asthma hospital admission, while July and August had the very low risk rate ratio for asthma hospital admission (*P* value < 0.001). It is also observed that 1998 and 1999 had a lower admission rate ratio than 1997, suggesting a potential improvement of air quality over the years. Ozone, however, demonstrate a rate ration of 0.86 (with RR less than 1 indicating an inverse relationship), which contradicts the general expectation. In this univariate analysis, where the ozone index at the zip code level was the only independent variable, only the spatial relationship between ozone and asthmas was considered. It appears that ozone is protecting factor of asthma hospital admission.

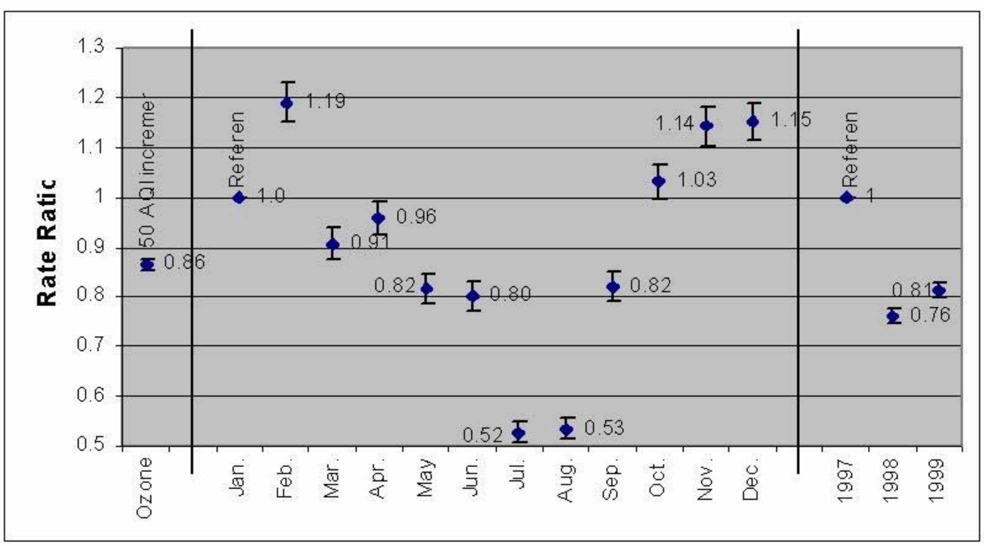


Figure 5. The results of univariate Poisson analysis expressed as rate ratio (RR).

In the multivariate analysis, the temporal factors, i.e. months and years, were included in the Poisson regression. Table 2 presents the results of such analysis, which demonstrate a quite different relationship. The rate ratio for ozone level index is 1.11 (95% CI: 1.09-1.13) per 50 AQI (about 0.01 ppm) increment after adjusting for months and years. This means that each time AQI increases by 50, hospital admission rates the next day would increase 11% among the children with age less than 5 years old. The relationships between asthma admission rate and the months and years were similar to those observed at the univariate analyses.

Table 2. Multivariable Poisson Regression of Asthma Admission Rate Ratio for the children under 5 years old

Variable	**RR (95% CI)**
50 AQI increment	1.11 (1.09-1.13)
Jan	1.00 (Referent)
Feb	1.17 (1.13-1.21)
Mar	0.87 (0.84-0.90)
Apr	0.90 (0.87-0.93)
May	0.74 (0.72-0.77)
Jun	0.73 (0.71-0.76)
Jul	0.48 (0.45-0.50)
Aug	0.48 (0.46-0.50)
Sep	0.76 (0.73-0.79)
Oct	0.98 (0.94-1.01)
Nov	1.13 (1.10-1.17)
Dec	1.17 (1.13-1.21)
1997	1.00 (Referent)
1998	0.76 (0.75-0.78)
1999	0.83 (0.81-0.84)

Discussion and Conclusion

The prevalence of asthma is increasing around the world. However, the causes of this increased prevalence and the role of ozone as a factor are still debatable.

