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Effect Of Outdoor Air Pollution On Hospital Admissions For
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Effect Of Outdoor Air Pollution On Hospital Admissions For Asthma

In Detroit, Michigan

By

Alireza Sadeghnejad

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ABSTRACT

EFFECT OF OUTDOOR AIR POLLUTION ON HOSPITAL ADMISSIONS FOR ASTHMA IN DETROIT, MICHIGAN

By

Alireza Sadeghnejad

We investigated the spatio-temporal relationship between number of asthma hospital admissions and levels of air pollutants ozone, particulate matter, nitrogen dioxide and sulfur dioxide. For the period 1999-2000, data were obtained on daily asthma hospital admissions for a contiguous region covering 23 zip codes in the East Seven Mile and Linwood areas of Detroit, Michigan.

Each zip code falls within a 4-kilometer radius of an air quality monitoring station that provided detailed data on the air pollutants and meteorological assessments. Exposure to a pollutant was assessed based on its mean daily level in the 4-day period preceding a hospital admission. Linwood and East Seven Mile areas were predominantly African-American (about 66%). Mean daily admission rates per 100,000 for asthma were 1.4 in Linwood, and 1.1 in East Seven Mile. The month of September showed a very sharp increase in admissions. In a negative binomial model, we estimated an average of 8% increase in the number of daily asthma hospital admissions by 6 ppb increase in nitrogen oxide levels. We observed a significant protective effect for ozone. The levels of nitrogen dioxide and ozone were negatively correlated.

Higher levels of nitrogen dioxide might increase asthma hospital admissions. Individual level data are needed to verify air pollutant effects on asthma.

DEDICATIONS

This work is specially dedicated to my parents and my wife Negin.

ACKNOWLEDGEMENTS

The planning, designing, implementation and completion of this work is the result of a team of dedicated individuals. Sincere gratitude to my thesis advisor, Dr. Wilfried Karmaus, for his insight, supervision and moral support in the process of completing this thesis.

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LIST OF ABBREVIATIONS

CO .... Carbon Monoxide

CI .... Confidence Interval

ED .... Emergency Department

MDCH .... Michigan Department of Community Health

MDEQ .... Michigan Department of Environmental Quality

NA .... Not Available

NO_2 .... Nitrogen Dioxide

NO_x .... Nitrogen Oxides

O_3 .... Ozone

P_5 .... 5^{th} Percentile

P_{50} .... Median

P_{95} .... 95^{th} Percentile

$PM_{2.5}$ .... Particulate Matter with a diameter less than 2.5 micrometer

PM_{10} .... Particulate Matter with a diameter less than 10 micrometer

ppb .... Parts Per Billion

ppm .... Parts Per Million

SAS .... Statistical Analysis Software

SO_2 .... Sulfur dioxide

VOCs .... Volatile Organic Compounds

μ .... Mean

$\mu g/m^3$ .... Microgram per cubic meter

BACKGROUND

Asthma prevalence has been increasing since the mid 1970s [1] and has emerged as a major public health problem over the past 20 years in the United States [2]. The overall rate of hospitalization for asthma increased during the late 1980s and has since plateaued. However, the rate among African Americans remained 2-3 times higher than for white Americans [2]. Air pollution is considered as a risk factor for asthma hospital admission. Asthmatics appear to be more susceptible to short-term peak concentration of air pollutants [3]. Research has strongly shown that air pollution increases asthma hospitalization through exacerbation of attacks in asthmatics. We tabulated previous published studies (Appendix). The following studies are from the North America.

In 1993, a study conducted over a 13-month period in Seattle reported that the relative risk of asthma emergency room visits for a 30µg/m^3 increase in particulate matter PM_{10} was 1.12 (95% confidence interval: 1.04, 1.20) [4]. They noted that the mean of the previous 4 days' PM_{10} was a better predictor than shorter lag periods. In addition for the number of asthma emergency room visits, an evident peak was observed during September.

In New Brunswick during 1984-1992, for the period May-September, Stieb et al. examined the relationship between asthma emergency department visits and air pollutants nitrogen dioxide (NO_2), ozone (O_3), and sulfur dioxide (SO_2) Daily emergency department (ED) visit frequencies were filtered to remove day of the week and long wave trends. Filtered values were regressed on air pollution and weather variables for the same day and the 3 days previous to the ED visits. They found a positive relationship for higher levels of O_3 and the increased number of ED visits, but not for other pollutants [5].

For the period 1987-1994 in Seattle, Washington, Sheppard et al. reported the effects of ambient air pollution on non-elderly asthma hospital admissions [6]. In a Poisson regression model controlling for time trends, seasonal variations, and temperature-related weather effects, they regressed daily hospital admissions on levels of O_3, particulate matter with a diameter, both less than 2.5µm and less than 10µm ($PM_{2.5}$ and PM_{10}) and SO_2. An estimated 4-5% increase in the rate of asthma hospital admissions associated with an interquartile range increase PM_{10} and $PM_{2.5}$ levels with one-day lag (19.0 $\mu g/m^3$ for PM_{10} and 11.8 $\mu g/m^3$ for $PM_{2.5}$). Similar findings for carbon monoxide (CO) and O_3 but not SO_2 were observed. Correlations between levels of pollutants were: +0.8 for (PM_{10}, $PM_{2.5}$)-CO, -0.23 for O_3-$PM_{2.5}$, +0.34 for O_3-SO_2 and +0.22 for $PM_{2.5}$-SO_2[6].

In 2000, Tolbert et al. reported Pediatric emergency room visits for asthma in relation to O_3, PM_{10}, NO_2 in Atlanta, Georgia during the summers of 1993-1995 [7]. The estimated relative risk per 20 parts per billion (ppb) increase in the maximum 8-hour O_3 level was 1.04 ($p < 0.05$). The estimated relative risk per 15 $\mu g/m^3$ increase in PM_{10} was 1.04 ($p < 0.05$). Exposure-response trends ($p < 0.01$) were observed for ozone (>100 ppb vs. <50 ppb: odds ratio = 1.23, $p = 0.003$) and PM_{10} (>60 $\mu g/m^3$ vs. <20 $\mu g/m^3$: odds ratio = 1.26, $p = 0.004$). In models with ozone and PM10, both terms became nonsignificant because of collinearity of the variables (r=0.75). Correlation between pairs of pollutants were: +0.51 for O_3-NO_x and +0.44 for PM_{10}-NO_x [7].

In 2001, Ritchie et al. studied 1 to 17 year old children admitted to one of 20 hospitals within nine counties in the Indianapolis metropolitan area. For warmer months (May-September), during 1997-1999, they found that as O_3 concentrations increased, asthma hospitalization probability decreased. During the study period, the mean for 24-daily O_3 concentration was 0.038 ppm and the daily one-hour maximum was 0.066 ppm [8].

Although study design varies in previous studies, but in almost all of them, exposure was allocated by aggregative method. The period that has been used to assess exposure prior to admission (lag period) varied between 1-5 days. For all pollutants these studies found an adverse or no effect on asthma hospital admissions. The only exception was O_3. Some studies, including Ritchie et al. reported a protective effect of O_3 on the number of asthma hospital admissions [8-11]. Correlation coefficients between pairs of pollutants were reported as positive in previous studies. The only exception to this was O_3 that showed both positive and negative correlation with other pollutants [6,10].

Most of the above-mentioned studies have demonstrated seasonal patterns in hospitalizations associated with asthma. A Canadian study examined the seasonal patterns of asthma hospitalizations for a 15–34 year age group, and found that hospitalizations peaked in the autumn season [12]. Marked differences between the number of asthma hospitalization for males and females have been reported in the literature, with admissions for young males being higher than for young females [13].

The only previous study conducted in Michigan to investigate the relationship between the daily air pollution levels and asthma hospital admissions was by Thorell. He examined the relationship between the daily air pollution levels and occurrences of asthma hospitalization as well as emergency department visits at Hurley Medical Center, Flint, MI. The study was limited to children under age 16 residing in ten zip codes in Flint. He found increases in emergency department visits and hospitalization when O_3 levels increased by 135.1 $\mu g/m^3$ above the mean daily maximum. There was also an increase in emergency visits when SO_2 levels increased by 21.8 $\mu g/m^3$ above the mean daily maximum [14].

In 1998 the Michigan Department of Community Health (MDCH) reviewed inpatient hospital records and death certificates for children less than age 15 with asthma diagnoses for the period 1985-94 [15]. The overall annual state childhood asthma hospitalization rate for this period was 34.3 cases per 10,000 children, with much higher rates for African American children. Wayne County (with an annual rate of 53.7/10,000) was among a group of counties with rates above the overall annual state rate for childhood asthma. The highest Detroit rates were for those children residing in zip codes* 48208, 48201, 48202, 48206, 48226, and 48238. Ingham County had an annual hospitalization rate lower than the state as a whole (22.5/10,000).

* They were included in this thesis.

The purpose of this aggregative study is to investigate potential associations between different air pollutants (NO_2, O_3, $PM_{2.5}$ and SO_2, as described below [16]) and asthma hospital admissions. In order to conduct this investigation, we used four data series (air pollution, meteorological, hospitalization and census data) on two geographical areas in Detroit, Michigan. The units of analysis were sites of residence stratified by age, gender, and race. Institutional Review Board at Michigan State University approved us to work on these existing data sets.

