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Ozone Pollution and Asthma Emergency Department Visits in Fresno, California, USA, During the Warm Season (June-September) of the Years 2005 to 2015: A Time-Stratified Case-Crossover Analysis.

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Ozone Pollution and Asthma Emergency Department Visits in Fresno, California, USA, During the Warm Season (June-September) of the Years 2005 to 2015: A Time-Stratified Case-Crossover Analysis

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Abstract

This time-stratified case crossover study investigates whether short term exposure to ozone (O_3) is associated with asthma emergency departments (ED) visits during warm seasons (June-September) of 2005 to 2015 in Fresno, California, USA. We identified 8102 ED visits from 2005 to 2015 in Fresno, California who lived within 15 km of active air monitors. Conditional logistic regression models were used to obtain the odds ratio (OR) and 95% confidence interval associated with 5 ppb increase in the air pollutants. A 5 ppb increase in the concentration of O_3 at lag 7 is associated with 10.1% increase in the odds of having asthma ED visits [OR: 1.101 (95% confidence intervals: 1.075, 1.128)]. We explored potential effect modification by land-use (commercial, and residential), sex (female, and male), race (White, Black, and Hispanic), and age (2-5, 6-18, 19-40, 41-64 and >= 65). We found that 5 ppb increase in the concentration of O_3 at lag 7 is associated with 17% [OR: 1.170 (95% confidence intervals: 1.127, 1.215)] and 11.3% [OR: 1.113 (95% confidence intervals: 1.067, 1.160)] increase in the odds of having asthma ED visits in commercial and residential areas, respectively. Sex was not a modifier in this study. For race, we found that the asthma ED visits among all the races to be associated with O_3 exposure, considering that Blacks and Hispanics showed faster response to O_3 exposure. Furthermore, the association between O_3 exposure and asthma ED visits among children (2 to 5 years old), adolescents (6 to 18 years old) and elderlies (>= 65 years old) were greater than those of other age groups in this study. This study showed that O_3 exposure is associated with asthma ED visits in Fresno during the warm seasons (June-September) of 2005 to 2015.

Keywords: Asthma; emergency visits; time-stratified case crossover; warm season; Ozone

Introduction

Fresno, located at the central part of the San Joaquin Valley (SJV), California, USA is one of the most air polluted cities in North America (1). The air pollution in Fresno often exceeds the standard levels for ozone, particularly during the warm seasons (June-September) (2). This is mostly due to the geographical characteristics of the San Joaquin Valley Air Basin in which Fresno is located (i. e. creates a giant air corridor susceptible to air pollution creation and retention) (3). It should be noted that the temperature is higher during June to September (4), providing ideal conditions for ozone formation (5). Therefore, during the warmer months of the year, the atmospheric reactions that produce ground level ozone are accelerated by the higher temperatures, contributing to ozone accumulation in the air.

Previous research has found that ozone at the ground level is an air pollutant associated with numerous harmful effects on respiratory health, even at levels commonly found in urban areas throughout the world (6). It has been documented that exposure to ozone produces inflammatory changes in the lung, inducing clinically meaningful pulmonary responses (7). Clinical research has found that exposure to ozone at standard levels produces respiratory symptoms related to decrease in the forced expiratory volume in 1 sec (FEV1) in healthy adults (7-8). Ozone contributes to mortality (9), morbidity and hospital admissions related to respiratory disease (10-12), even at low ambient levels (13-14). Ozone pollution is particularly harmful for children (15-17), and elderlies (18) who are already affected by lung diseases such as asthma. Asthma, a clinical condition characterized by intermittent obstructive respiratory symptoms and airway hyperresponsiveness to a variety of stimuli may be worsened by exposure to ozone (19). There have been studies showing no significant association between O_3 exposure and asthma exacerbations (20-22). Nonetheless, there have been studies reporting a positive association between O_3 exposure and asthma exacerbations (23-24). Therefore, a need for more studies on the association between O_3 exposure and asthma ED visits is calling for more investigation.

The present study examines the relationship between O_3 exposure and asthma ED visits during the warm seasons (June-September) in Fresno California from 2005 and 2015 through a time-stratified case crossover design. We hypothesize that acute exposure to O_3 is associated with increased odds of having an ED visit related to asthma.

Materials and Method

Data and Participants

We obtained the hospital data from California's Office of Statewide Health Planning and Development (OSHPD) for the warm seasons (June-September) of 2005 to 2015 in Fresno, California, USA. The dataset contains the abstracted information from individual patient records, including patient’s ZIP code, gender, birthdate, and principal language, service date, diagnoses, cause of injury, treatments/procedures, and expected source of payment which are submitted every three months by emergency departments to OSHPD. We selected emergency department visits due to asthma attacks identified by the International Classification of Diseases, 9^{th} Revision (ICD-9). Multiple visits by a single person cannot be identified because the data is not linked by person longitudinally due to the lack of access to social security number; therefore, each valid observation was taken as an independent observation.

