



Associations between ozone, PM_{2.5}, and four pollen types on emergency department pediatric asthma events during the warm season in New Jersey: A case-crossover study[☆]

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ABSTRACT

Background: Asthma is one of the most common chronic diseases among school-aged children in the United States. Environmental respiratory irritants exacerbate asthma among children. Understanding the impact of a variety of known and biologically plausible environmental irritants and triggers among children in New Jersey – ozone, fine particulate matter (PM_{2.5}), tree pollen, weed pollen, grass pollen and ragweed – would allow for informed public health interventions.

Methods: Time-stratified case-crossover design was used to study the transient impact of ozone, PM_{2.5} and pollen on the acute onset of pediatric asthma. Daily emergency department visits were obtained for children aged 3–17 years with a primary diagnosis of asthma during the warm season (April through September), 2004–2007 (inclusive). Bi-directional control sampling was used to select two control periods for each case for a total of 65,562 inclusion days. Since the period of exposure prior to emergency department visit may be the most clinically relevant, lag exposures were investigated (same day (lag0), 1, 2, 3, 4, and 5 as well as 3-day and 5-day moving averages). Multivariable conditional logistic regression controlling for holiday, school-in-session indicator, and 3-day moving average for temperature and relative humidity was used to examine the associations. Odds ratios are based on interquartile range (IQR) increases or 10 unit increases when IQR ranges were narrow. Single-pollutant models as well as multipollutant models were examined. Stratification on gender, race, ethnicity and socioeconomic status was explored.

Results: The associations with ozone and PM_{2.5} were strongest on the same day (lag0) of the emergency department visit (RR_{IQR} = 1.05, 95% CI 1.04–1.06) and (RR_{IQR} = 1.03, 95% CI 1.02–1.04), respectively, with a decreasing lag effect. Tree and weed pollen were associated with pediatric ED visits; the largest magnitudes of association was with the 5-day average (RR_{IQR} = 1.23, 95% CI 1.21–1.25) and (RR₁₀ = 1.13, 95% CI 1.12–1.14), respectively. Grass pollen was only minimally associated with the outcome while ragweed had a negative association.

Conclusions: The ambient air pollutant ozone is associated with increases in pediatric emergency department asthma visits during the warm weather season. The different pollen types showed different associations with the outcome. High levels of tree pollen appear to be an important risk factor in asthma exacerbations.

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1. Introduction

Asthma is one of the most common chronic diseases among school-aged children in the United States (Eaton et al., 2010). In

New Jersey over 14% of the pediatric population has a history of asthma while over 10% have current asthma (NJ DHSS, 2013). Each year there are approximately 50,000 emergency department visits for asthma in New Jersey; about 40% of these are for children (NJ DHSS, 2013).

Children with asthma are disproportionately impacted by warm weather patterns of ozone and fine particulate matter (PM_{2.5}) (Mar and Koenig, 2009; Silverman and Ito, 2010). Children may be the most vulnerable to the effects of ambient air pollutants since their defense mechanisms are still evolving and they inhale a higher volume of air per body weight than adults (Salvi, 2007). Increased ambient air levels of ozone and PM_{2.5} lead to asthma

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exacerbation for children who are especially susceptible (Samoli et al., 2011; Silverman and Ito, 2010). Increases in childhood emergency department (ED) visits and hospitalizations are associated with ozone and PM_{2.5} (Babin et al., 2007; Boutin-Forzano et al., 2004; Giovannini et al., 2010; Mar and Koenig, 2009; Pereira et al., 2009; Silverman and Ito, 2010; Strickland et al., 2010). Increases in emergency department visits among children have also been associated with increased pollen concentrations (Heguy et al., 2008). However, the role of pollen in the complex genetic and ambient air pollutant interactions leading to asthma exacerbation remains unclear (Heguy et al., 2008).

The susceptibility of asthmatic children to ambient air triggers is further compounded since 72% of all persons in the northeast region – New England, New Jersey and New York – live in urban areas with increased PM_{2.5} exposure profiles (Johnson and Graham, 2005). Although New Jersey air quality has improved in the last 40 years it still has not met some current standards of air quality (Lioy and Georgopoulos, 2011; NJ DEP, 2013a). The entire state of New Jersey is classified in nonattainment under the current 8-hour ozone National Ambient Air Quality Standard (NAAQS) of 75 parts per billion (ppb) and portions of the state are classified in nonattainment under the 24-hour and annual average NAAQSs for PM_{2.5} of 35 micrograms per cubic meter (μg/m³) (NJ DEP, 2013a).

Many environmental respiratory irritants and allergens are predicted to increase with changes in the climate and population (Bielory et al., 2012; Blando et al., 2012; Dapul-Hidalgo and Bielory, 2012). Increasing urbanization rates result in increased traffic that contributes significantly to the pollution of the atmosphere (D'Amato et al., 2010; Mahbub et al., 2011; Moodley et al., 2011; Riedl and Diaz-Sanchez, 2005). Increases in pollen concentrations, lengthening pollen seasons and increases in the allergenicity of pollen have been forecasted (Bielory et al., 2012; Heguy et al., 2008; Ziska et al., 2011).

In this large, multi-year study, a time-stratified case-crossover design was used to investigate the impacts of ozone, PM_{2.5}, tree, grass, weed and ragweed pollen on the acute onset of pediatric asthma. Daily ED visits for pediatric asthma in New Jersey during the warm seasons of four years, 2004–2007, have been matched using bi-directional control sampling. We explore modeled daily- and location-varying estimates of ozone and PM_{2.5} in addition to four pollen types as both independent predictors and as control factors in multi-pollutant models. Understanding the impact of a variety of known and biologically plausible environmental irritants and triggers among children across New Jersey will allow informed public health intervention.