<u>Nitrogen dioxide (NO_2)</u> [16]

Nitrogen oxides (NO_x) are byproducts of fuel burned at high temperatures, as in a combustion process. The primary sources of NO_x are motor vehicles (49%), electric utilities (27%), and other industrial, commercial, and residential sources that burn fuels (24%).

In a complex reaction, NO reacts with volatile organic compounds (VOCs) to produce NO_2 (Figure 1). Then NO_2 and oxygen reaction is catalyzed by sunlight to produce NO and O_3.

$$NO + VOCs \longrightarrow NO_2$$

$$NO_2 + O_2 \xrightarrow{\text{Sunlight}} NO + O_3$$

Figure 1. NO_2 in the pathway of O_3 production

Ozone (O_3)

Within the scope of this thesis, ozone refers to ground level (tropospheric) ozone, such as smog, and not to stratospheric ozone. Stratospheric ozone is the layer of ozone gas in the upper atmosphere that screens out harmful ultraviolet radiation from the sun. Ground level ozone is not emitted directly into the air, but is formed through complex chemical reactions between precursor emissions VOCs and nitrogen oxides (NO_x) in the presence of sunlight (Figure 1). VOCs are emitted from sources such as automobiles, dry cleaners, and paint shops. NO_x, as stated earlier come from sources including coal-fired power plants and motor vehicles. The chemical reactions that produce O_3 are activated by sunlight and high temperature; therefore peak O_3 levels occur mostly during the summer when the weather is warmer and in the middle of the day as emissions build up and the temperature rises [16].

Typically, the length of the O_3 season is May through October, coinciding with the warmer months of the year. Since varying meteorological conditions influence ambient levels and year-to-year trends, O_3 monitoring seasons may vary from one area of the country to another.

Particulate Matter (PM)

Particulate matter includes dust, dirt, soot, smoke and liquid droplets that are directly emitted into the air from sources such as windblown dust, automobiles, construction sites, factories, and fires. PM is also formed in the atmosphere by condensation or by the transformation of emitted gases such as

SO_2, NO_x, and VOCs. Particulate matter is distinguished by it diameter. Fugitive sources such as agricultural tilling, construction, fires, and unpaved roads contribute much more PM_{10} (PM with a diameter less than 10μm) emissions in specific regions than others (this include dry forested areas susceptible to fire and agricultural areas).

Sulfur dioxide (SO_2)

SO_2 is a gaseous product from stationary and mobile sources burning coal and oil-containing sulfur. Processes found in pulp and paper mills and in nonferrous metal smelters also contribute to SO_2. The largest contributors to SO_2 emissions are coal-burning power plants. Once released, SO_2 and other oxides of sulfur combine with oxygen to form sulfates, and with water vapor to form aerosols of sulfurous and sulfuric acid. This mixture is a precursor of acid rain. Many emissions originate from tall stacks enabling them to be dispersed according to the pattern of the wind and variable wind speed. For example, Vermont's air quality is partly affected by emissions carried from more industrialized areas both close by and far away. Sulfur compounds also contribute to visibility impairment in areas other than the primary source area.

METHODS

First, we will define the two geographical sites included in this study. Then population and the four data sets of study will be addressed. After defining exposure, outcome and potential confounders, we will describe methods proposed for descriptive and regression analysis in “Statistical analysis”.

Information from Linwood and East Seven Mile, two geographical areas in Detroit, Michigan was used in this study. Each site was defined by an air pollution monitoring station and zip codes that were wholly or partially contained within a 4-kilometer radius of the air pollution monitoring station (Figure 2). The 4-kilometer radius around the East Seven Mile and Linwood sites wholly or partially contained 10 zip codes and 13 zip codes respectively (Table 1).

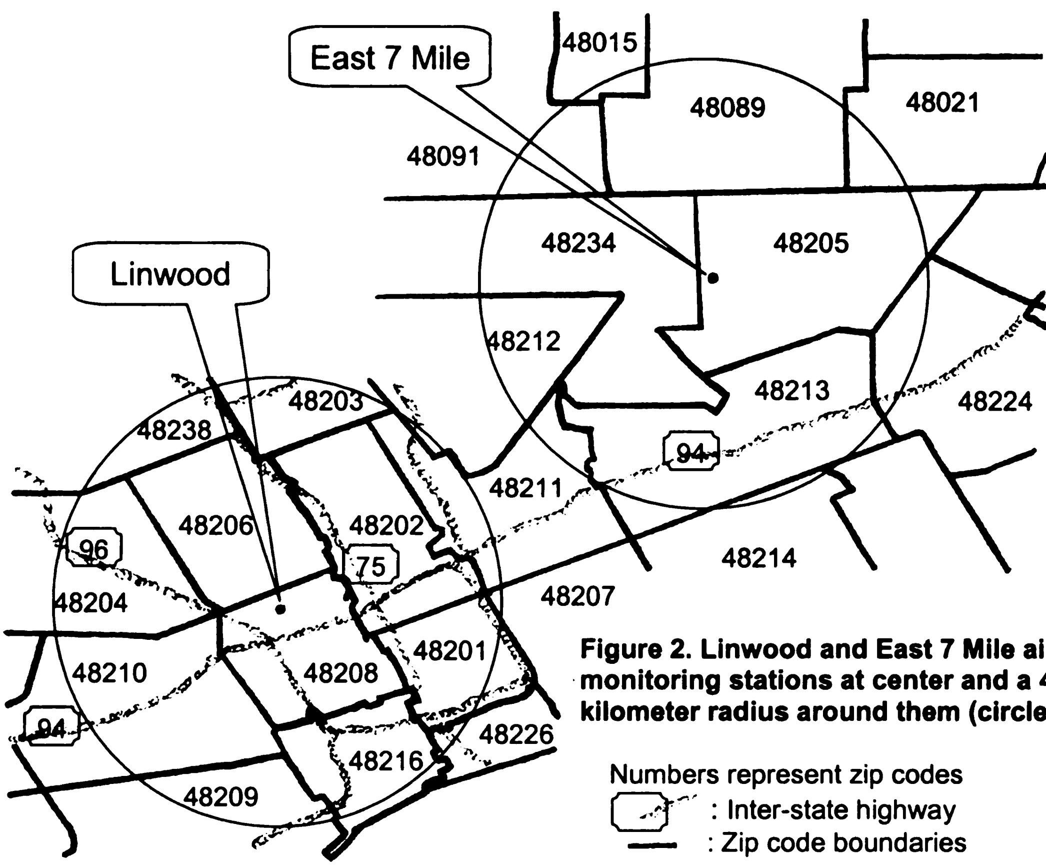

Figure 2. Linwood and East 7 Mile air monitoring stations at center and a 4-kilometer radius around them (circles)

Numbers represent zip codes
: Inter-state highway
: Zip code boundaries

Table 1. Zip codes contained in each of the two sites

East 7 Mile		Linwood	
48015	48214	48201	48209
48021	48224	48202	48210
48089	48234	48203	48211
48091		48204	48216
48205		48206	48226
48212		48207	48238
48213		48208	

Study population and data

Residents of the two sites at who aged one to 45 years' people comprised the study population. We used data on census, air pollution, meteorological indices and hospital admissions in this study. Census data was obtained from the United States Census Bureau, the later three data sets were provided by MDCH and Michigan Department of Environmental Quality (MDEQ).

Census data

By assuming that the population was steady during the two years of study period, we used year 2000 census data as the reference. Data was available online through the United States Census Bureau [17]. We downloaded census data for the desired zip codes by race, gender and age in years and converted the data to SAS (Statistical Analysis Software) format for the two sites.

Air pollution data

The Michigan Air Sampling Network measures air quality throughout the state. The pollutants that we used were nitrogen dioxide (NO_2), ozone (O_3), particulate matters with a diameter less than 2.5 micrometer ($PM_{2.5}$) and sulfur dioxide (SO_2). Pollutant concentrations were monitored using a direct reading instrument by standardized methods. These methods and their units were:

- Gas-phase chemiluninescence, ppb for NO_2
- Ultra violet analysis, ppb for O_3
- R&P 2025 sequential sampler /gravimetric method, $\mu g/m^3$ for $PM_{2.5}$
- Ultra violet fluorescence, ppb for SO_2

Hourly measurements were recorded and electronically sent to the Air Quality Division of MDEQ. In the two air monitoring stations, air pollution data has been incompletely collected from January 1, 1999 through December 31, 2001. For each site, MDCH calculated daily mean and maximum levels of SO_2, NO_2 and O_3 as well as daily $PM_{2.5}$ values. We used mean daily levels of the pollutants and built up a SAS file.

Meteorological data

Both sites shared the same daily measurement for minimum and maximum temperatures as well as mean daily relative humidity during 1999 and 2000. This information was gathered in Detroit-Linwood station. We made a SAS formatted data from this information.

Hospital admission data

Information from almost all Michigan hospitals is included in the Michigan Inpatient Database. We received a file with the data on the number of patients with a discharge diagnosis of asthma. Data structure was based on the date of admission, zip code of residence, age in years, gender and race. We used data from January 1, 1999 till December 31, 2000 based on the date of admission. We organized final hospital admission data set as a SAS-formatted data set by date of admission, site (versus zip code in the original data set) of residence, age in years, gender and race.