Study design

The time-stratified case-crossover design is an alternative to conventional time series regression for analyzing associations between short-term air pollution exposure and the risk of an acute adverse health event [15-16]. This design compares exposures of individual patients during the hazard period (i.e. the day of asthma ED admission) to their exposures on up to 3 referent days occurring on the same day of the week during the same month. Because each individual serves as his/her own control, there is no confounding by factors that do not vary within a month. The simple lag models, up to 7 days before the event days, and cumulative lag models were used to study the acute effect of O_3 on the occurrence of asthma ED visit. Specifically, in the simple lag model, we used the concentration of the day before the event day (lag 1), two days before the event day (lag 2) and up to seven days before the event (lag 7). The cumulative lag model used the mean concentration of the pollutant in the day of the event and the previous day was used as lag 0-1, and 7 days mean concentration of the pollutant as lag 0-7.

Exposure Assessment

The data for air pollutants were obtained from EPA's Air Quality System (AQS). The data in the AQS dataset is provided by tribal, state, and local agencies and must pass several quality control tests before these data are saved into the AQS dataset. Furthermore, each monitor must pass several quality assurance assessments and audits to be eligible for passing its data to the EPA database (25). Air pollution data as well as meteorological data were collected from 5 active sampling stations during the warm seasons (June-September) of the year 2005 to 2015. In this study, daily-average values were collected for Nitrogen Dioxide (NO_2), Particulate Matter 2.5 ($PM_{2.5}$), Carbon Monoxide (CO), and Sulfate Dioxide (SO_2); and, 8-hr maximum-averages were used for O_3. Relative humidity is presented in the dataset in percent and atmospheric pressure in bar. For temperature, the mean daily temperature in degrees Celsius (C°) was used. For meteorological factors, we applied restricted cubic spline (RCS) with 3 degrees of freedom (3 d.f.). Air pollution exposures were assigned to the patients' ZIP code of residence located within 15 km of the sampling station to minimize measurement errors. In previous studies, the radius of 20 km in California was applied (23); however, we decided to apply 15 km to have a closer assignment of the patients to the relevant concentration of O_3 in Fresno. In addition, the elevation within the city of Fresno does not vary that considerably that might result in sudden change of O_3 concentration. A total of 20 ZIP codes were included. Geographical assignment was performed using GIS V. 10.5.1.

Statistical analysis

ICD-9 code 493 for asthma related visits (National Center for Health Statistics, 2011) was used to select asthma related ED visits in Fresno, California in the warm seasons of 2005 to 2015. We used patient's date of visit, principal diagnosis, residential ZIP code, the patient's age, race, and sex from OSHPD dataset.

To estimate the association between short-term exposure to O_3 (8-hr maximum-average; continuous) and the odds of having asthma ED visit in Fresno, California, we used conditional logistic regression models. We controlled for meteorological factors (i. e. temperature, barometric pressure and relative humidity) via restricted cubic spline, and $PM_{2.5}$, NO_2, SO_2 and CO during the same exposure window. The time-stratified case-crossover analysis using conditional logistic regression can be written as follows:

$$l_c(\beta) = \sum_{k=1}^{n} Y_k \times \{ \beta.(O_{3_{k1}}, PM_{2.5_{k1}}, NO_{2_{k1}}, SO_{2_{k1}}, CO_{k1}, spline(T_{k1}), spline(P_{k1}), spline(RH_{k1})) - \log\left[\sum_{j=3}^{7} exp\left(\beta.(O_{3_{kj}}, PM_{2.5_{kj}}, NO_{2_{kj}}, SO_{2_{kj}}, CO_{kj}, spline\left(T_{kj}\right), spline\left(P_{kj}\right), spline\left(RH_{kj}\right))\right)\right]\}$$

Where, Y_k is daily counts of asthma events on k-th day; and $\beta = \beta_1, \beta_2, \beta_3, \beta_4, \beta_5, \beta_6, \beta_7, \beta_8$ refers to the coefficient for each covariate. In addition, $O_{3_{k1}}, PM_{2.5_{k1}}, NO_{2_{k1}}, SO_{2_{k1}}$, CO_{k1}, $spline(T_{k1}), spline(P_{k1}), and\ spline(RH_{k1})$ stand for the covariates for the case; and, $O_{3_{kj}}, PM_{2.5_{kj}}, NO_{2_{kj}}, SO_{2_{kj}}, CO_{kj}, spline\left(T_{kj}\right), spline\left(P_{kj}\right), and\ spline\left(RH_{kj}\right)$ are covariates for the three matched controls. The reported odds ratios (OR) and 95% confidence intervals (CI) in this study are based on 5 ppb increase in the concentration of O_3. Potential effect modifications were evaluated by stratifying models for land-use (commercial, and residential), sex (female and male), race and ethnicity (White, Black, and Hispanic), and age (2-5, 6-18, 19-40, 41-64, and >=65). All analyses were performed using STATA V. 14 (College Station, TX).

