REPOSURE TO OZONE EXPOSURE TO OZONE Martine

Association Between Asthma Hospital Visits and Ozone Concentration in Maricopa County, Arizona (2007–2012)

Ahmed Mohamed, MSc, PhD Kate Goodin, MPH Office of Epidemiology Maricopa County Department of Public Health

Ronald Pope, PhD Mark Hubbard Maricopa County Department of Air Quality

> Michael Levine, PhD Department of Statistics Purdue University

Abstract The objective of this study was to evaluate the association of asthma hospital visits with ozone concentrations in Maricopa County, Arizona. We used time plots and distributed lag nonlinear models to achieve these objectives while accounting for some potential confounders including temperature and day of the week. A total of 90,381 asthma hospitalizations were retrieved from the dataset (daily median = 39, range: 8-122). Asthma hospitalizations were highest in 2008 (16,949), during the months of November through December, and lowest in 2011 (13,213), during the months of June through July. By contrast, the average daily ozone concentration ranged from 27.05 parts per billion (ppb) in 2012 to 30.15 ppb in 2008 and from 13.96 ppb in December to 40.58 ppb in May. The association between asthma hospitalizations (relative risk [RR/per 10 ppb increase of ozone]) start at ~1.046 (95% confidence interval [1.029, 1.064] at lag 0) and gradually decrease over several days. Our findings suggest exposure to ozone is associated with increased RR of asthma hospital visits in Maricopa County lasting several days. This study used recently developed methods that are freely available and could be used to evaluate other health events that are measured over time.

Introduction

Asthma is a chronic disease that affects a considerable number of adults and children. It has been a growing public health challenge in industrialized countries for the last few decades where it has reached epidemic levels, despite the introduction of new medications (Eder, Ege, & von Mutius, 2006; Le Moual et al., 2013). While there is a general consensus that, based on available data, the prevalence of asthma has been on the rise in western countries, the underlying causes of this increase are much less clear. On the one hand, it could be partially attributed to the advent of diagnostic tools and improved reporting; on the other hand, the role of air pollution, other environmental factors, genetics, and lifestyle changes cannot be ignored (Ebi & McGregor, 2008; Sheffield, Knowlton, Carr, & Kinney, 2011). Nonetheless, based on available evidence, it is now accepted that air pollution is a risk factor for asthma (Oosterlee, Marjon, Lebret, & Brunekreef, 1996; Venn, Lewis, Cooper, Hubbard, & Britton, 2001). Not only has this effect been found to be statistically significant, the biological mechanism through which exposure to air pollutants exacerbates the severity of asthma symptoms has been explained (Ciencewicki, Trivedi, & Kleeberger, 2008; Gent et al., 2003; Slaughter, Lumley, Sheppard, Koenig, & Shapiro, 2003).

Ozone is one of the pollutants that was found to be associated with increased risk of asthma hospitalizations and deaths in studies worldwide, including in the United States (Babin et al., 2007; Centers for Disease Control and Prevention, 2014; Delfino, Gong, Jr., Linn, Pellizzari, & Hu, 2003; Delfino et al., 2014; Jerrett et al., 2009; Mortimer, Tager, Dockery, Neas, & Redline, 2000). Additionally, ozone was found to be associated with development of new asthma cases in some studies (Künzli et al., 2009; McDonnell, Abbey, Nishino, & Lebowitz, 1999; Modig, Torén, Janson, Jarvholm, & Forsberg, 2009).

Although there is a general consensus in the literature on the adverse effect of ozone on asthma symptoms and hospitalizations (Burnett, Brook, Yung, Dales, & Krewski, 1997), some studies have produced inconclusive or conflicting results. This discordance is not completely unexpected and can be partly explained by differences in study population, designs, and analytic approach (Akinbami, Lynch, Parker, & Woodruff, 2010; Delamater, Finley, & Banerjee, 2012). Several studies have examined the association between asthma hospitalizations and/or emergency department visits in some metropolitan areas including Los Angeles and Seattle because



FIGURE 2

Geographic Distribution of Asthma Patients Visiting Hospitals in Maricopa County (2007–2012)



of the known link between air pollution in highly populated areas and asthma hospital visits and admissions (Akinbami et al., 2010; Delamater et al., 2012).