Outcome, exposure and confounders

Outcome

We defined outcome as the number of patients admitted to Michigan hospitals, per day and by the site of residence, age, gender and race. Outcome quantification was based on the following criteria:

- Patient age, between one year and 45 years
- Diagnosis of asthma at discharge (code 493 in the International Classification of Diseases, version 9)
- Use of date of admission for calculating number of daily asthma hospitalization

Exposure

We assessed exposure to NO_2, SO_2, $PM_{2.5}$ and O_3. Using an aggregative method we allocated exposure to individuals. Residents in zip codes that completely or incompletely felt into a 4-kilometer radius of each air monitoring station were assumed to have the same amount of exposure to the pollutants. There were two zip codes that felt in both sites. We assigned each of these zip codes to the site that predominantly encountered it.

In previous studies exposure to pollutants was assessed using different lag periods between daily levels of pollutants and subsequent hospital admissions. Previously lag periods with a range between one day and 5 days were used, however there is no universally agreed standard. In this study we used mean level of pollutants during preceding four days of admissions [4,6,9,18].

Confounders

Variables that could be related to the level of air pollutants as well as daily number of hospital admissions assumed to be year, month and the weekday of admission; race, age and gender of admitted patients; and meteorological indices [5,7,9].

For each of the meteorological variables (minimum, maximum and mean temperature as well as mean relative humidity), we calculated an average in the preceding 4-day period of admission and controlled for that in the models.

Statistical analysis

We used SAS software, Release 8.2 [19] to conduct statistical analysis. In this part, we present the way to get a working data set from the four data sets (Figure 3). Then methods for descriptive analysis and regression will be explained. Finally, we will discuss modeling strategies.

Working data set

We created a working data set (Figure 3) by merging hospital admission, census, meteorological and air pollution data sets. Following are the steps of getting final data set

1. A data frame (linkage file) made to resemble all potential combinations of sites and dates of admission as well as age groups, gender and racial groups of admittees. We used this data frame as a base for merging the four data sets.
2. Hospital data set was merged with the linkage file by site, date, age group, gender and racial group.
3. Census data set was merged with the data from step 2 by site, age group, gender and racial group.
4. As both sites shared the same meteorological data, we assigned information to both sites and then merged it with the data set from step 3 by site and date.
5. Air pollution data set was merged by site and date with the data set derived from step 4.
6. At the last step, we calculated average level for each of the pollutants and meteorological indices in the 4 preceding days of admission in the final data set (Figure 3).

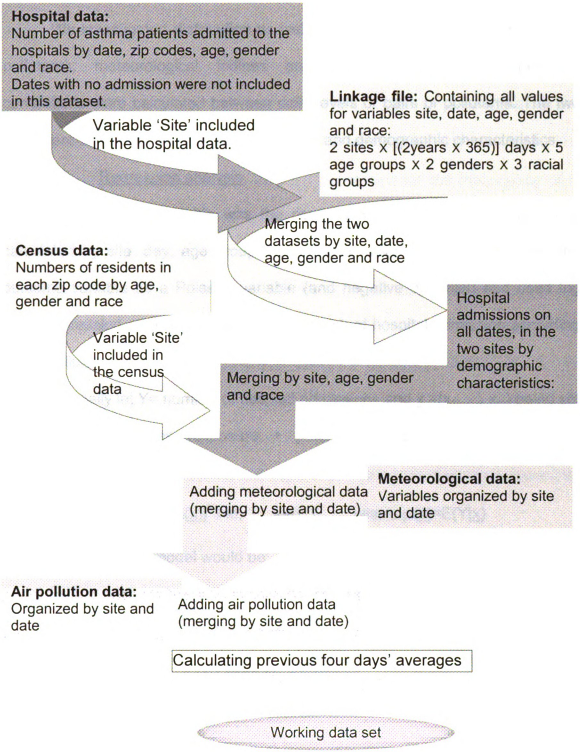

Figure 3. Different steps for merging the four data sets to get working data set

Descriptive analysis

We investigated distribution as well as spatial and temporal trends of air pollutants, meteorological indices and hospital admissions. Spearman correlations were calculated between daily levels of pairs of pollutants. The two sites were compared on their pollutant levels and demographic characteristics.

Regression analysis

The outcome variable was the count of hospital admissions that was calculated by site, day, age group, gender and racial group. We modeled the outcome variable as a Poisson variable (and negative binomial) and used log linear regression analysis to assess relative risk of hospital admission according to the pollutants level.

Formally let Y= number of hospital admissions and $\underline{x}=(x_1,\ldots,x_m)$ being set of relevant covariates (exposure + potential confounders). The Poisson assumption is:

$$P(Y=k|\underline{x}) = e^{-\mu(\underline{x})}[\mu(\underline{x})]^k / k!, \quad k=0, 1, \ldots \text{ where } \mu(\underline{x})=E(Y|\underline{x})$$

The log-linear model would be: $\log \mu(\underline{x}) = \beta_0 + \beta_1 x_1 + \ldots + \beta_m x_m$

In our analysis we should include an offset term which represents the population at risk ($=N(\underline{x})$). So, the modification to the above equation is:

$$\log \mu(\underline{x}) = \log N(\underline{x}) + \beta_0 + \beta_1 X_1 + \ldots + \beta_m X_m$$

Parameter interpretation

We modeled $E(Y/N(\underline{x})\,|\underline{x}) = \mu(\underline{x})/N(\underline{x})$. The analysis of the incidence index with a Poisson or negative binomial regression allows the estimation of Relative

Risks (RR), which are equal to the ratio y_j / y_0 where y_j is the incidence of admissions in level j, and y_0 corresponds to the reference (first) level [20].

Assessing the fitted model

GENMOD procedure in SAS was used to fit log linear models. We applied deviance and scaled Pearson χ^2 statistics in order to gauge adequacy of fit. The scaled values should be close to one [21]. The reason for the inadequacy of fit could be due to over-dispersion (a condition that occurs when variance of the distribution is larger than its mean). If the fit seems inadequate one should use the negative binomial method instead of Poisson to incorporate over-dispersion [20]. In order to choose the appropriate method of analysis we looked at the distribution of the outcome variable and criteria for 'Goodness of fit'.

($Y \sim NB$ $E(Y)=\mu$ $Variance(Y)= \mu+k\mu^2$, $k>0$). This also provides an approach to test H_0 : $k=0$ (the alternative hypothesis, H_a : $k>0$). Statistically this test must be performed carefully because the null hypothesis places the dispersion parameter on the boundary of the parameter space [20].

Modeling strategies

Average of pollutants and meteorological indices over a 4-day period preceding hospital admissions were ranked by their quartiles. Fully saturated models were run with only one pollutant in each along with all the potential confounders. If the risk ratio was significant for the pollutant, backward elimination was used to get the most parsimonious model. While rate ratios of pollutants in several reduced single-pollutant models show significance, models with combinations of pollutants were run.

RESULTS

The first two part of this section will focus on descriptive analysis of air quality, meteorological, hospital admission and census data. In the third part, results of regression analyses will be provided.

Descriptive analyses of air quality and meteorological data

In this part, we present distribution of mean daily levels of NO_2, SO_2, $PM_{2.5}$ and O_3 along with their monthly variations and their variations upon weekdays. Correlations among daily levels of pollutants are also provided in this part. For meteorological data, statistics in terms of mean and percentiles along with monthly variations of minimum, mean and maximum temperature as well as relative humidity investigated.

Distributions of daily mean levels of pollutants were generally skewed to the left (Figure 4). This was more prominent for SO_2 and $PM_{2.5}$. O_3 possessed the most symmetrical distribution in comparison to the other pollutants.

NO_2 and SO_2 levels were available for all months of the study period in the two sites (Figure 5 and Figure 6). The yearly measurement period for O_3 was April through September in both sites. In East Seven Mile, $PM_{2.5}$ was not measured during first three months of each year.

Monthly variation was present for all the four pollutants. While O_3 levels showed obvious peaks in June and July, concurrent drop of mean monthly NO_2 levels in these two months was evident. Mean monthly levels of SO_2 and $PM_{2.5}$ did not resemble a pattern.

Mean daily levels of pollutants varied during week (Figure 7 and Figure 8). On weekends (Saturday and Sunday), there was a decrease in NO_2 levels and an increase in O_3 levels. SO_2 and $PM_{2.5}$ were almost stable during the week in Linwood, but not East Seven Mile.

The highest correlations among pollutants were observed in Linwood between NO_2 and SO_2 during cold months (Table 2). Generally, NO_2, $PM_{2.5}$ and SO_2 were significantly correlated. Significant correlations between O_3 and $PM_{2.5}$ were found. O_3 was not correlated significantly with NO_2 or SO_2. All pollutants were significantly correlated with $PM_{2.5}$.

Mean daily levels of NO_2 were higher in colder periods of the two years in the two sites (Table 3), a situation that was true in the case of SO_2 just in East Seven Mile. $PM_{2.5}$ also had higher mean daily levels in colder period of year. In Linwood, mean daily levels of O_3 were lower and of NO_2 were higher than their levels in East Seven Mile.

The year 2000 was colder and more humid than 1999 in the Detroit area (Table 4). The warmest month in the study period was July and the coldest, January (Figure 9).