2. Materials and methods

2.1. Emergency department data

Data on daily ED visits were obtained from the New Jersey Department of Health, Health Care Quality Assessment program, for children aged 3–17 years with a primary diagnosis of asthma (International Classification of Diseases, Ninth Revision [ICD-9] code 493.xx) for the warm seasons (April 1st to September 30th) in the years 2004–2007 (Strickland et al., 2010). The reliability of a diagnosis of asthma in children younger than 3 years of age has been questioned, therefore these children were excluded from this study (Boutin-Forzano et al., 2004; PHASE, 2007).

2.2. Ambient air pollutant data

The New Jersey Department of Environmental Protection Bureau of Air Monitoring currently maintains 40 ambient air monitoring sites, which include 15 sites for ozone and 20 sites for PM_{2.5} (NJ DEP, 2013b). Data from these sites contributed to the U.S. Environmental Protection Agency's Bayesian space-time hierarchical model combining air quality monitoring data with gridded output from the Multi-Scale Air Quality Model. The national model provides estimates of

daily PM_{2.5} (daily average) and ozone (daily 8-hr maximum) values for 2001–2007 at a 12 km (km) square grid scale (NJ DEP, McMillan et al., 2010; US EPA, 2012).

2.3. Meteorological data

Daily mean temperature and relative humidity values were obtained from the New Jersey State Climatologist. During the study period, 26 weather stations across the state were active throughout. Each station was geocoded to an overlay of the 12 km × 12 km grid and each grid centroid was assigned the daily values of the closest station. In the instance that data on a given day was unavailable the grid was assigned the next closest station with available data for that day.

2.4. Pollen data

The National Allergy Bureau, a section of the American Academy of Allergy, Asthma and Immunology's Aeroallergen Network, reports pollen and mold grain levels to the public. Specific counts for various pollen types – tree, grass, weed and ragweed – are collected daily, except for weekends and some winter months, using volumetric sampling devices from a counting station located in Springfield, New Jersey (Port et al., 2006). Samples are taken in the morning and reflect the past 24 h periods. For each pollen type, 3.1% of days during the study period were missing pollen values. If a pollen value was missing on a given day that day was assigned the pollen value from the previous day for up to three consecutive days with missing values. If more than three consecutive days were missing pollen values then the remainder of the days were given the pollen value from the succeeding day. Data from this monitoring station, which is one of only two stations in the State of New Jersey, served as representative for the whole state, as pollen season peaks are similar throughout the state (Dvorin et al., 2001; Im and Schneider, 2005).

2.5. Design and analysis

Time-stratified case-crossover design was used to control for time trends by dividing the study period into fixed 21-day strata; the last stratum in the study period is only 18 days. (PHASE, 2007). Although there is no hardened rule for stratum selection, following recommendations and considerations from the PHASE Case-Crossover Technical Background Report, 2007; time stratification into 21-day strata was selected. This strata size was chosen for several reasons: first it is a multiple of seven therefore controls are selected on the same day of the week as the case, additionally 21 days is a wide enough period of time to allow for the selection of two control periods per case therefore increasing statistical power, and finally the period is narrow enough to avoid capturing a long-term temporal pattern and can more effectively control for time-varying confounding. Asthma events which are recurrent for the same child within the time-stratum of 21-days were excluded to maintain an assumption of independence (Li et al., 2011; PHASE, 2007).

Each child included in the study population was geocoded to the address that was provided at the time of the ED visit. The child's address was spatially linked to a 12 km × 12 km grid and assigned the corresponding value of ozone and PM_{2.5} for the same day (lag0) of the ED visit. The most clinically relevant exposure may be the exposures just prior to the ED visit, therefore 1-day through 5-day lag, 3-day average (average of lags 0–2) and 5-day average (average of lags 0–4) were explored (PHASE, 2007). Since the most relevant lag period(s) has been shown to differ by study location, exploring multiple lagged exposures will provide insight into the role of these exposures on pediatric asthma emergency department events in New Jersey (Darrow et al., 2012; Ji et al., 2011; Mar and Koenig, 2009; Strickland et al., 2010; Tobias et al., 2003; Villeneuve et al., 2007; Zeka et al., 2005). Bi-directional control sampling was employed in which two control periods, one preceding and one proceeding is selected for each case day (Navidi, 1998). This method avoids bias due to temporal trends since controls are selected at a time prior to and following an event and selection by week avoids any effects of day of week (Fung et al., 2003; Navidi, 1998; Navidi et al., 1999; PHASE, 2007). Controls were only selected from weeks before or after that are within the 21-day stratum. If the control's stratum did not match the case's stratum a new control date was selected two weeks in the appropriate time direction such that case and controls would be from the same stratum. Case-control sets were excluded if exposure data was missing due to pollutant lagging occurring outside of the study period.

Multivariate conditional logistic regression was performed using SAS software PROC PHREG to calculate odds ratios (Statistical Analysis Software (SAS) Institute Inc., 2002–2008; Boutin-Forzano et al., 2004; Navidi, 1998; Tolbert et al., 2000; Villeneuve et al., 2007). Adjusted odds ratios of pediatric ED visits and exposures of interest were calculated using either the same-day IQR increase or a 10-unit increase when IQR ranges were narrow (< 5 units). Estimation of odds ratios by (IQR) increases in the pollution lag days allows for comparability of exposures (Pereira et al., 2010; Silverman and Ito, 2010). IQR was calculated using the same-day case-referent concentrations rather than the full time-series in order to avoid extrapolating beyond the observed ranges (PHASE, 2007). Additionally, adjusted odds ratios were calculated using a binary categorization based on existing standards and cut-offs (AAAAI, 2012; US EPA, 2011). Ozone, PM_{2.5} and tree pollen

lags were categorized into quintiles and the lowest quintile served as the referent category to calculate odds ratios.