Maricopa County has grown considerably in the recent decades from less than a million inhabitants to one of the most populous counties in the nation with close to four million residents (U.S. Census Bureau, 2013). This rapid growth probably was accompanied by a comparable increase in traffic volume producing high levels of volatile organic compounds, which are one of the main precursors of ozone (Ebi & McGregor, 2008; Hodnebrog et al., 2012). Consequently, epidemiological studies have found a higher risk of asthma hospitalizations and admissions among those living in close proximity to highways and streets with high traffic volume (Oosterlee, Drijver, Lebret, & Brunekreef, 1996; van Vliet et al., 1997). Given this reality and the fact that the Phoenix metropolitan area is among the most polluted cities in the nation (American Lung Association, 2013), it is important to examine the potential effect of ozone level on hospital visits and admissions among Maricopa County residents.

Therefore, the objective of this study was to evaluate the association between ozone concentration and asthma hospitalization from inpatient hospitalizations and emergency department visits in Maricopa County for the period from January 2007 through December 2012.

Materials and Methods

Data Sources

Inpatient and emergency department visits occurring in Maricopa County with an asthma diagnosis code (49300, 49301, 49302, 49310, 49311, 49320, 49321, 49322, 49381, 49382, 49390, 49391, and 49392) from January 1, 2007, through December 31, 2012, were extracted from the hospital discharge database accessible to the Maricopa County Department of Public Health. Extracted data include the date of visit (the day of the visit but not the time was available) and the patient's address, which was used to geocode the records. The Maricopa County Air Quality Department provided hourly ozone and temperature measurement from 16 monitoring stations distributed throughout Maricopa County urban and suburban areas (Figure 1).



Data Management

Thiessen polygons were drawn around each air quality monitoring station to determine the most plausible source of exposure for each individual patient. Thiessen polygons are generated to ensure that any point (an asthma patient) inside the polygon is closer to the polygon center (ozone monitor) than any other polygon center (ozone monitor) in the area. This approach was used to ensure that all patients were assigned an ozone reading from the closest monitor.

Mean daily ozone and temperature measurements were calculated from hourly measurements in preparation to merge them with patient data. Daily measurements were chosen to match the time scale of hospitalization records, which were available only in daily format. Patient data were then divided by location into subsets corresponding to each Thiessen polygon, as previously discussed. Each patient subset was merged with daily ozone and temperature data from the corresponding monitoring station by date, and all subsets were appended together to form the full dataset containing the patient's admission date along with ozone and temperature measurements. Lastly, the total patient daily counts indexed by visit date (days) and the overall daily mean of ozone and temperature measurement were calculated, along with the day of the week, to prepare the dataset for time-series analysis. Hospitalization records and ozone/temperature readings in two exposure areas (Cave Creek and Rio Verde) had very small numbers of asthma visits during the study period and therefore were exclude from the analysis (Figure 2).

Statistical Analysis

We used time plots and the distributed lag linear and nonlinear model (Bhaskaran, Gasparrini, Hajat, Smeeth, & Armstrong, 2013; Gasparrini, 2011) to evaluate the association between asthma hospital visits and ozone levels while accounting for trend, season, temperature, and day of the week. Time plots were used to illustrate the overall pattern over time. The association between the daily number of asthma hospital visits and ozone concentration was evaluated using a Poisson model, taking into account the effect of seasonality, long-term trend, temperature, and day of the week. Also, a lag component was added to the model to evaluate how long the effect of ozone exposure on the number of asthma hospitalizations lasts. Distribution of the model residuals over time was checked for sign of anomalies or indications for deviation from the model assumptions.

Results

A total of 90,381 asthma hospitalizations were retrieved from the dataset (daily median = 39, range: 8–122). Asthma hospitalizations were highest in 2008 (16,949), from November through December, and lowest in 2011 (13,213) and from June through July (Figure 3). By contrast, the average daily ozone concentration ranged from 27.05 parts per billion (ppb) in 2012 to 30.15 ppb in 2008 and from 13.96 ppb in December to 40.58 ppb in May (Figure 3). Additionally, the median number of daily asthma hospitalized visits during weekdays [median = 39; range (16–115)] did not vary considerably from the number of visits during weekends [median = 40; range (14-122)]. Similarly, mean daily ozone concentration ranged from 29.34 ppb on weekdays to 30.09 ppb in weekends (Table 1).

TABLE 1

Descriptive Statistics

						1
Variable	# of Observations	Mean	Median	SD	Minimum	Maximum
Asthma hospitalizations count (per day)	2192	41.23	39	15.37	8	122
Mean daily temperature (°F)	2192	74.05	73.7	15.9	35.11	102.62
Mean daily ozone (ppb ^a)	2192	28.67	29.53	11.39	3.37	59.09
Year					2007	2012
apph = parts per billion						

appb = parts per billion.