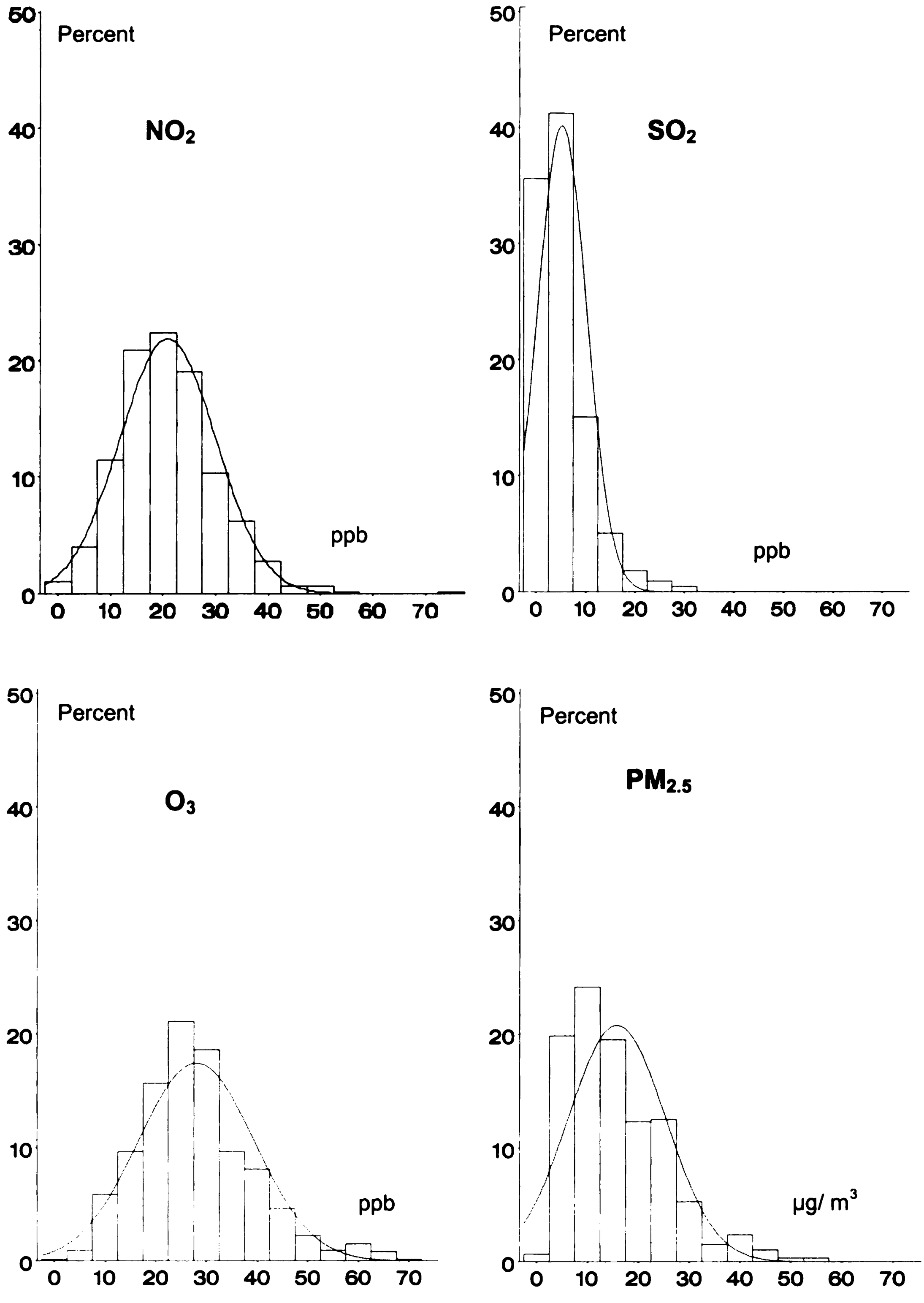

Figure 4. Distributions of pollutants during the study period
Abbreviations; ppb, part per billion; µg/ m^3, microgram per cubic meter; NO_2, nitrogen dioxide; O_3, ozone; $PM_{2.5}$, particulate matter with a diameter less than 2.5 micrometer; SO_2, sulfur dioxide

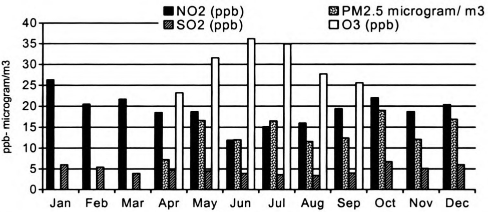

Figure 5. Mean monthly levels of pollutants in East 7 Mile during the study period

Abbreviations; ppb, part per billion; µg/ m^3, microgram per cubic meter; NO_2, nitrogen dioxide; O_3, ozone; $PM_{2.5}$, particulate matter with a diameter less than 2.5 micrometer; SO_2, sulfur dioxide

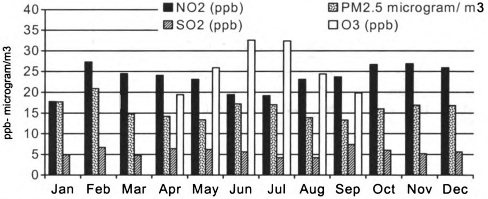

Figure 6. Mean monthly levels of pollutants in Linwood during the study period

Abbreviations; ppb, part per billion; µg/ m^3, microgram per cubic meter; NO_2, nitrogen dioxide; O_3, ozone; $PM_{2.5}$, particulate matter with a diameter less than 2.5 micrometer; SO_2, sulfur dioxide

Table 2. Correlation among various pollutants in the two sites during specified periods

Site name / Period	Pollutant	Spearman correlation coefficient (P value) / Number of days: NO_2	$PM_{2.5}$	SO_2	O_3
East 7 Mile					
Apr- Sep	NO_2	1.00 344			
	$PM_{2.5}$	0.14 (.36) 40	1.00 41		
	SO_2	0.41(<. 001) 315	0.31(.07) 35	1.00 319	
	O_3	−0.10(.05) 337	0.47 (.001) 41	0.15 (.006) 314	1.00 356
Oct- Dec Jan- Mar	NO_2	1.00 208			
	$PM_{2.5}$	0.63 (<. 001) 27	1.00 29		
	SO_2	0.55 (<. 001) 204	0.30 (.10) 28	1.00 239	
Linwood					
Apr- Sep	NO_2	1.00 249			
	$PM_{2.5}$	0.54 (<. 001) 211	1.00 259		
	SO_2	0.57(<. 001) 249	0.51(<. 001) 259	1.00 366	
	O_3	−0.10(.10) 249	0.52 (<. 001) 259	−0.02 (.64) 360	1.00 360
Oct- Dec Jan- Mar	NO_2	1.00 267			
	$PM_{2.5}$	0.51(<. 001) 248	1.00 255		
	SO_2	0.69 (<. 001) 267	0.70 (<. 001) 255	1.00 365	

Abbreviations: NO_2, nitrogen dioxide; O_3, ozone; $PM_{2.5}$, particulate matter with a diameter< 2.5 µm

Table 3. Means and percentiles for daily average levels of pollutants during the study period

Site/ Year	Period	Pollutant (unit)															
		NO_2 (ppb)				$PM_{2.5}$ (µg/m3)				SO_2 (ppb)				O_3 (ppb)			
		μ	P_5	P_{50}	P_{95}	μ	P_5	P_{50}	P_{95}	μ	P_5	P_{50}	P_{95}	μ	P_5	P_{50}	P_{95}
E. 7 Mile/ 1999	Apr- Sep	16.7	2.7	17.2	29.0	NA	NA	NA	NA	3.7	0.1	3.0	9.5	32.4	11.0	30.9	59.0
	Jan- Mar Oct- Dec	20.2	6.7	18.9	33.2	NA	NA	NA	NA	5.3	0.4	3.4	15.9	NA	NA	NA	NA
E. 7 Mile/ 2000	Apr- Sep	16.5	6.7	14.7	28.8	13.8	3.5	11.8	28.5	4.5	1.2	3.7	11.4	27.7	13.1	26.9	46.9
	Jan- Mar Oct- Dec	21.5	9.7	21.0	35.7	16.0	3.8	14	40.6	6.2	0.4	5.5	14.8	NA	NA	NA	NA
Linwood/ 1999	Apr- Sep	21.7	9.9	21.2	35.0	16.7	5.2	13.8	40.6	5.9	0.5	3.6	17.4	27.9	11.6	26.5	47.9
	Jan- Mar Oct- Dec	25.4	14.0	24.3	41.3	16.2	4.5	13.5	39	5.9	0.4	3.5	18.4	NA	NA	NA	NA
Linwood/ 2000	Apr- Sep	22.6	10.4	21.6	37.2	13.7	4.5	12.3	27.7	5.4	0.4	3.2	20.0	24.0	9.5	23.9	40.3
	Jan- Mar Oct- Dec	25.4	10.4	24.6	40.7	17.3	4.8	16.0	36.0	5.2	0.3	4.2	13.3	NA	NA	NA	NA

Abbreviations: µ, Mean; P_5, 5th percentile; P_{50}, Median; P_{95}: 95th percentile; NO_2, nitrogen dioxide; O_3, ozone; $PM_{2.5}$, particulate matter with a diameter< 2.5 µm; SO_2, sulfur dioxide; ppb, part per billion; NA, not available

Table 4. Means and percentiles for daily meteorological variables during the study period