Every combination of mean temperature and mean humidity lags was explored. Coefficient estimation was not meaningfully affected based on the lag selection of mean temperature or mean humidity, therefore 3-day average temperature and 3-day average humidity were selected to provide adequate control in single pollutant models (Boutin-Forzano et al., 2004; Mohr et al., 2008; PHASE, 2007; Silverman and Ito, 2010). Additionally, a school-in-session indicator for days before Memorial Day and after Labor Day was included because school status among children is associated with increases in viral upper respiratory infections, and also an indicator of holidays was controlled for; both indicators were associated with both the outcome and same-day (lag0) exposures (Johnston et al., 1996; Strickland et al., 2010).

Multipollutant models were fit to assess how associations changed after adjusting for other exposures, using same day (lag0) values for ozone and PM_{2.5} and 3-day moving average for each pollen type. Stratification by gender, race, ethnicity and socioeconomic status (SES) of a fully-adjusted multipollutant model, using an *a priori* variable selection, was performed to assess whether effect estimates were modified among these socio-demographic groups. Using 2000 United States Census Data, SES was defined as proportion of population living in poverty for each census tract. A high proportion of population living in poverty results in a low SES categorization (high SES is < 5% living in poverty, moderate SES is 5–20% living in poverty, and low SES is > 20% living in poverty). A sensitivity analysis restricting the study population to an area located close by the pollen monitoring station was performed to assess whether effect estimates differed among those closest to the pollen monitoring station.

To examine possible effect modification between the air pollutants ozone and PM_{2.5} with pollen, odds ratios and 95% CIs of high versus low pollen categories (based on existing standards and cut-offs referenced previously) for each quintile of ozone and PM_{2.5} were estimated. Also, ORs and 95% CI of each quintile of ozone and PM_{2.5} versus the lowest quintile for both high and low categories of pollen were estimated. These models controlled for 3-day average temperature, 3-day average humidity, and school in session and holiday indicators.

3. Results

After exclusions there were 21,854 visits to the ED for pediatric asthma (case days) that were matched with two control days for a total of 65,562 case and control days. Cases were more likely to be male than female, white than black or other race, non-Hispanic than Hispanic, and categorized as moderate SES than low or high SES (Table 1). Compared to the state population cases appear over representative of males, black race and low SES (Table 1). The largest percentage of ED pediatric asthma visits occurred in the month of May while the lowest occurred in July; the monthly distribution of ED visits appeared similar across the four years of the study period.

Among environmental variables, the highest pairwise correlation was between ozone and PM_{2.5} ($r=0.56$), followed by grass pollen and weed pollen ($r=0.34$). Fig. 1A through 1F are daily time-series plots of ED pediatric visits overlaid by each of the six exposures of interest for the year 2004, shown for illustration. Ozone and PM_{2.5} plots are of average daily concentrations across grid cells, weighted by the count of pediatric asthma ED visits in each cell. Fig. 1C, the daily time-series plot of pediatric asthma ED counts overlaid with the weighted average of tree pollen, illustrates an overlap of peaks in late April to early May, while Fig. 1F of the weighted average of ragweed shows unaligned peaks.

3.1. Single pollutant models

Adjusted odds ratios of pediatric ED visits and exposures of interest are presented for lag periods (same day, 1-day lag, 2-day lag, 3-day average and 5-day average) with the exposure categorized as continuous (either IQR increase or a 10-unit increase) (Table 2 and Fig. 2) or as binary categorization based on existing environmental standards (Table 2). Adjusted odds ratios and 95% confidence intervals for ozone, PM_{2.5} and tree pollen categorized into quintiles across lags (same day, lag1, lag2, 3-day and 5-day average) are presented in Table 3.

Table 1

Distribution of sex, race, ethnicity and socioeconomic status among cases and New Jersey population and month and year of case diagnosis.^a

Characteristics	Cases ^b		State % ^c
	N	%	
Gender			
Male	13,232	60.6	51.0
Female	8622	39.5	49.0
Race			
Black	8380	38.4	16.0
Other	3674	16.8	19.8
White	9800	44.8	64.2
Ethnicity			
Hispanic	4176	21.3	19.0
Non-Hispanic	15,417	78.7	81.0
Socioeconomic status			
Low	6209	28.4	10.9
Moderate	9795	44.8	43.3
High	5850	26.8	45.8
Month of diagnosis			
April	3601	16.5	—
May	7391	33.8	—
June	2930	13.4	—
July	2099	9.6	—
August	2448	11.2	—
September	3385	15.5	—
Year of diagnosis			
2004	4973	22.8	—
2005	5615	25.7	—
2006	5886	26.9	—
2007	5380	24.6	—

^a Due to rounding percentages may not add to 100.

^b Missing and unknown values are removed.

^c Gender, race and ethnicity state percentages obtained from U.S. Census Bureau, American Community Survey (2006) for population under 18 years of age. State socioeconomic status percentage obtained from U.S. Census Bureau (2000) as percentage of population living in a census tract below poverty.

Ozone as a continuous variable showed associations with pediatric asthma ED visits for same day exposure, 1-day lag, and 3-day average. The strongest association was with same day exposure (RR_{IQR}=1.05, 95% CI 1.04–1.06) (Table 2 and Fig. 2). When classified as a binary variable with a cut-point of 75 ppb, there was an association with same day exposure (RR=1.14, 95% CI 1.02–1.27) (Table 2). When classified into quintiles, there was an association with pediatric asthma ED visits for the highest quintile of exposure compared to the lowest for same-day, 3-day average, and 5-day average exposure (Table 3).