Results

Descriptive analysis of the hospital data

Table 1 describes the characteristics of asthma ED visits during the warm seasons (June-September) of the years 2005 to 2015 in Fresno, California, USA. During this period, 8102 individuals in the area under the study visited ED due to asthma attacks. As shown in the table, 55.51% and 45.05% of the patients were living in the residential and commercial areas of Fresno during the warm seasons (June-September) of the years 2005 to 2015. In addition, 55.6% of the study population were females, while 44.4% were males.

Table 1: Characteristics of asthma ED visits during the warm season (June-September) of the year 2005 to 2015 in Fresno, California, USA (n=8,102)

Variables	Number of Participants	Percent (%)
Land-use		
Residential	4498	55.510
Commercial	3569	44.050
Sex		
Female	4505	55.600
Male	3597	44.400
Race		
White	2596	33.000
Black	1115	14.000
Hispanic	3965	49.000
Age		
2-5	960	11.850
6-18	1819	22.450
19-40	2403	29.660
41-64	1959	24.180
>=65	465	5.740
Total Population	8102	100.00

We found that 33%, 14%, and 49% are White, Black, and Hispanic, respectively. The mean age for the population in this study is 26.8 years old. We categorized the age into five categories; 11.85%, 22.45%, 29.66%, 24.18% and 5.74% of the population in this study are between the age of 2 and 5 years old, 6 and 18 years old, 19 and 40 years old, 41 and 64 years old and higher than 65 years old, respectively.

Descriptive analysis of the air pollutants

Table 2: The distribution of air pollutants and meteorological factors in Fresno, California during the warm seasons (June-September) of 2005 to 2015

Variable	Mean	SD	Minimum	Percentile			Maximum
				25	50	75	
O_3 (ppb)	43.330	10.230	13.000	36.020	43.170	50.293	85.700
$PM_{2.5}$ (μg/m^3)	12.870	5.880	0.700	8.450	14.550	16.590	103.800
NO_2 (ppb)	11.640	5.060	2.470	7.700	10.950	14.700	37.860
SO_2 (ppb)	1.230	0.710	0.000	0.930	0.930	1.470	5.170
CO (ppb)	270.540	120.330	0.000	200.000	300.000	325.000	1691.000
Relative Humidity (%)	45.650	9.390	21.200	38.120	44.720	57.090	73.830
Barometric Pressure (bar)	0.990	0.003	0.980	0.990	0.990	1.001	1.009
Temperature (C°)	25.520	4.360	15.290	22.800	26.360	28.610	37.260

Abbreviations: SD, Standard Deviation

O_3 (ppb): 8-hr maximum average

$PM_{2.5}$ (μg/m^3): daily-average

CO (ppb): daily-average

NO_2 (ppb): daily-average

As shown in Table 2, the mean concentration of O_3 during the warm seasons of 2005 to 2015 was 43.3 ppb. In order to compare O_3 concentration with its level during the cold season, we obtained the corresponding amount of O_3 and also other pollutants and meteorological factors and indicated in Appendix I (Table I.1). As can be seen from Table I. 1, the mean concentration of O_3 during the warm season is higher than that of cold season (November-February) by 29.540 ppb. In addition, for other pollutants, it can be seen that their corresponding concentrations during the cold season are higher than those of warm seasons. Table 3 presents the correlation coefficients between the air pollutants and meteorological factors in Fresno, California during the warm seasons (June-September) of the years 2005 to 2015. The highest correlation was found between NO_2 and CO (0.377, $P < 0.01$), and O_3 and temperature (0.368, $P < 0.01$). as can be seen from the table, O_3 is positively correlated with $PM_{2.5}$, NO_2, CO, and SO_2.

Table 3: Correlation analysis of the air pollutants and meteorological factors in Fresno, California during warm seasons (June-September) of the years 2005 to 2015

Variable	O_3	$PM_{2.5}$	NO_2	CO	SO_2	Relative Humidity	Barometric Pressure	Temperature
O_3 (ppb)	1.000							
$PM_{2.5}$ ($\mu g/m^3$)	0.200*	1.000						
NO_2 (ppb)	0.029	0.242*	1.000					
CO	0.178*	0.209*	0.376*	1.000				
SO_2	0.205*	0.161*	0.138*	0.035	1.000			
Relative Humidity (%)	-0.236*	-0.072*	-0.049	0.105*	-0.243*	1.000		
Barometric Pressure (bar)	-0.093*	-0.133*	-0.081*	0.047	-0.206*	0.323*	1.000	
Temperature (C°)	0.368*	0.174*	0.136*	0.021	0.276*	-0.471	-0.357	1.000

*P < 0.01 **P < 0.05

Single-Pollutant Model

Table 4: The association between O_3 exposure and asthma ED visits in Fresno, California during the warm seasons (June-September) of 2005 to 2015: single and multi-pollutant models.