TABLE 2

Ozone Coefficients and Relative Risk (RR) for Asthma Hospital Visit Counts Obtained From Poisson Model

Model	Coefficient	SE	z-Score	<i>p</i> -Value	RR	95% <i>Cl</i> ª
Model 1 ^b	-0.051	0.007	-7.404	<.0001	0.95	0.937, 0.963
Model 2 ^c	1.046	0.009	5.107	<.0001	1.047	1.029, 1.065
Model 3 ^d	1.045	0.008	5.386	<.0001	1.047	1.029, 1.064

 ${}^{a}CI = confidence interval.$

^bNot adjusted.

°Adjusted for trend and seasonality.

^dAdjusted for trend, seasonality, temperature, and day of the week.



The final model was Poisson regression with daily asthma hospitalization count as the dependent variable and ozone as the independent variable adjusted for temperature and day of the week (Table 2). There was a significant association between the daily count of asthma hospitalizations and ozone concentration with a relative risk (RR) of 1.046; 95% confidence interval [1.029, 1.064] or equivalently 4.6% for every 10 ppb increase in ozone level. The ozone effect seemed to decrease gradually after the first day of exposure and level off by lag day 5 (Figure 4).

Discussion and Conclusions

Our findings suggest that ozone level is positively associated with asthma hospital visits and that this effect lasts for several days after the exposure. Our results are in agreement with other studies that reported comparable, but slightly varying, effect size or RR estimates (Barnett et al., 2005; Cakmak, Dales, & Coates, 2012; Fauroux, Sampil, Quenel, & Lemoullec, 2000; Holmen et al., 1997). These variations are not surprising and probably could be due to the differences in study population and statistical modeling methods (Akinbami et al., 2010; Delamater et al., 2012; Mar & Koenig, 2009). For instance, a study conducted in Seattle reported an approximate 10% increase in asthma emergency department visits per 10 ppb increase in ozone, which may seem substantially higher from the estimate (RR = 4.6%) reported here in Maricopa County. A closer look, however, reveals that the Seattle study used data only from May through October, months characterized by high ozone levels, which may explain the higher RR estimates.

Maricopa County has been growing noticeably over the past decades and its ozone concentrations often exceed the national ambient air quality standards (NAAQS). Accordingly, it is important from a public health standpoint to estimate the effect of ozone concentrations on asthma hospital visits. This is the first study, to our knowledge, to evaluate this effect in Maricopa County.

Two of the main challenges in environmental and time-series analysis pertain to the method of exposure assessment and the time scale of the analysis. To increase the validity of the exposure variable and account for geographic variation, we chose to assign individuals to the closest air monitoring station rather than use a countywide average over all stations. We were particularly interested in the lag time from exposure to hospitalization, so we wanted to use a finer time scale than monthly or weekly. Additionally, the hospitalization information did not have time of admission, which prevented us from examining a time scale smaller than daily.

The range of daily average ozone measurements reported in this study was within the acceptable standards set by the U.S. Environmental Protection Agency (U.S. EPA). Data presented here, however, are based on a daily average, which is an aggregation of the hourly recordings. This means that an individual station could have exceeded the U.S. EPA limit at a given hour of the day and that would not be discernable from the data presented here. In fact, there were 12 high ozone days (8-hour maximum ozone >75 ppb) in the Phoenix metropolitan area in 2012 alone.

Similarly, the daily number of asthma hospital visits probably varied by admission type, age groups, and other demographic characteristics not considered here. It has been reported, however, that for asthma and respiratory disease, children are more sensitive to ozone concentrations compared with adults (Delfino et al., 2014; Künzli et al., 2009; Oosterlee et al., 1996) and were probably affected disproportionately (Mar & Koenig, 2009). Day of the week did not have any considerable effect on the asthma RR, indicating that ozone's persistence in the ambient environment does not-in general-vary by different day of the week over our study area. This is supported by known temporal dynamics of ozone, which tends to follow a diurnal pattern within urban areas, even on weekends, and a more constant pattern in suburban and rural areas (Gregg, Jones, & Daws, 2003; Seinfeld & Pandis, 2006).

Currently, the NAAQS list ozone concentrations higher than 75 ppb in an 8-hour average as unhealthy for sensitive groups. According to some advocate groups, however, the current standards need to be reviewed and updated (American Lung Association, 2013); this review is currently in progress by the U.S. EPA in accordance with requirements in the 1990 Amendment to the Clean Air Act (U.S. EPA, 1990).

Future areas for research include examining the number of high ozone days as well as the magnitude of ozone levels and their impact on asthma hospital visits among the local population. As with other hospital discharge data, it should be acknowledged that some asthmatic patients might not seek treatment at hospitals depending on the severity of their conditions and the influence of socioeconomic factors on healthcare access. Consequently, the actual number of people with asthma as well as the magnitude of symptoms experienced in Maricopa County is probably higher than reported here.