PM_{2.5} exposure as a continuous variable was associated with pediatric asthma ED visits for same day exposure (RR_{IQR}=1.03, 95% CI 1.02–1.04), but not for lagged exposures. No associations were observed for PM_{2.5} as a binary variable (cutpoint 35 µg/m³ for any lag or average) (Table 2). Similarly, no pattern of positive association was seen for PM_{2.5} exposure classified into quintiles (Table 3).

As continuous variables, tree pollen and weed pollen produced strong associations with all lag and average periods examined, with the 5-day averages showing the highest relative risks (RR_{IQR}=1.23, 95% CI 1.21–1.25) and (RR₁₀=1.13, 95% CI 1.12–1.14), respectively (Table 2). Both tree and weed pollen show a sustained association over time and remained positively associated for up to at least five days prior to ED visit for asthma (Fig. 2). A statistically significant association for a 10-grain increase in 5-day average grass pollen and pediatric asthma ED visits was also found (RR₁₀=1.02, 95% CI 1.01–1.03) (Table 2). For ragweed, 10-grain increases for all lag periods, were negatively associated with increases in pediatric asthma ED visits. Similar results for tree and weed pollens were observed when classified as binary

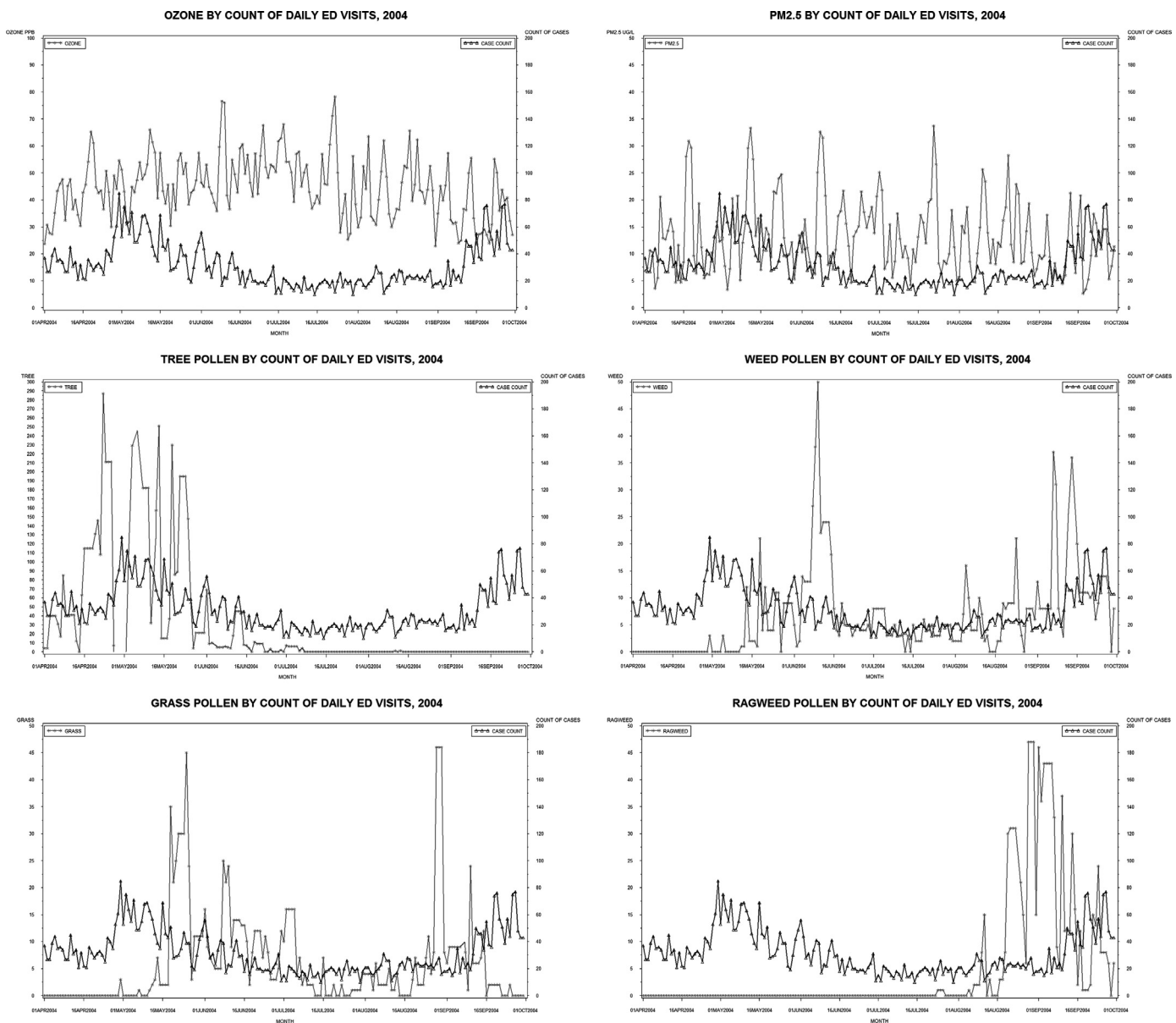


Fig. 1. Daily time-series plots of emergency department pediatric visits counts versus weighted exposure in New Jersey during April to September warm season, 2004. (Exposures were weighted by population).

variables, with the strongest associations seen for 5-day average exposures (Table 2); relative risks were $RR=1.61$ (95% CI 1.52–1.71) and ($RR=1.94$, 95% CI 1.79–2.12) for 5-day average tree and weed pollen, respectively. When classified into quintiles, tree pollen showed associations with pediatric asthma ED visits for at least the highest two quintiles compared to the lowest, across all lags and averages examined (Table 3). A statistically significant association for 5-day average tree pollen was present at the second quintile compared to the lowest quintile. The association with pediatric asthma ED visits was strongest when comparing the highest to lowest quintiles of 5-day average tree pollen ($RR=1.96$, 95% CI 1.73–2.22).