Ozone can build up to dangerous concentrations when heat, sunlight, and hydrocarbons from fuel exhaust combine. This study focused on a significant relationship between ambient ozone exposure, a modifiable risk factor, and hospital admission of asthma for children less than 5 years old. Our results strongly support that ambient ozone level relates to children hospital admission of asthma when both spatial and temporal factors were taken into consideration. Our study also demonstrated that asthma hospital admission rate is highly related to seasons, an unmodified risk factor, at a much high magnitude than to ambient ozone level. This suggests that ozone may not a major risk factor or an allergen for childhood asthma. Ambient ozone could be only a sufficient trigger of asthma.

The biologically mechanisms of ozone and asthma are complicated. Inhaled ozone is absorbed by the surface liquid lining the airways. In animal studies, exposure causes morphologic injury along the entire respiratory tract (Harkema JR, 1995), but most controlled human exposure studies that have involved asthmatic subjects have not shown them to be especially sensitive to ozone (Balmes JR, 1993).

Considering the relative homogeneity of meteorological factor among our study area, we did not included temperature, humidity, pollen, mold, or other meteorological information in this study. Another limitation of this study is that we did not include other pollutant such as suspended particulates, black smoke, sulfur dioxide, or SO_2 in this study. These pollutants may also cause asthma. However, all of these pollutants were reported to be significantly correlated with ozone (Fauroux B, 2000).

We conclude that while there are large seasonal fluctuations of hospital admission rate of asthma, the ambient ozone level has contributed to the increasing risk of asthma hospital admission among children with age of 5 yeas old or younger.

Acknowledgments

This study was part of the NSF project entitled "Sensitivity of concentration response function to the explicitly modeling of spatial time dependence" (NSF142521). The authors would like to extend their appreciation to Dr. James Murdoch for his support and guidance. The authors would also like to thank Ms. Annie Hsu for her assistant in preparing the manuscript.

References

Balmes JR. The role of ozone exposure in the epidemiology of asthma. *Environ Health Perspect* 1993;101 Suppl 4:219-24.

Bates DV, Sizto R. Air pollution and hospital admissions in Southern Ontario: the acid summer haze effect. *Environ Res* 1987;43:317-31.

EPA, AirNow Publications (http://www.epa.gov/airnow/publications.html#aqi). Last accessed on June 11, 2003,

Fauroux B, Sampil M, Qenel P, Lemoullec Y. Ozone: a trigger for hospital pediatric asthma emergency room visits. *Pediatr Pulmonol* 2000;30:41-46.

Friedman MS, Power KE, Hutwagner L, Graham LM, Teague WG. Impact of changes in transportation and commuting behaviors during the 1996 Summer Olympic Games in Atlanta on air quality and childhood asthma. *JAMA* 2001;285:897-905.

Harkema JR, Plopper CG, Hyde DM, St George JA, Wilson DW, Dungworth DL. Response of the macaque nasal epithelium to ambient levels of ozone. A morphologic and morphometric study of the transitional and respiratory epithelium. *Am J Pathol* 1987 Jul;128:29-44.

O'Sullivan D, and Unwin DJ. *Geographic Information Analysis,* John Wiley & Sons, Inc, Hoboken, NJ, 436 p. 2003

Sadahiro Y. Accuracy of areal interpolation: A comparison of alternative methods, J. Geography Syst, 1999; 1:323-346.

Woodruff PG, Fahy JV. Asthma: prevalence, pathogenesis, and prospects for novel therapies. *JAMA* 2001;286:395-398.

Author's Contact Information

Hua Lu, MS
GIS Analyst
Department of Planning and Development
City of Allen
305 Century Parkway
Allen, TX 75080
Phone: 972-747-4119
E-mail: hlu@cityofallen.org

Fang Qiu, Ph.D
Assistant Professor of GIS and Remote Sensing
School of Social Sciences
The University of Texas at Dallas
2601 North Floyd Road
Richardson, Texas 75080
Phone: 972-883-4143
E-mail: ffqiu@utdallas.edu

Yiling Cheng, M.D, Ph.D.
Epidemiologist
Northrop Grumman Mission Systems
CDC Information Technology Support
Davidson Bldg, Mail Stop K-10
2858 Woodcock Blvd
Atlanta, GA 30341
Phone: 770-488-1269
Email: ycc1@cdc.gov