Corresponding Author: Ahmed Mohamed, Public Health Scientist, Office of Epidemiology, Maricopa County Department of Public Health, 4041 North Central Avenue, Phoenix, AZ 85012.

E-mail: AhmedMohamed@mail.maricopa.gov.

References

- Akinbami, L.J., Lynch, C.D., Parker, J.D., & Woodruff, T.J. (2010). The association between childhood asthma prevalence and monitored air pollutants in metropolitan areas, United States, 2001– 2004. Environmental Research, 110(3), 294–301.
- American Lung Association. (2013). *State of the air*. Washington, DC: Author. Retrieved from http://www.stateoftheair.org/2013/states/
- Babin, S.M., Burkom, H.S., Holtry, R.S., Tabernero, N.R., Stokes, L.D., Davies-Cole, J.O., DeHaan, K., & Lee, D.H. (2007). Pediatric patient asthma-related emergency department visits and admissions in Washington, DC, from 2001–2004, and associations with air quality, socio-economic status and age group. *Environmental Health*, 6, 9.
- Barnett, A.G., Williams, G.M., Schwartz, J., Neller, A.H., Best, T.L., Petroeschevsky, A.L., & Simpson, R.W. (2005). Air pollution and child respiratory health: A case-crossover study in Australia and New Zealand. American Journal of Respiratory and Critical Care Medicine, 171(11), 1272–1278.

- Bhaskaran, K., Gasparrini, A., Hajat, S., Smeeth, L., & Armstrong, B. (2013). Time series regression studies in environmental epidemiology. *International Journal of Epidemiology*, 42(4), 1187–1195.
- Burnett, R.T., Brook, J.R., Yung, W.T., Dales, R.E., & Krewski, D. (1997). Association between ozone and hospitalization for respiratory diseases in 16 Canadian cities. *Environmental Research*, 72(1), 24–31.
- Cakmak, S., Dales, R.E., & Coates, F. (2012). Does air pollution increase the effect of aeroallergens on hospitalization for asthma? *Journal of Allergy and Clinical Immunology*, 129(1), 228–231.
- Centers for Disease Control and Prevention. (2014). Asthma, respiratory allergies, and airway diseases. Retrieved from http://www.cdc.gov/ climateandhealth/effects/air_pollution.htm
- Ciencewicki, J., Trivedi, S., & Kleeberger, S.R. (2008). Oxidants and the pathogenesis of lung diseases. *Journal of Allergy and Clinical Immunology*, 122(3), 456–468.
- Delamater, P.L., Finley, A.O., & Banerjee, S. (2012). An analysis of asthma hospitalizations, air pollution, and weather conditions in

References

Los Angeles County, California. *Science of the Total Environment*, 425, 110–118.

- Delfino, R.J., Gong, H., Jr., Linn, W.S., Pellizzari, E.D., & Hu, Y. (2003). Asthma symptoms in Hispanic children and daily ambient exposures to toxic and criteria air pollutants. *Environmental Health Perspectives*, 111(4), 647–656.
- Delfino, R.J., Wu, J., Tjoa, T., Gullesserian, S.K., Nickerson, B., & Gillen, D.L. (2014). Asthma morbidity and ambient air pollution: Effect modification by residential traffic-related air pollution. *Epidemiology*, 25(1), 48–57.
- Ebi, K.L., & McGregor, G. (2008). Climate change, tropospheric ozone and particulate matter, and health impacts. *Environmental Health Perspectives*, 116(11), 1449–1455.
- Eder, W., Ege, M.J., & von Mutius, E. (2006). The asthma epidemic. *The New England Journal of Medicine*, 355(21), 2226–2235.
- Fauroux, B., Sampil, M., Quenel, P., & Lemoullec, Y. (2000). Ozone: A trigger for hospital pediatric asthma emergency room visits. *Pediatric Pulmonology*, 30(1), 41–46.
- Gasparrini, A. (2011). Distributed lag linear and non-linear models in R: The package dlnm. *Journal of Statistical Software*, 43(8), 1–20.
- Gent, J.F., Triche, E.W., Holford, T.R., Belanger, K., Bracken, M.B., Beckett, W.S., & Leaderer, B.P. (2003). Association of low-level ozone and fine particles with respiratory symptoms in children with asthma. *Journal of the American Medical Association*, 290(14), 1859–1867.
- Gregg, J.W., Jones, C.G., & Daws, T.E. (2003). Urbanization effects on tree growth in the vicinity of New York City. *Nature*, 424, 183–187.
- Hodnebrog, Ø., Berntsen, T.K., Dessens, O., Gauss, M., Grewe, V., Isaksen, I.S.A., Koffi, B., Myhre, G., Olivié, D., Prather, M.J., Stordal, F., Szopa, S., Tang, Q., van Velthoven, P., & Williams, J.E. (2012). Future impact of traffic emissions on atmospheric ozone and OH based on two scenarios. *Atmospheric Chemistry and Phys*ics, 12(24), 12211–12225.
- Holmen, A., Blomqvist, J., Frindberg, H., Johnelius, Y., Eriksson, N.E., Henricson, K.A., Herrstrom, P., & Hogstedt, B. (1997). Frequency of patients with acute asthma in relation to ozone, nitrogen dioxide, other pollutants of ambient air and meteorological observations. *International Archives of Occupational and Environmental Health*, 69(5), 317–322.
- Jerrett, M., Burnett, R.T., Pope, C.A., III, Ito, K., Thurston, G., Krewski, D., Shi, Y., Calle, E., & Thun, M. (2009). Long-term ozone exposure and mortality. *The New England Journal of Medicine*, 360(11), 1085–1095.
- Künzli, N., Bridevaux, P.O., Liu, L.J.S., Garcia-Esteban, R., Schindler, C., Gerbase, M.W., Sunyer, J., Keidel, D., & Rochat, T. (2009). Traffic-related air pollution correlates with adult-onset asthma among never-smokers. *Thorax*, 64(8), 664–670.