3.2. Multipollutant models

Adjusted odds ratios for the fully-adjusted multipollutant model are provided in Table 4. With all other exposures of interest controlled for, the association of same-day ozone with pediatric asthma ED visits increased slightly ($RR_{IQR}=1.08$, 95% CI 1.06–1.10)

in comparison to the single pollutant model, while the same-day association with $PM_{2.5}$ was no longer present. The positive association of tree and weed pollen remained. When we removed ozone from the multipollutant model, $PM_{2.5}$ was positively associated ($RR_{IQR}=1.04$, 95% CI 1.02–1.05). Placing all subsets of the four pollen types into the model did not change the effect magnitudes of $PM_{2.5}$ or any of the other pollen types. Tree pollen heightened the effect magnitude of ozone regardless of the inclusion of other pollutants in the model. A sensitivity analysis restricted to an area located close by the pollen monitoring station resulted in effect estimates which were generally comparable (almost identical) to the state-wide estimates.

3.3. Stratification

The fully-adjusted model was stratified by gender, race, ethnicity and SES (Table 5). Tree pollen (3-day average), has a stronger association among males ($RR_{IQR}=1.21$, 95% CI 1.20–1.23) than among females ($RR_{IQR}=1.14$, 95% CI 1.12–1.16), while 3-day

Table 2
Adjusted odds ratios for environmental exposures and pediatric emergency department visits.^{a,b}

Exposure	Continuous			Binary		
	Unit ^c	OR	95% CI	Ref	OR	95% CI
Ozone (ppb)				75		
Same day		15.53	1.05		1.14	1.02–1.27
1-day lag		15.17	1.04		1.04	0.92–1.17
2-day lag		14.97	1.00		1.01	0.90–1.14
3-day average		12.23	1.04		1.20	0.96–1.49
5-day average		10.79	1.01		0.95	0.42–2.15
PM _{2.5} (µg/m ³)				35		
Same day		8.61	1.03		1.02	0.87–1.19
1-day lag		8.50	1.01		1.00	0.85–1.17
2-day lag		8.55	0.98		1.04	0.89–1.23
3-day average		6.87	1.01		1.10	0.68–1.77
5-day average		6.25	0.97		1.09	0.68–1.76
Tree pollen				1000		
Same day		567.00	1.11		1.42	1.34–1.51
1-day lag		567.00	1.13		1.52	1.43–1.61
2-day lag		587.00	1.11		1.53	1.45–1.62
3-day average		565.67	1.17		1.60	1.51–1.69
5-day average		664.00	1.23		1.61	1.52–1.71
Grass pollen				30		
Same day		10.00	0.99		0.93	0.85–1.02
1-day lag		10.00	0.99		0.93	0.85–1.03
2-day lag		10.00	1.01		1.04	0.95–1.14
3-day average		10.00	0.99		0.92	0.85–1.01
5-day average		10.00	1.02		0.98	0.88–1.09
Weed pollen				30		
Same day		10.00	1.06		1.54	1.42–1.68
1-day lag		10.00	1.07		1.53	1.40–1.66
2-day lag		10.00	1.08		1.64	1.51–1.78
3-day average		10.00	1.10		1.72	1.58–1.86
5-day average		10.00	1.13		1.94	1.79–2.12
Ragweed				30		
Same day		10.00	0.97		0.90	0.83–0.97
1-day lag		10.00	0.96		0.82	0.77–0.89
2-day lag		10.00	0.97		0.83	0.78–0.90
3-day average		10.00	0.95		0.77	0.72–0.83
5-day average		10.00	0.94		0.83	0.77–0.89

^a Adjusted for 3-day moving average temperature, 3-day moving average relative humidity, holiday indicator and school-in-session indicator.

^b Values in bold are statistically significantly different and assessed at a significance level of 5%.

^c Interquartile range increases are the respective multiplier of the given lag period for ozone, PM_{2.5} and tree pollen in calculating the risk ratio. Due to narrow interquartile ranges, a 10-unit increase is used for grass pollen, weed pollen and ragweed.

average weed pollen has a stronger association among blacks as compared to whites or other race. Same-day ozone had a stronger association among non-Hispanics than among Hispanics, while PM_{2.5} was more strongly associated with ED asthma visits among Hispanics than among non-Hispanics.

3.4. Effect modification

There was no apparent effect modification when examining ORs and 95% CIs of high pollen as compared to low pollen at quintiles of ozone and PM_{2.5}. As the level of ozone increased there were no patterns of increasing risk among the four pollen types (Supplementary Table 1). However, examination of ORs and 95% CIs of quintile 2 through 5 versus the lowest quintile 1 for high and low categories of pollen showed that effect estimates increased with increasing levels of ozone and PM_{2.5} on high 3-day average weed days. No other patterns of effect modification were noted (Supplementary Table 2).

4. Discussion

Nationally, asthma affects one in every eleven children and one in every five children with asthma visited the emergency department in 2009 (CDC, 2012). Our study examined over 20,000 ED pediatric asthma visit days matched with two control days during the warm season from 2004 through 2007 for associations with ozone, PM_{2.5}, tree pollen, grass pollen, weed pollen and ragweed. We observed associations with ED pediatric asthma visits and same day increases in ozone. Additionally, we observed an association sustained across lags with tree and weed pollen.