	O_3 (ppb)	
	OR	**95% CI**
Single-Pollutant Model (warm season)		
Lag 0	1.019	0.996, 1.041
Lag 1	1.042	1.019, 1.065
Lag 2	1.055	1.031, 1.079
Lag 3	1.069	1.045, 1.093
Lag 4	1.069	1.045, 1.093
Lag 5	1.086	1.062, 1.111
Lag 6	1.096	1.070, 1.121
Lag 7	1.101	1.075, 1.128
Lag 0-1	1.032	1.008, 1.055
Lag 0-7	1.078	1.051, 1.104
Multi-Pollutant Model for Lag 7		
Adjusted for $PM_{2.5}$	1.105	1.055, 1.155
Adjusted for NO_2	1.108	1.064, 1.152
Adjusted for CO	1.100	1.050, 1.151
Adjusted for SO_2	1.021	0.999, 1.045
Adjusted for all	1.128*	1.069, 1.197

Abbreviations: CI, confidence interval;

OR, odds ratio

O_3 was associated with asthma ED visits at all the lags, except for the event day (lag 0). A 5 ppb increase in the concentration of O_3 at the lag 7 was associated with 10.1% increase in the odds of having asthma ED visits [OR: 1.101 (95% confidence intervals: 1.075, 1.128)](Table 4). In addition, we found that 5 ppb increase in the average concentration of O_3 during the past 7 days before the event day (lag 0-7) is associated with 7.8% increase in the odds of having asthma ED visits [OR: 1.078 (95% confidence intervals: 1.051, 1.104)]. We found that the odds ratio at lag 7 is higher than that of other lags, both simple and cumulative lags. Considering this, we used this lag for multi-pollutant analysis. When we controlled for other pollutants, shown in the table under the multi-pollutant model, we observed an increase in the ORs. For example, by controlling for all the concomitantly present pollutants and splined meteorological factors, 5 ppb increase in the concentration of O_3 at the event day is associated with 12.8% increase in the odds of having asthma ED visits [OR: 1.128 (95% confidence intervals: 1.069, 1.197)]. In this regard, we controlled for all the concomitantly present pollutants (i. e. $PM_{2.5}$, NO_2, CO, and SO_2) in the stratification analysis of sex, race, age and land-use.

Stratification by land-use

Figure 2 shows the ORs per 5 ppb increase in O_3 concentration controlled for meteorological factors (restricted cubic spline mode of temperature, relative humidity and barometric pressure), $PM_{2.5}$, CO, NO_2, and SO_2 by simple and cumulative lag models for asthma ED visits during the warm seasons (June-September) of 2005 to 2015, stratification by land-use (i. e. commercial, and residential).