		Variables															
		Minimum Temperature				Mean Temperature				Maximum Temperature				Mean Relative Humidity			
Year	Period	μ	P_5	P_{50}	P_{95}	μ	P_5	P_{50}	P_{95}	μ	P_5	P_{50}	P_{95}	μ	P_5	P_{50}	P_{95}
1999	Apr- Sep	56.6	38.0	57.0	71.0	65.8	45.0	67.7	79.7	74.7	51.0	76.0	90.0	66.3	42.8	65.8	86.1
	Jan- Mar Oct- Dec	28.5	7.0	30.0	48.0	36.5	14.4	36.6	57.2	44.2	20.0	43.0	69.0	70.0	51.8	71.0	87.8
2000	Apr- Sep	55.0	36.0	57.0	68.0	63.6	45.0	66.0	75.5	72.3	51.0	75.0	85	70.9	48.0	71.3	88.6
	Jan- Mar Oct- Dec	28.3	5.0	30.0	52.0	36.3	13.2	35.4	60.0	43.3	19.0	40.0	69.0	73.2	53.4	72.9	91.0

Abbreviations: μ, Mean; P_5, 5th percentile; P_{50}, Median; P_{95}: 95th percentile

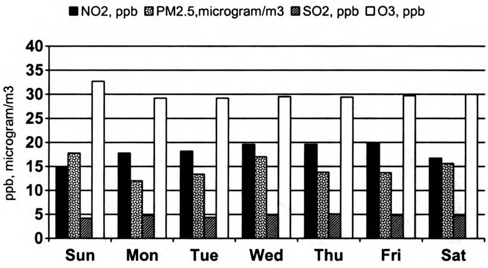

Figure 7. Variation of mean daily levels of pollutants during week in East 7 Mile in the two years of study

Abbreviations; ppb, part per billion; NO_2, nitrogen dioxide; O_3, ozone; $PM_{2.5}$, particulate matter with a diameter less than 2.5 micrometer;
SO_2, sulfur dioxide

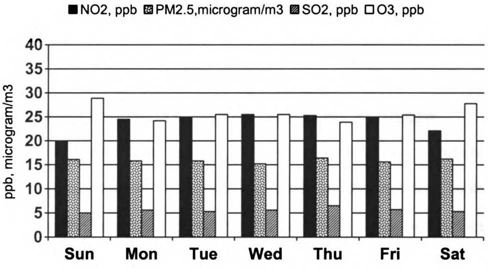

Figure 8. Variation of mean daily levels of pollutants during week in Linwood in the two years of study

Abbreviations; ppb, part per billion; NO_2, nitrogen dioxide; O_3, ozone; $PM_{2.5}$, particulate matter with a diameter less than 2.5 micrometer;
SO_2, sulfur dioxide

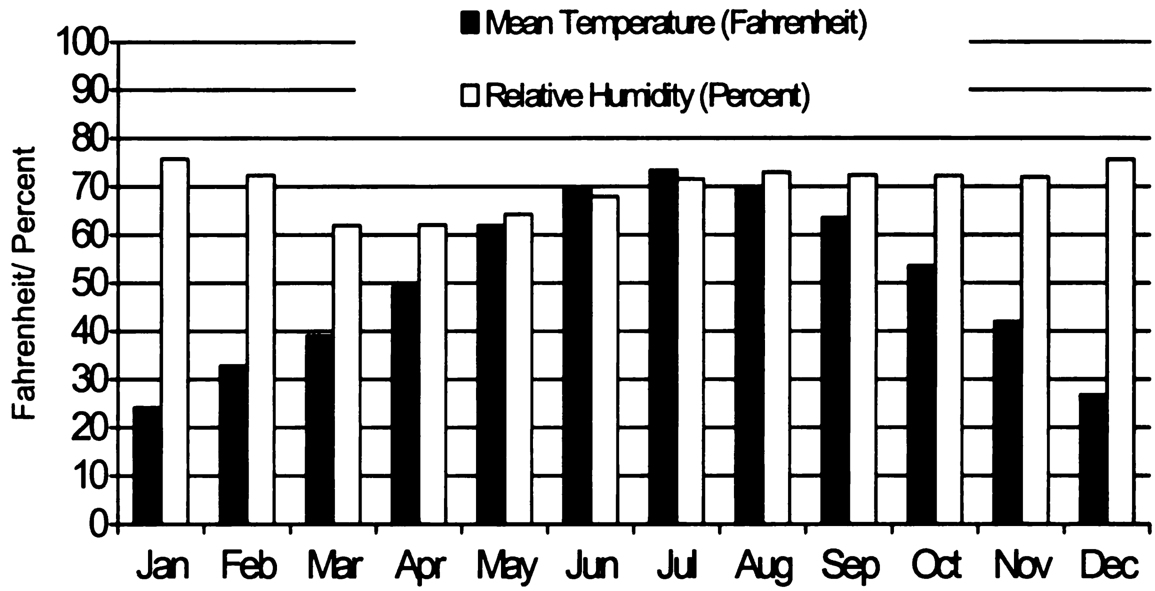

Figure 9. Monthly averages for the mean daily temperature and the mean daily relative humidity in the two sites during the study period.

Descriptive analyses of hospital admissions and census data

Hospital admissions along with census data are presented by demographic characteristic, site of residence and year of admission (Table 7).

During 1999 and 2000, a total number of 4,847 hospital admissions with a discharge diagnosis of asthma were recorded in the Michigan inpatient database for patients who were one to 45 years of age and resided in the 23 zip codes used in this study.

Distribution of the number of daily hospitalizations per site (Figures 10 and 11) represents an asymmetric left skewed curve. The average of the above-mentioned hospital admissions was 3.3, with a variance of 6.02, median of 3 and mode of 2 (Table 5 and 6).

Asthma hospital admission ratios in African-Americans compared to Caucasians were about 5:1 in Linwood and 3:1 in East 7 Mile. Residents up to 18 years old showed a higher rate of hospital admissions in both sites. Linwood had more admissions than East Seven Mile. In 2000 more admissions were recorded in comparison to the previous year, 1999 (Table 7).

For ages less than 19 years, male had greater number of asthma admissions. On the other hand, for ages 19 years and older, females were more often admitted due to asthma (Figure 12). In warmer months, the total monthly admissions dropped in June and July, then increased in August and peaked in September (Figure 13). Mondays and Tuesdays had the maximum number of admissions among weekdays (Figure 14). African-Americans had a higher proportion in Linwood in comparison to East 7 Mile (68.6% versus 59.6%, Table 7). Mean daily admissions rate was higher in Linwood than East 7 Mile (1.4 versus 1.1 per 100,000).

Table 5. Statistics for daily hospital admissions in East 7 Mile

Variable	Estimate
100% Max	20
99%	12
95%	7
50% Median	3
5%	0
0% Min	0
Mode	3
Mean	3.11
Variance	5.76

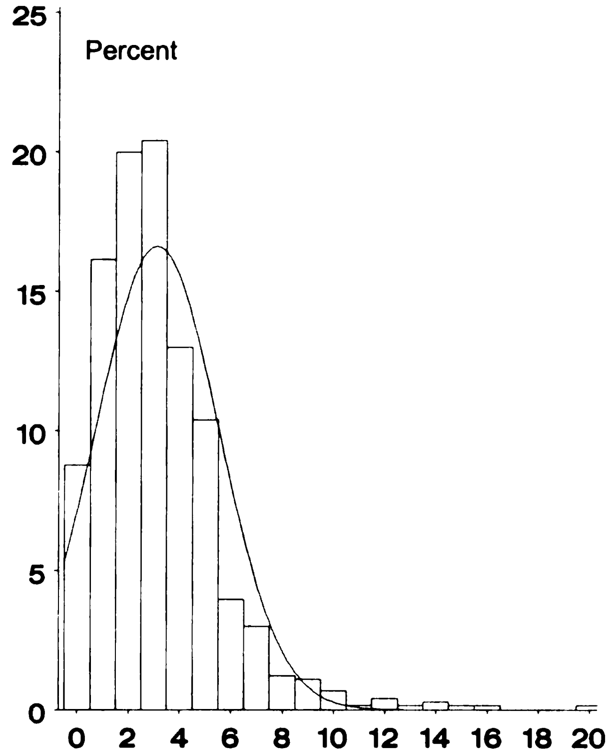

Figure 10. Distribution of total daily asthma admissions during 1999-2000 in Detroit, East 7 Mile

Table 6. Statistics for daily hospital admissions in Linwood

Variable	Estimate
100% Max	19
99%	11
95%	8
50% Median	3
5%	0
0% Min	0
Mode	2
Mean	3.51
Variance	6.21