We limited our study period to the warm season months of April to September that are high ozone and low asthma occurrence months, but also correspond to New Jersey's tree allergy season of March through May followed by the grass season in May and June, weed season in June through September with ragweed being released in August till the first frost (Port et al., 2006). Additionally, this seasonal restriction minimizes the influence on daily case counts of upper respiratory infections on asthma exacerbations (Peel et al., 2005). Many studies have found stronger associations between asthma and air pollution during the warm season months which may indicate that during the warm season more asthma ED visits are due to air pollution (Barnett et al., 2005; Jalaludin et al., 2008; Strickland et al., 2010; Szyszkowicz, 2008; Villeneuve et al., 2007).

Our study employed a case-crossover design that is suited for studying acute health events such as pediatric asthma ED visits. The use of bi-directional control selection and time-stratification has been shown to yield less biased results in simulation studies (Carracedo-Martinez et al., 2010). Case-crossover study design allows the examination of regionally varying exposures while controlling for non-time varying confounding. Although children may have different biological sensitivities to each of the exposures as well as different personal behaviors and daily exposure profiles these potential confounders are controlled for by the study design. Yet, without information about these factors we could not examine effect modification such as was explored for the variables gender, race, ethnicity and SES.

Inhalation of ozone at high concentration is associated with increases in the risk of asthma development, airway inflammation, and responsiveness resulting in increased risk of asthma exacerbation among subjects already affected by asthma (D'Amato and Cecchi, 2008). In addition exposure to fine particles has been shown to increase allergen sensitization, increase the risk of worsening asthma and decrease lung function (Salvi, 2007; Seaton et al., 1995). Ozone showed associations on the same day (lag0) and up to one day prior (lag1) to the pediatric asthma ED visit. This association remained in a multipollutant model adjusting for PM_{2.5} and the four pollen types. Similar findings are well documented in the literature (Jalaludin et al., 2008; Mar and Koenig, 2009; Samoli et al., 2011; Strickland et al., 2010; Villeneuve et al., 2007). The lag period for ozone with the strongest association varies across different studies, ranging from the same day lag to 5 days prior to the ED visit (Galan et al., 2003; Mar and Koenig, 2009; Szyszkowicz, 2008). It was necessary to adjust for tree pollen to get an accurate estimate of ozone association, if tree season is included in the study period. We also observed a same day positive association for PM_{2.5}; however this association was removed when ozone was controlled for in the multipollutant model. The published literature on the association of PM_{2.5} and pediatric asthma ED visits is inconsistent (Jalaludin et al., 2008; Mar and Koenig, 2009; Sheppard et al., 1999). Because the methods, study populations, exposures and lag periods examined vary widely across studies of ambient air pollution and asthma, results should be compared across studies with caution (Carracedo-Martinez et al., 2010).