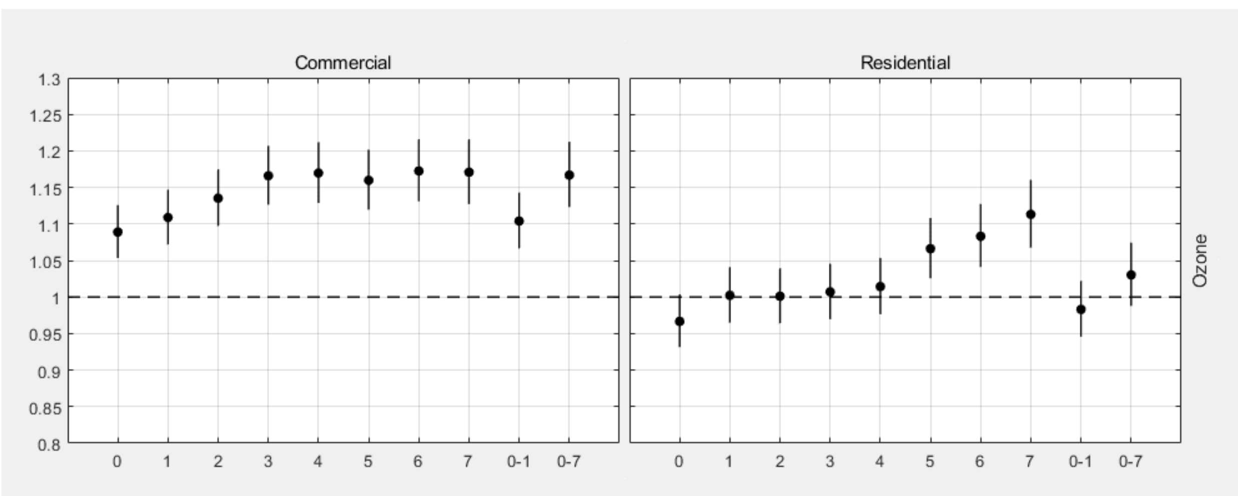

Figure 2: the odds ratio (95% CI) per 5 ppb increase in O_3, controlled for $PM_{2.5}$, NO_2, SO_2, CO, and meteorological factors (restricted cubic spline mode of temperature, relative humidity and barometric pressure) by simple lag model (i. e. Lag 0 = same-day exposure, lag 1 = exposure 1 day prior, etc.), and cumulative lag (i. e. Lag 0-1 = mean of lag 0 and lag 1, lag 0-7= mean of lags 0 through 7) for asthma ED visits during June to September of 2005 to 2015 in Fresno, California, USA; stratifying for land-use (i. e. Commercial, and Residential)

As shown in the figure, the association between O_3 and asthma ED visits in commercial areas is positively associated in all the lags. Specifically, 5 ppb increase in the concentration of O_3 at lag 7 is associated with 17% [OR: 1.170 (95% confidence intervals: 1.127, 1.215)] and 11.3% [OR: 1.113 (95% confidence intervals: 1.067, 1.160)] increase in the odds of having asthma ED visits in commercial and residential areas, respectively.

Stratification by sex

Figure 3 shows the fully adjusted ORs per 5 ppb increase in O_3 concentration stratificatified by sex (i. e. female, and male).

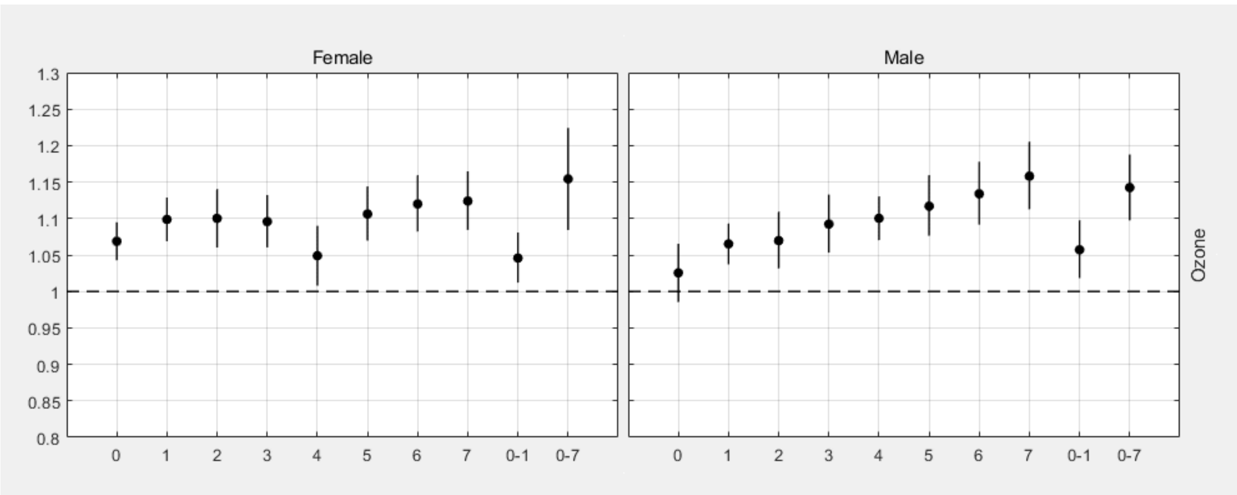

Figure 3: the odds ratio (95% CI) per 5 ppb increase in O_3, controlled for $PM_{2.5}$, NO_2, CO, and meteorological factors (restricted cubic spline mode of temperature, relative humidity and barometric pressure) by simple lag model (i. e. Lag 0 = same-day exposure, lag 1 = exposure 1 day prior, etc.), and cumulative lag (i. e. Lag 0-1 = mean of lag 0 and lag 1, and lag 0-7= mean of lags 0 through 7) for asthma ED visits during June to September of 2005 to 2015 in Fresno, California, USA; stratifying by sex (i. e. female, and male).

The results show that O_3 is positively associated with both female and male asthma ED visits. A 5 ppb increase at Lag 0-7 is associated with 15.4% [OR: 1.154 (95% confidence intervals: 1.084, 1.224)] and 14.2% [OR: 1.142 (95% confidence intervals: 1.097, 1.187)] increase in asthma ED visits in females and males, respectively. It should be noted that the difference between the obtained OR for female and male is not statistically significant.

Stratification by race

Figure 4 shows the fully adjusted ORs per 5 ppb increase in O_3 concentration stratified by race (i. e. White, Black, Hispanic).