- Le Moual, N., Jacquemin, B., Varraso, R., Dumas, O., Kauffmann, F., & Nadif, R. (2013). Environment and asthma in adults. *La Presse Médicale*, 42(9, Pt. 2), e317–e333.
- Mar, T.F., & Koenig, J.Q. (2009). Relationship between visits to emergency departments for asthma and ozone exposure in greater Seattle, Washington. *Annals of Allergy, Asthma & Immunology* 103(6), 474–479.
- McDonnell, W.F., Abbey, D.E., Nishino, N., & Lebowitz, M.D. (1999). Long-term ambient ozone concentration and the incidence of asthma in nonsmoking adults: The AHSMOG study. *Environmental Research*, 80(2, Pt. 1), 110–121.
- Modig, L., Torén, K., Janson, C., Jarvholm, B., & Forsberg, B. (2009). Vehicle exhaust outside the home and onset of asthma among adults. *European Respiratory Journal*, 33(6), 1261–1267.
- Mortimer, K.M., Tager, I.B., Dockery, D.W., Neas, L.M., & Redline, S. (2000). The effect of ozone on inner-city children with asthma: Identification of susceptible subgroups. *American Journal of Respiratory and Critical Care Medicine*, 162(5), 1838–1845.
- Oosterlee, A., Drijver, M., Lebret, E., & Brunekreef, B. (1996). Chronic respiratory symptoms in children and adults living along streets with high traffic density. *Occupational and Environmental Medicine*, 53(4), 241–247.
- Seinfeld, J.H., & Pandis, S.N. (2006). Atmospheric chemistry and physics: From air pollution to climate change (2nd ed.). Hoboken, NJ: John Wiley & Sons.
- Sheffield, P.E., Knowlton, K., Carr, J.L., & Kinney, P.L. (2011). Modeling of regional climate change effects on ground-level ozone and childhood asthma. *American Journal of Preventive Medicine*, 41(3), 251–257.
- Slaughter, J.C., Lumley, T., Sheppard, L., Koenig, J.Q., & Shapiro, G.G. (2003). Effects of ambient air pollution on symptom severity and medication use in children with asthma. *Annals of Allergy, Asthma & Immunology*, 91(4), 346–353.
- U.S. Census Bureau. State & county quickfacts. Retrieved from http:// quickfacts.census.gov/qfd/states/04/04013.html
- U.S. Environmental Protection Agency. (1990). The clean air act amendments of 1990. Retrieved from http://www.epa.gov/laws-regulations/summary-clean-air-act
- van Vliet, P., Knape, M., de Hartog, J., Janssen, N., Harssema, H., & Brunekreef, B. (1997). Motor vehicle exhaust and chronic respiratory symptoms in children living near freeways. *Environmental Research*, 74(2), 122–132.
- Venn, A., Lewis, S., Cooper, M., Hubbard, R., & Britton, J. (2001). Living near a main road and the risk of wheezing illness in children. American Journal of Respiratory and Critical Care Medicine, 164(12), 2177–2180.