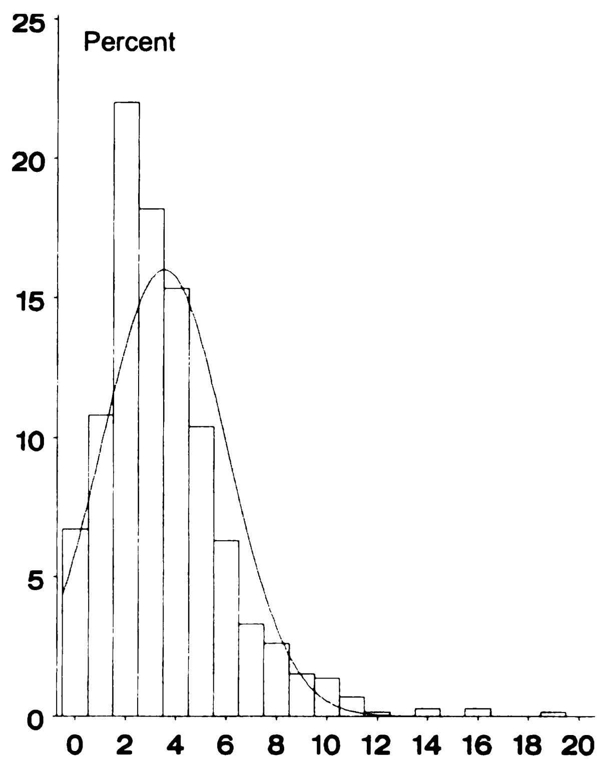

Figure 11. Distribution of total daily asthma admissions during 1999-2000 in Detroit, Linwood

Table 7. Demographic characteristics, site of residence and year of admission for census data along with hospital admissions

	E. Seven Mile				Linwood			
	Year 2000 population (Percent)	Yearly admissions			Year 2000 population (Percent)	Yearly admissions		
		Year	N	Rate (per 10^5)		Year	N	Rate (per 10^5)
Race								
African-American	*165988 (59.6%)*	*1999: 2000:*	*881 1091*	*530 657*	*171337 68.6%*	*1999: 2000:*	*1108 1290*	*647 723*
Caucasian	*76675 (27.6%)*	*1999: 2000:*	*124 178*	*161 232*	*54658 21.9%*	*1999: 2000:*	*64 85*	*117 155*
Other races	*35572 (12.8%)*	*1999: 2000:*	*0 4*	*0 11*	*23690 9.5%*	*1999: 2000:*	*10 12*	*42 51*
Age (years)								
1-5	*32148 (11.6%)*	*1999: 2000:*	*257 338*	*799 1051*	*29840 (11.9%)*	*1999: 2000:*	*276 378*	*925 1267*
6-18	*89934 (32.3%)*	*1999: 2000:*	*375 476*	*417 529*	*74545 (29.8%)*	*1999: 2000:*	*343 399*	*460 535*
19-22	*20319 (7.3%)*	*1999: 2000:*	*31 48*	*152 236*	*21959 (8.8%)*	*1999: 2000:*	*37 49*	*168 223*
23-29	*40310 (14.5%)*	*1999: 2000:*	*83 90*	*206 223*	*41170 (16.5%)*	*1999: 2000:*	*94 139*	*228 338*
30-45	*95524 (34.3%)*	*1999: 2000:*	*259 321*	*271 336*	*82171 (32.9%)*	*1999: 2000:*	*432 422*	*526 513*
Gender								
Female	*141449 (50.8%)*	*1999: 2000:*	*523 633*	*370 447*	*123331 (49.4%)*	*1999: 2000:*	*597 686*	*484 556*
Male	*136786 (49.2%)*	*1999: 2000:*	*482 640*	*352 468*	*126354 (50.6%)*	*1999: 2000:*	*585 701*	*463 555*
Total	*278235 (100%)*	*1999: 2000:*	*1156 1122*	*415 403*	*249685 (100%)*	*1999: 2000:*	*1283 1286*	*514 515*

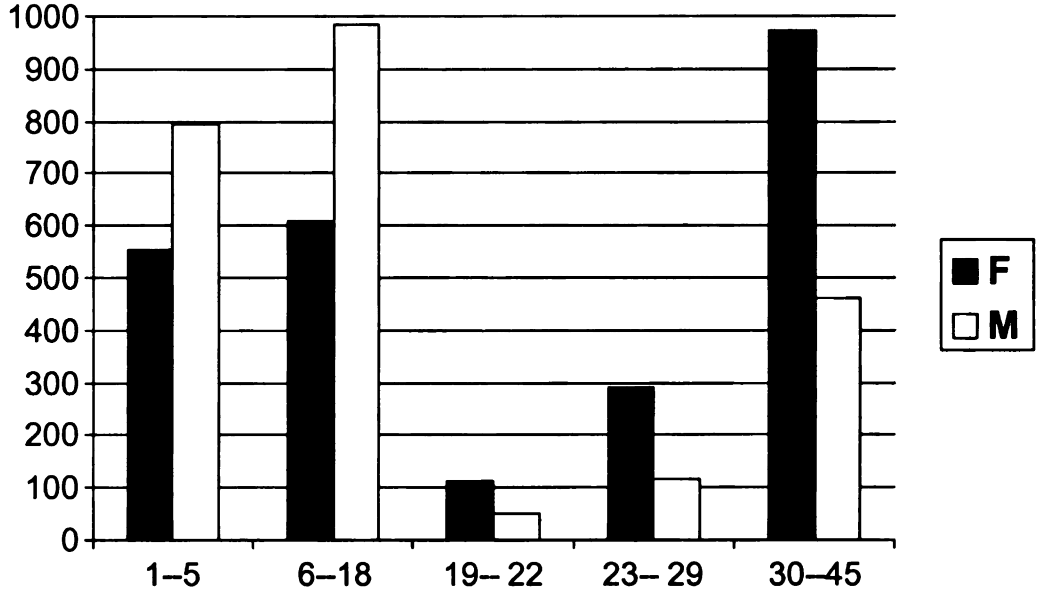

Figure 12. Total number of asthma hospital admissions by age group and gender during the study period

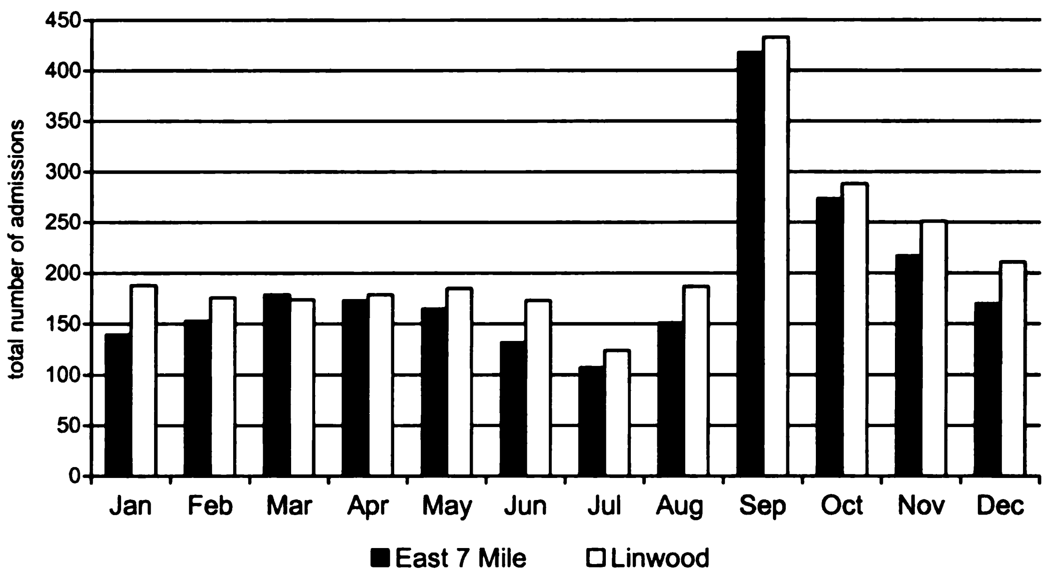

Figure 13. Monthly number of asthma hospital admissions in the two sites during the study period

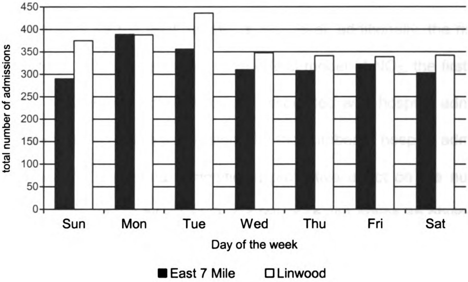

Figure 14. Asthma hospital admissions by day of the week during the study period

Regression analyses

The variance of daily hospital admission (6.02) was greater than its mean (3.3) and the distribution of daily hospital admissions was over-dispersed. We used negative binomial regression to investigate possible associations between air pollution levels and daily hospital admissions. Potential confounders were assumed to be year, month, weekday of admission; with age group, racial group, and gender of admittees; as well as average of relative humidity, minimum, mean and maximum temperature for the 4 days preceding of admission. Among fully saturated models (Table 8) with only one pollutant, models for NO_2, SO_2 and O_3 were significantly associated with hospital admissions for certain levels of the pollutant. Final (the most parsimonious) models were models with variables that dropping them could have changed RR more than 10%. In other words, year or month or both were the only confounders. In the final model for SO_2, risk ratio was significant only for the third quartile of SO_2 level; additionally, the risk ratios did not pursue a trend in this model. In the final model of NO_2, the first quartile level of the pollutant was not significantly associated with hospital admissions, but higher levels of NO_2 were associated with the number of hospital admissions. All three levels of O_3 showed a significant protective effect on the number of hospital admissions. In the NO_2 and O_3 models, one can notice an obvious trend in RR for different levels of the pollutants. At the next step, a model with year, month, SO_2, NO_2 and O_3 was run (Tri-pollutant model, Table 9). SO_2 failed to show significance in the tri-pollutant model. Finally we ran a model with two pollutants, NO_2 and O_3, controlling for year and month of admissions. This model was considered as our final model with having significant RR for both NO_2 and O_3 (Table 10). The interaction term of NO_2 and O_3 did not gain statistical significance.