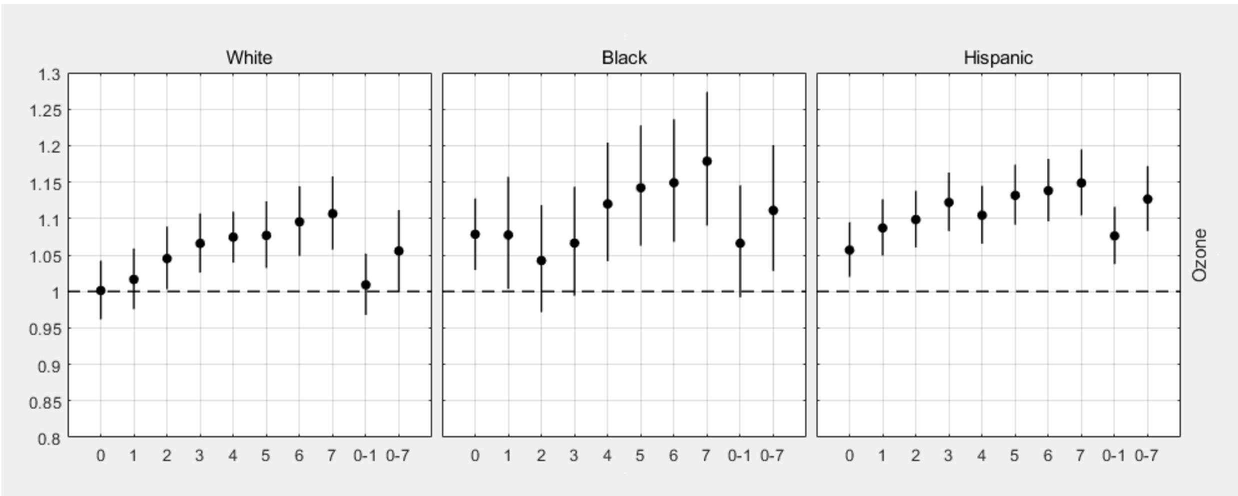

Figure 4: the odds ratio (95% CI) per 5 ppb increase in O_3, controlled for $PM_{2.5}$, NO_2, CO, and meteorological factors (restricted cubic spline mode of temperature, relative humidity and barometric pressure) by simple lag model (i. e. Lag 0 = same-day exposure, lag 1 = exposure 1 day prior, etc.), and cumulative lag (i. e. Lag 0-1 = mean of lag 0 and lag 1, and lag 0-7= mean of lags 0 through 7) for asthma ED visits during June to September of 2005 to 2015 in Fresno, California, USA; stratifying for race (i. e. White, Black and Hispanic).

O_3 is associated with asthma ED visits among Whites, Blacks, and Hispanics. However, the highest OR was among Blacks. A 5 ppb increase in the concentration of O_3 at lag 7 is associated with 17.8% [OR: 1.178 (95% confidence intervals: 1.090, 1.273)] increase in the odds of having asthma ED visits among this population. The corresponding ORs for Whites and Hispanics at the same lag were respectively 10.6% [OR: 1.106 (95% confidence intervals: 1.057, 1.157)] and 14.8% [OR: 1.107 (95% confidence intervals: 1.104, 1.194)], respectively.

Stratification by age

Figure 5 shows the fully adjusted ORs per 5 ppb increase in O_3 concentration stratified by age (i. e. 2-5, 6-18, 19-40, 41-64 and >= 65).