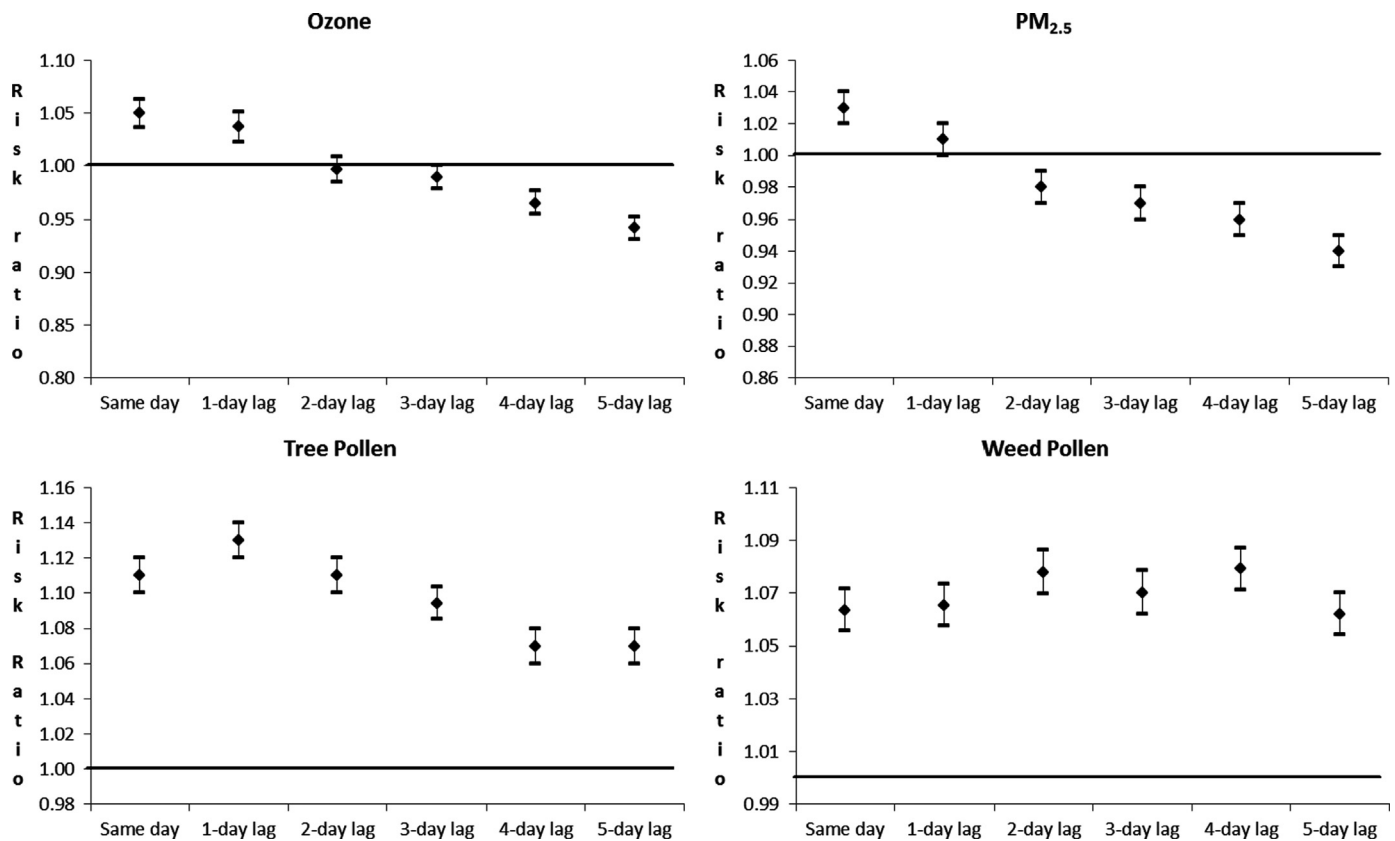


Fig. 2. Lag-specific effects for ozone, PM_{2.5}, tree pollen and weed pollen. (Lag-specific (lags 0–5) odds ratios and 95% confidence intervals corresponding to IQR increases, adjusted for 3-day moving average temperature, 3-day moving average relative humidity, holiday indicator and school-in-session indicator and interquartile range increases are the respective multiplier of the given lag period for ozone, PM_{2.5} and tree pollen in calculating the odds ratio. Due to narrow interquartile ranges, a 10-unit increase is used for weed pollen).

Table 3

Adjusted odds ratios of environmental exposures and pediatric emergency department visits in quintiles.^{a,b,c}

Exposures	Same day		1-day lag		2-day lag		3-day average		5-day average	
	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
Ozone (ppb)										
Q1 (8.38–35.83)	–	–	–	–	–	–	–	–	–	–
Q2 (35.84–42.47)	0.97	0.92–1.03	0.92	0.87–0.97	0.93	0.88–0.98	0.94	0.89–0.99	0.98	0.93–1.04
Q3 (42.48–48.18)	1.06	1.00–1.12	1.02	0.96–1.08	1.03	0.97–1.09	1.05	1.00–1.12	0.98	0.93–1.04
Q4 (48.19–55.73)	1.05	0.99–1.11	1.07	1.01–1.13	1.07	1.01–1.13	1.08	1.02–1.15	1.02	0.96–1.08
Q5 (55.74–96.12)	1.10	1.03–1.16	1.05	0.99–1.12	1.00	0.95–1.06	1.08	1.01–1.15	1.09	1.02–1.17
PM_{2.5} (μg/m³)										
Q1 (0.53–6.05)	–	–	–	–	–	–	–	–	–	–
Q2 (6.06–8.45)	1.00	0.95–1.06	0.97	0.92–1.03	0.99	0.94–1.05	1.06	1.01–1.12	0.95	0.90–1.00
Q3 (8.46–11.43)	0.99	0.94–1.04	1.00	0.95–1.06	1.02	0.96–1.07	1.00	0.94–1.05	0.90	0.85–0.95
Q4 (11.44–16.84)	1.01	0.96–1.06	0.99	0.94–1.04	0.94	0.89–0.99	0.96	0.91–1.01	0.85	0.80–0.90
Q5 (16.85–47.21)	1.05	0.99–1.11	1.01	0.95–1.07	0.96	0.91–1.01	1.04	0.98–1.10	0.91	0.85–0.97
Tree pollen										
Q1 (0–2)	–	–	–	–	–	–	–	–	–	–
Q2 (3–20)	1.06	0.98–1.13	1.06	0.99–1.14	1.07	0.99–1.15	1.03	0.95–1.10	1.12	1.04–1.21
Q3 (21–178)	1.20	1.10–1.32	1.25	1.14–1.37	1.07	0.98–1.18	1.16	1.05–1.29	1.16	1.05–1.30
Q4 (182–808)	1.29	1.17–1.42	1.28	1.16–1.41	1.17	1.07–1.29	1.25	1.12–1.39	1.23	1.10–1.38
Q5 (829–4581)	1.77	1.58–1.97	1.86	1.67–2.08	1.73	1.55–1.93	1.85	1.65–2.09	1.96	1.73–2.22

^a Adjusted for 3-day moving average temperature, 3-day moving average relative humidity, holiday indicator and school-in-session indicator.

^b Values presented for quintile ranges are based on same day estimates.

^c Values in bold are statistically significantly different and assessed at a significance level of 5%.

Pollen can induce bronchial obstruction resulting in increased risk of asthma exacerbation (Barnig and Casset, 2012; D'Amato and Cecchi, 2008). There is evidence that airway mucosal damage and impaired mucociliary clearance induced by air pollution may

facilitate the penetration and access of inhaled allergens to the cells of the immune system (D'Amato and Cecchi, 2008; D'Amato et al., 2001, 2010). Studies have found that increases in asthma exacerbations have been associated with both tree and weed

pollen (Dales et al., 2008; Im and Schneider, 2005; Tobias et al., 2003). We found only a minimal association with a 5-day average grass pollen and childhood asthma ED visits. Although there is limited literature on the specific impact of grass pollen on childhood asthma ED visits, studies have found associations with varying relevant lag periods (Erbas et al., 2005; Heguy et al., 2008). DellaValle et al. found no association with grass pollen and asthma symptoms among users of asthma maintenance medication, but found an association among non-users, although this finding was not statistically significant (DellaValle et al., 2012). Ragweed had a negative association, which has also been shown previously (Heguy et al., 2008). It is possible that a positive

association of ragweed may exist with longer lag periods, perhaps up to two weeks or longer.