In mono-pollutant models, SO_2 and NO_2 were positively and O_3 was negatively associated with the daily asthma hospital admissions. Association between $PM_{2.5}$ and hospital admissions was not evident.

In a tri-pollutant model including those pollutants that showed any association in mono-pollutant models (SO_2, NO_2 and O_3), SO_2 was no more associated with the outcome. NO_2 had still a positive and ozone a negative association with the outcome.

Table 8. Mono-pollutant models† (SO_2, NO_2 or O_3) controlling for year and/ or month of admission

Model	Pollutant* (unit)	Equidistant levels	RR (95% CI)	k (95% CI)	Quartile levels	RR (95% CI)	k (95% CI)
SO_2+ Month	SO_2 (ppb)	0.1-4.0 (Ref.)	1.00		0.1-3.0 (Ref.)	1.00	
		4.1-8.0	1.06 (0.94, 1.18)	0.08	3.1-4.7	1.07 (0.93, 1.24)	0.07
		8.1-12	1.26 (1.02, 1.54)	(.05-.13)	4.8-6.9	1.08 (0.94, 1.25)	(.04-.1)
		12.1-16.2	1.51 (1.18, 1.94)		7.0-16.2	1.37 (1.17, 1.60)	
NO_2+ Month	NO_2 (ppb)	1.7-13.0 (Ref.)	1.00		1.7-16.5 (Ref.)	1.00	
		13.1-24.3	1.01 (0.84, 1.21)	0.08	16.6-20.3	1.01 (0.87, 1.16)	0.07
		24.4-35.6	1.29 (1.04, 1.06)	(.05-.13)	20.4-24.8	1.25 (1.07, 1.44)	(.04-.1)
		35.7-46.9	1.22 (0.76, 1.98)		24.9-46.9	1.37 (1.17, 1.66)	
O_3+ Year+ Month	O_3 (ppb)	5.9-19.2 (Ref.)	1.00		5.9-22.1 (Ref.)	1.00	
		19.3-32.5	0.79 (0.69, 0.90)	0.03	22.2-27.0	0.90 (0.78, 1.04)	0.03
		32.6-45.8	0.71 (0.59, 0.86)	(.009-.09)	27.1-32.7	0.85 (0.74, 0.99)	(.01- .09)
		45.9-59.1	0.67 (0.49, 0.92)		32.8-59.1	0.79 (0.66, 0.93)	

† The period involved in these models was April-September, each year and the number of observations (days in the two site) were 582.
In fully saturated models all the potential confounders were controlled for.
*Average level for 4 preceding days of admission
Abbreviations; CI, confidence interval; ppb, part per billion; µg/ m^3, microgram per cubic meter; Ref., reference level; RR, risk ratios; k. Dispersion parameter; NO_2, nitrogen dioxide; O_3, ozone; SO_2, sulfur dioxide

Table 9. Tri-pollutant model† (SO_2, NO_2 and O_3) controlling for year and month of admission

Pollutant* (unit)	Equidistant levels	RR (95% CI)	k (95% CI)	Quartile levels	RR (95% CI)	k (95% CI)
SO_2 (ppb)	0.1-4.0 (Ref.)	1.00		0.1-3.0 (Ref.)	1.00	
	4.1-8.0	1.07 (0.96, 1.19)		3.1-4.7	1.11 (0.98, 1.27)	
	8.1-12	1.14 (0.94, 1.39)		4.8-6.9	1.07 (0.93, 1.22)	
	12.1-16.2	1.21 (0.95, 1.55)		7.0-16.2	1.15 (0.98, 1.35)	
NO_2 (ppb)	1.7-13.0 (Ref.)	1.00		1.7-16.5 (Ref.)	1.00	
	13.1-24.3	0.98 (0.82, 1.16)	0.02	16.6-20.3	1.06 (0.93, 1.21)	
	24.4-35.6	1.07 (0.87, 1.33)	(.004-.09)	20.4-24.8	1.20 (1.05, 1.38)	0.02
	35.7-46.9	1.09 (0.70, 1.71)		24.9-46.9	1.19 (1.00, 1.40)	(.004-.09)
O_3 (ppb)	5.9-19.2 (Ref.)	1.00		5.9-22.1 (Ref.)	1.00	
	19.3-32.5	0.79 (0.67, 0.87)		22.2-27.0	0.90 (0.79, 1.04)	
	32.6-45.8	0.69 (0.57, 0.83)		27.1-32.7	0.85 (0.74, 0.98)	
	45.9-59.1	0.64 (0.47, 0.87)		32.8-59.1	0.78 (0.66, 0.93)	

† The period involved in this model was April-September, each year and the number of observations (days in the two site) were 582.
*Average level for 4 preceding days of admission
Abbreviations; CI, confidence interval; ppb, part per billion; μg/ m^3, microgram per cubic meter; Ref., reference level; RR, risk ratios; k. Dispersion parameter; NO_2, nitrogen dioxide; O_3, ozone; SO_2, sulfur dioxide

Table 10. Bi-pollutant model† (NO_2 and O_3) controlling for year and month of admission

Pollutant* (unit)	Equidistant levels	RR (95% CI)	k (95% CI)	Quartile levels	RR (95% CI)	k (95% CI)
NO_2 (ppb)	1.7-13.0 (Ref.)	1.00		1.7-16.5 (Ref.)	1.00	
	13.1-24.3	1.00 (0.85, 1.18)		16.6-20.3	1.07 (0.94, 1.21)	
	24.4-35.6	1.16 (0.96, 1.41)		20.4-24.8	1.24 (1.09, 1.40)	
	35.7-46.9	1.18 (0.76, 1.82)	0.02 (.006-.09)	24.9-46.9	1.25 (1.09, 1.43)	.025 (.007-.08)
O_3 (ppb)	5.9-19.2 (Ref.)	1.00		5.9-22.1 (Ref.)	1.00	
	19.3-32.5	0.78 (0.69, 0.89)		22.2-27.0	0.92 (0.81, 1.05)	
	32.6-45.8	0.70 (0.59, 0.85)		27.1-32.7	0.87 (0.76, 1.00)	
	45.9-59.1	0.65 (0.48, 0.89)		32.8-59.1	0.81 (0.69, 0.95)	

† The period involved in this model was April-September, each year and the number of observations (days in the two site) were 582.
*Average level for 4 preceding days of admission
Abbreviations; CI, confidence interval; ppb, part per billion; µg/ m^3, microgram per cubic meter; Ref., reference level; RR, risk ratios; k. Dispersion parameter; NO_2, nitrogen dioxide; O_3, ozone

DISCUSSION

Among residents of 23 zip codes in Detroit, Michigan, we conducted an aggregative study to investigate the relationship between daily asthma hospital admissions and levels of four pollutants nitrogen dioxide (NO_2), ozone (O_3), particulate matter with a diameter less than 2.5 µm ($PM_{2.5}$) and sulfur dioxide (SO_2).

Using negative binomial models and taking into account the average levels of pollutants over the 4-day period preceding daily asthma hospital admissions, regression analysis revealed that number of daily asthma hospital admissions was positively associated (increased) with NO_2 levels and negatively associated (decreased) with O_3 levels (adjusted for year and month of admissions). Asthma hospital admissions showed a positive association with SO_2 levels in single-pollutant model, but this association disappeared when we controlled for NO_2 and O_3. No association was evident between particulate matter ($PM_{2.5}$) and asthma hospital admissions.

For NO_2, the only pollutant that consistently showed a positive association with the outcome, an exposure-response trend was suggested. The estimated relative risk per 6 ppb increase in NO_2 (an increment roughly equal to one standard deviation) was 1.08.

It has been shown that both NO_2 and O_3 increase inflammatory response in lung and bronchial tissues [22]. Although it is in debate whether or not these pollutants are associated with the incidence of new diagnosis of asthma [23], most of the previous studies support at least a triggering effect for them even at low levels [24]. Our finding that increasing NO_2 levels are positively associated with asthma hospital admissions is consistent with previous studies.

A conflicting finding in this study was the protective effect of increasing O_3 levels on the number of daily asthma hospital admissions (As O_3 levels increased, the number of admissions dropped). However in several previous studies with the same methodology as ours, increasing O_3 levels appeared to be negatively associated with the number of asthma hospital admissions [8-11].

In fact O_3 is not emitted to the air directly and it is the product of a complex reaction between volatile organic compounds (VOCs) and nitrogen oxides in the presence of sunlight [16]. We did not have data on the pollutants that are related to O_3 levels, except for NO_2. Our data showed that O_3 and NO_2 were negatively correlated. Additionally, the negative effect of O_3 levels on average numbers of daily asthma hospital admissions was best seen when NO_2 was low in contrast to situations when level of NO_2 was high (Figure 15). Based on these explanations and the fact that O_3 is a byproduct of other pollutants, we think that the negative association between O_3 and the daily number of asthma hospital admission, found in this study might be due to the simultaneous lower levels of other pollutants, such as VOCs and not independently due to O_3 levels.