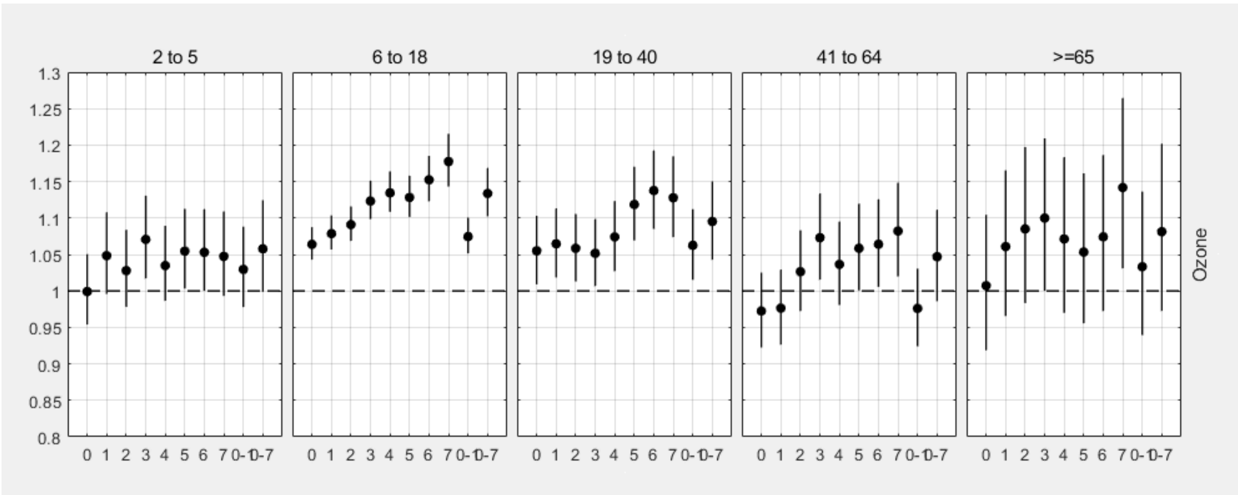

Figure 5: the odds ratio (95% CI) per 5 ppb increase in O_3, controlled for $PM_{2.5}$, NO_2, SO_2, CO, and meteorological factors (restricted cubic spline mode of temperature, relative humidity and barometric pressure) by simple lag model (i. e. Lag 0 = same-day exposure, lag 1 = exposure 1 day prior, etc.), and cumulative lag (i. e. Lag 0-1 = mean of lag 0 and lag 1, and lag 0-7= mean of lags 0 through 7) for asthma ED visits during June to September of 2005 to 2015 in Fresno, California, USA; stratifying for age (i. e. 2-5, 6-18, 19-40, 41-64 and >= 65).

We found positive association between O_3 and odds of having asthma ED visits among different age categories. A 5 ppb increase in the concentration of O_3 at lag 7 is associated with 17.7% [OR: 1.177 (95% confidence intervals: 1.111, 1.247)], 12.7% [OR: 1.127 (95% confidence intervals: 1.073, 1.184)], 8.2% [OR: 1.082 (95% confidence intervals: 1.019, 1.148)], 14.1% [OR: 1.141 (95% confidence intervals: 1.030, 1.264)] increase in the odds of having asthma ED visits among 6 to 18, 19 to 40, 41 to 64 and >=65 years old, respectively.

Discussion

In this time-stratified study, we investigated the association between short term exposure to O_3 and asthma ED visits during the warm season (June-September) of 2005 to 2015 in Fresno, California, USA was investigated, using a time-stratified case-crossover analysis. Our findings suggest that the increases in O_3 exposure were associated with asthma related ED visits in Fresno. Positive associations between O_3 exposure and asthma ED visits were observed in all lags, except at lag 0 (e.g event day), and the highest was observed at lag 7. There have been studies reporting positive associations during the warm season between O_3 concentration and asthma ED visits, which is consistent with our findings (27-28). Malig et al., conducted a study on O_3 pollution and asthma related ED visits; they reported a positive association between O_3 and asthma related ED visits (23). A study by Glad et al., on the relationship between air pollution and asthma related ED visits, O_3 was found to be positively associated with asthma ED visits (24). The results of these two studies are consistent with our findings. In a systematic meta-analysis of multi-community asthma prevalence studies by Anderson H. R. et al., (20) it was concluded that there was no significant association between O_3 and asthma attacks. In addition, a study by Laurent et al., on the association between ambient air pollution estimated in small geographic areas and asthma attacks in Strasbourg, France, in 2000–2005, no significant association was found between O_3 and asthma attacks (21). The difference between these results may be due to the level of O_3 concentration in these studies. Fresno has one of the highest concentrations of O_3 in the country with a significant difference in its concentration in warm and cold season (1-2). This difference was also considered to be a reason of why different studies report different findings in this matter by Lin M., et al., who investigated the associations between short-term exposure to gaseous pollutants and asthma hospitalizations (17). In addition, the two mentioned studies did not stratify for season; in other words, the concentration of O_3 differs drastically in warm and cold season, as we showed here in this study in Table 2 and Table I. 1. Additionally, the ORs in conditional logistic regression is a combination of all individually grouped patients, comparing the event day to three control days; hence, having a significant number of ORs not significant and smaller than 1 (i. e. the ORs obtained between O_3 and asthma ED visits during the cold season which has a stable and low concentration of O_3) can greatly affect the output. They also did not use the spline method to adjust the non-linearity of the meteorological factors which can greatly affect the results.

We hypothesized that living in different areas (i.e. commercial, residential) can be a significant modifier for the association between O_3 exposure and asthma ED visits. Our findings showed that asthma ED visits for those who live in commercial areas was higher than those of residential areas. To the best of our knowledge, this is the first time a study is looking into this issue; and, it could be of interest for further research. Therefore, living in commercial areas may increase the likelihood of the asthma ED visits; suggesting that urbanicity and residence characteristics may also have an effect on respiratory health. The difference can be due to the fact that in residential areas people are mostly inside house which prevent them from pollution exposure and (29) O_3, especially during the warm season.

Previous research has found that there is a possible difference on sensitivity among subpopulations of individuals exposed to the same O3 levels (30-31). Hence, we assumed that patients' characteristics could modify the effect of air pollutants on the asthma ED visits. Our findings showed that exposure to O_3 is positively associated with asthma ED visits for both male and female; the observed ORs between male and female is not significant. This is in line with the findings of previously conducted studies (32-34). A study by Ding et al., on air pollution and asthma attacks in children showed that sex was not a significant modifier (22). A possible explanation for these findings may be due to an Ozone effect on the respiratory system damage that is common to both sexes such as inflammation (35-38).

Our findings suggest a difference in susceptibility to ozone depending on race. We observed positive associations between O_3 and asthma ED visits among Black, White and Hispanic during the warm seasons (June-September) of 2005 to 2015 in Fresno; O_3 was found to have highest association with asthma ED visits among Blacks. It should be noted that Black and Hispanic showed a faster response to O_3 exposure, in comparison to that of Whites. In a study conducted by Alhanti B. A. et al., (39) on short-term relationships between asthma related ED visits and ambient air pollutants including O_3, they reported that non-white racial groups are more vulnerable to short term increase of O_3. In addition, in previous epidemiological studies, the association between O_3 exposure and asthma ED visits were reported to be mostly among Blacks (40-41). These results may be explained by factors such as social inequalities in racial minorities who could be more prone to asthma exacerbation when they are exposed to asthma triggers (40-42). Furthermore, previous research supports that human biologic variation has influence in asthmatics, supporting the differences encountered between races (43-44). Additionally, the response of each age group (2-5, 6-18, 19-40, 41-64 and >= 65) to the O_3 exposure was assessed. We found positive associations between O_3 exposure and asthma ED visits among all age groups. However, the greater association was found among those who are between 2 to 5, 6 to 18 and 65 years old and above. Several studies have found similar results (38-39, 45). The differences encountered among different age groups may be due to structural and immunological characteristics that differ with as individuals aging processes. Previous research has shown that the developmental factors modifying the maturation of the immune cells and airway remodeling of the respiratory system during infancy have the most important role in childhood asthma (29-46). Elderly individuals may be more sensitive to asthmatic triggers due to aging-related changes on the respiratory systems. It has been documented that chest wall compliance and pulmonary function tests are decreased in elderlies (47-48), making them especially susceptible to respiratory diseases. This scientific evidence on how different populations may respond to ozone exposure and respiratory disease, specifically asthma, aids to set regulations and safety margins for standards levels of air pollutants based on the most susceptible populations (49). Therefore, understanding at State level agencies may use this information to ensure that the levels of these air pollutants may be more tightly regulated.

Conclusion

We aimed to investigate the association between short term exposure to O_3 and asthma ED visits during the warm season (June to September) of 2005 to 2015 in the Fresno, California, USA, using a time-stratified case-crossover design. We found that O_3 is associated with asthma ED visits in Fresno during the warm seasons. Considering the difference in land use, we found a stronger association between O_3 exposure and asthma ED visits among those who reside in commercial areas, compared to those of residential areas. For the patients' characteristics as modifiers, we could not find sex as a significant modifier. Although O_3 exposure and asthma ED visits is positive among all the three studied races, Blacks and Hispanics showed faster response to O_3 exposure. Furthermore, the association between O_3 exposure and asthma ED visits among children (2 to 5 years old), adolescents (6 to 18 years old) and elderlies (>= 65 years old) were greater than those of other age groups in this study. Given the growing concerns related to anthropogenic air pollution sources and the increasing diversity within our community, these findings merit further investigation. Meanwhile, continued efforts to minimize air pollution exposures may help to reduce asthma risk.

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Appendix I

Table I. 1: The distribution of air pollutants in Fresno, California during the cold seasons (November-February) of the years 2005 to 2015

Variable	Mean	Standard Deviation	Minimum	Percentile			Maximum
				25	50	75	
O_3 (ppb)	13.79	7.45	0.23	8.2	12.52	18.5	42.7
$PM_{2.5}$ (μg/m^3)	23.62	15	1	16.5	16.59	29.95	99.6
NO_2 (ppb)	18.49	6.5	2.5	14.4	17.64	22.73	46.9
SO_2 (ppb)	0.75	0.4	0	0.5	0.93	0.93	2.22
CO (ppb)	486.71	258.9	0	304.4	400.2	615.1	1904
Relative Humidity (%)	70.36	12.7	6.33	57.09	70.83	80.12	99
Barometric Pressure (bar)	1.006	0.005	0.97	1.001	1.006	1.01	1.025
Temperature (C°)	10.76	3.78	1.54	7.89	10.39	13.21	22.1

Abbreviations: SD, Standard Deviation

O_3 (ppb): 8-hr maximum average

$PM_{2.5}$ (μg/m^3): daily-average

CO (ppb): daily-average

NO_2 (ppb): daily-average

Temperature C°: daily-average