Additional investigation, in the presence of data on pollutants involved in the pathway of O_3 production such as VOCs and various nitrogen oxides (Figure 1), may help to further explain the effect of O_3 levels on asthma hospital admission.

In the analysis, race emerged as a strong independent predictor of hospital admissions (asthma hospital admission was 3-5 times higher in African-Americans compared to Caucasians). Our results are inconclusive whether 'race' can affect asthma hospital admission due to air pollution. The pattern of hospital admission by gender is in agreement with previously reported studies (Figure 12).

The effect of seasonality on asthma hospital admissions is a well-known phenomenon. We noticed a sharp rise of asthma hospital admissions in September. Other studies reported a seasonal variation in the asthma hospital admission [12,25] and Sheppard et al. had identical findings [6].

It has been argued that parents pay more attention to their children's preventive measures for asthma during holiday, as well as children being under less stress than when at school [12]. Indeed those who travel and become admitted out of the state are no longer being calculated for the number of hospital admissions. In our study, the September peak was evident for all age groups, particularly for ages less than 19 years. Holiday travels facilitate the acquisition of new viral strains by the community. It is possible that children share new strains of viruses and carry them to their families when they first come back to school. Viral upper respiratory infections, especially rhinovirus, are reported to be the most common cause of acute asthma exacerbations. Looking at asthma hospital admissions, Johnston et al. showed that viruses are associated with 80 to 85% of asthma exacerbations in school-age children [26].

Limitations and strengths

In this study we assumed that residents of zip codes within the 4-kilometer radius of each air-monitoring station were exposed to the same amount of pollutants. This assumption may evoke information bias, because the monitoring stations were not necessarily at the point that the overall effect of pollution in the site had been exhibited. For example the distance of the Linwood station to the three Interstate highways (I-75, I-94 and I-96) is less than a mile, while distance of most other points at this site is much further from these highways (Figure 2).

Ecological fallacy may apply to this investigation as we assumed all residents exposed to the same amount of the pollutants. Data that might affect individual exposures was not available (such as the duration the residents spent outside and individual level factors such as cigarette smoking). Although we did not have data on pollen count and flu episodes (that are related to asthma), however they are not likely to be related to air pollution. The data included information on the daily number of hospital admissions by age, gender and race, so we were unable to account for re-admissions and severity of attacks. Daily hospital admissions may have been biased due to different level of access to hospital among the study population, but the data had the potential to capture nearly all asthma hospital admissions because all hospitals in Michigan are committed to participate in the Michigan Inpatient Database.

We attempted to analyze the data using Poisson regression models as similar previous studies explained but the fit was not adequate in Poisson regression models. Using negative binomial models we achieved an excellent goodness of fit for our models of regression analysis.

Conclusion

This thesis, adds to the body of evidence that supports an adverse effect of air pollution on the increase of asthma hospital admissions and is an example of using regression analysis for the count data in epidemiologic studies. Because of the ecological nature of this study, the results do not necessarily indicate a causal association.

Among the four pollutants studied in this thesis, increasing NO_2 levels seemed to be related to higher daily asthma hospital admissions. Our analyses did not support the adverse effect of $PM_{2.5}$ and SO_2 on asthma hospital admissions. The conflicting protective effect of O_3 on the number of asthma hospital admissions needs more investigation. We suggest designing future studies that take into account pollutants, which are important in the pathway of O_3 production, such as VOCs and nitrogen oxides. Additionally conclusion, the best setting to study the effect of the air pollutants on asthma would be the assessment of exposures, confounders and outcomes at the individual level.

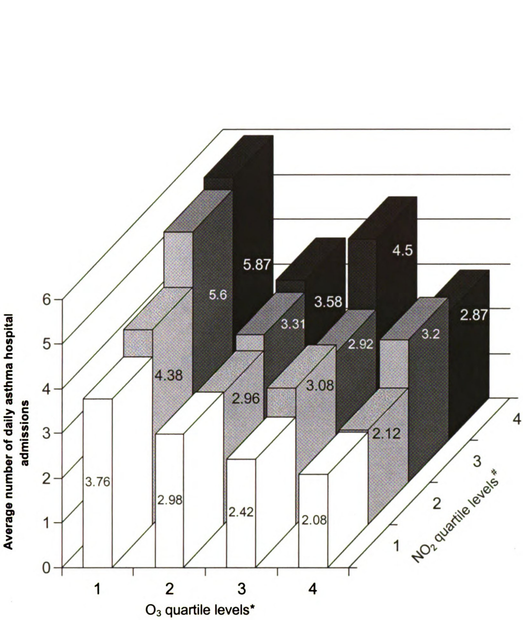

Figure 15. Average number of daily asthma hospital admissions for different quartiles of nitrogen dioxide (NO_2) and ozone (O_3)

*O_3 quartile levels (parts per billion): 1, *5.9-22.1*; 2, *22.2-27.0*; 3, *27.1-32.7*; 4, *32.8-59.1*

#NO_2 quartile levels (parts per billion): 1, *1.7-16.5*; 2, *16.6-20.3*; 3, *20.4-24.8*; 4, *24.9-46.9*

Appendix. Summary of previous studies

First author (Year)	Period of study	Ref.	Location	Population	Outcome	Pollutant				Comments
						NO_2	O_3	PM	SO_2	
Bates (1990)	1984-1986 Y-S-W		Vancouver Canada	All ages	ED visits	o	o	NA	o	In the 15-60 age group, asthma and respiratory visits were correlated in summer with SO2 and SO4 levels
Ponka (1991)	1987-1989		Helsinki	All ages	Hospital admissions	+	+	+	+	
Schwartz (1993)	1989-1990		Seattle	<65 years	ED visits	NA	+	o	o	Maximum number of admissions in September
White (1994)	1990 S		Atlanta	1-16 years	ED visits	NA	+	NA	NA	Study population was predominantly African-American
Romieu (1995)	1990 Jan-Jun		Mexico City	≤16 years	ED visits	NA	+	NA	o	
Buchdahl (1996)	1992-1993		London	≤16 years	ED visits	o	+	NA	+	Acute wheezy episodes as outcome
Stieb (1996)	1984-1992 S		Saint John Canada	All ages	ED visits	NA	+	NA	NA	

Abbreviations; +, positive effect; –, negative effect; o, no effect; NA, not available; S, summer; W, winter; Y, whole year; NO_2, nitrogen dioxide; O_3, ozone; SO_2, sulfur dioxide; PM, particulate matter; ED, emergency department

(Appendix Cont'd)

First author (Year)	Period of study	Ref.	Location	Population	Outcome	Pollutant NO$_2$	O$_3$	PM	SO$_2$	Comments
Holmen (1997)	1990-1993		Halmstad, Sweden	Kids≤ 15 Adults> 15	ED visits	+ in kids – in Adults	– in kids +in Adults	NA	o	– 0.70 correlation between ozone and nitrogen dioxide
Medina (1997)	1991-1995		Paris	All ages	Doctors' home calls	+	+	+	+	
Anderson (1998)	1987-1992 S						+ o			All pollutants found to have significant associations with daily hospital admissions for asthma, but there was a lack of consistency across the age groups in the specific pollutant
			London	All ages	Hospital admissions	+ o		+ o	+ o	
	1987-1992 W						– o			
Garty (1998)			Israel	1-18 years	ED visits	+	–	o	+	An exceptionally high incidence of ED visits of asthmatic children was observed during September
Chew (1999)	1990-1994		Singapore	3-12 years 13-21 years	ED visits	+ o	+ o	+ o	+ o	Positive associations found in younger age group and no association for older
Sheppard (1999)	1987-1994		Seattle, Washington	<65 years	Hospital admissions	NA	o	+	o	Both PM$_{2.5}$ and PM$_{10}$ were studied

Abbreviations; +, positive effect; –, negative effect; o, no effect; NA, not available; S, summer; W, winter; Y, whole year; NO$_2$, nitrogen dioxide; O$_3$, ozone; SO$_2$, sulfur dioxide; PM, particulate matter; ED, emergency department

(Appendix Cont'd)

First author (Year)	Period of study	Ref.	Location	Population	Outcome	Pollutant				Comments
						NO_2	O_3	PM	SO_2	
Tolbert (2000)	1999 S		Atlanta	≤16 years	ED visits	o	+	+ 10μm	NA	0.75 of correlation between PM_{10}- O_3
Wong (2001)	1993-1994		Hong Kong	<15 years	Hospital admissions	+	o	+ 10μm	+	
Ritchie (2001)	1997-1999 S		Indianapolis	1-17 years	Hospital admissions	+	–	NA	+	
Jaffe (2002)	1991-1996 S		Ohio	5-34 years	ED visits	o	o	+ 2.5-10μm	+	Summer months, June-August
Lin (2002)	1981-1993		Toronto	6-12 years	Hospital admissions	NA	NA	+	NA	5-6 day's average of both $PM_{2.5}$ and PM_{10} were in the study- Individual subjects
Wong (2002)	1992-1994		London	15-65 years	Hospital admissions	+	+	+	+	Significant negative association between O_3 and cardiac disease admissions in London
	1995-1997		Hong Kong	<65 years						

Abbreviations; +, positive effect; –, negative effect; o, no effect; NA, not available; S, summer; W, winter; Y, whole year; NO_2, nitrogen dioxide; O_3, ozone; SO_2, sulfur dioxide; PM, particulate matter; ED, emergency department

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