The associations of pediatric asthma ED visits with tree and weed pollen were sustained over lag periods. The association of tree pollen was strongest the day prior to the ED visit, while weed pollen peaked three days prior to the ED visit. These differences in peak lag associations may be a result of the amount of grain that a patient is exposed to. Tree pollen is present in the thousands of grains per cubic meter while other allergens such as weed is commonly present between 20 and 100 grains per cubic meter and may therefore need to accumulate over days before producing respiratory impacts. Lagged associations of pollen on asthma exacerbations have been shown in other studies, but the most clinically relevant periods are inconsistent across studies (Heguy et al., 2008; Lierl and Hornung, 2003; Tobias et al., 2003). Placing all subsets of the four pollen types into the model did not change the effect magnitudes of PM_{2.5} or any of the other pollen types; however tree pollen may confound the effect of ozone. There is also some evidence that a synergistic relationship between weed pollen and ozone and PM_{2.5} may exist, whereby the increasing effect of higher exposure levels of ozone and PM_{2.5} is greatest on days with high weed pollen levels.

The association of aeroallergens on pediatric asthma ED events had been established in a variety of research contexts (Anderson et al., 2001; Barnig and Casset, 2012; Cakmak et al., 2012; Dales et al., 2008; Tobias et al., 2003). However, comparing the impact of aeroallergens across studies is challenging due to the availability of pollen data and the variability of plant life in different regions. Some studies may have a single measure of pollen while others are able to differentiate a variety of types (Darrow et al., 2012; DellaValle et al., 2012; Galan et al., 2003; Newhouse and Levetin, 2004; Tobias et al., 2003). Still other studies presented information concerning pollen as a confounder; not as a main exposure of interest (Babin et al., 2007; Galan et al., 2003; Strickland et al., 2010).

Table 4

Adjusted odds ratios and 95% confidence intervals for multi-pollutant model.^{a,b}

Exposures and covariates	Unit ^c	OR	95% CI	
Ozone (ppb) same day	15.53	1.08	1.06	1.10
PM _{2.5} (μg/m ³) same day	8.61	0.99	0.98	1.01
Tree pollen 3-day average	566.00	1.19	1.17	1.20
Grass pollen 3-day average	10.00	1.00	0.99	1.01
Weed pollen 3-day average	10.00	1.10	1.09	1.11
Ragweed 3-day average	10.00	0.96	0.95	0.97
Temperature 3-day average	7.90	0.89	0.87	0.91
Humidity 3-day average	21.00	0.96	0.95	0.98
School-in-session	–	1.05	0.96	1.15
Holiday	–	1.15	1.05	1.25

^a Adjusted for 3-day moving average temperature, 3-day moving average relative humidity, holiday indicator and school-in-session indicator, ozone same day, PM_{2.5} same day, tree pollen 3-day average, grass pollen 3-day average, weed pollen 3-day average, ragweed 3-day average.

^b Values in bold are statistically significantly different and assessed at a significance level of 5%.

^c Interquartile range increases are the respective multiplier of the given lag period for ozone, PM_{2.5} and tree pollen in calculating the risk ratio. Due to narrow interquartile ranges, a 10-unit increase is used for grass pollen, weed pollen and ragweed.

Table 5

Adjusted odds ratios and 95% confidence intervals by sex, race, ethnicity and socioeconomic status.^{a,b,c,d}

Characteristics	Exposure											
	Ozone (ppb) (same day) IQR = 15.53		PM _{2.5} (μg/m ³) (same day) IQR = 8.61		Tree pollen (3-day average) IQR = 565.67		Grass pollen (3-day average) Unit = 10		Weed pollen (3-day average) Unit = 10		Ragweed (3-day average) Unit = 10	
	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
Gender												
Male	1.10	1.07–1.12	0.99	0.97–1.01	1.21	1.20–1.23	1.00	0.99–1.01	1.10	1.09–1.11	0.96	0.95–0.97
Female	1.06	1.03–1.09	0.99	0.97–1.02	1.14	1.12–1.16	1.00	0.98–1.02	1.11	1.09–1.13	0.96	0.95–0.98
Race												
White	1.09	1.06–1.11	1.01	0.99–1.03	1.18	1.16–1.20	0.99	0.98–1.01	1.09	1.08–1.11	0.97	0.96–0.98
Black	1.06	1.04–1.09	1.00	0.98–1.03	1.21	1.19–1.23	1.01	0.99–1.02	1.14	1.12–1.15	0.96	0.95–0.97
Other	1.10	1.06–1.15	0.94	0.90–0.97	1.15	1.12–1.18	0.99	0.97–1.02	1.07	1.04–1.09	0.95	0.93–0.97
Ethnicity												
Non-Hispanic	1.10	1.08–1.13	0.97	0.95–0.99	1.19	1.18–1.21	1.00	0.99–1.01	1.12	1.10–1.13	0.96	0.96–0.97
Hispanic	1.01	0.97–1.05	1.06	1.03–1.10	1.16	1.14–1.19	0.99	0.96–1.01	1.08	1.06–1.10	0.96	0.94–0.97
Socioeconomic status												
High	1.07	1.04–1.11	0.99	0.96–1.02	1.18	1.16–1.20	1.00	0.98–1.02	1.13	1.11–1.15	0.97	0.96–0.98
Moderate	1.08	1.05–1.11	0.98	0.96–1.01	1.19	1.18–1.21	1.01	0.99–1.02	1.09	1.08–1.11	0.96	0.95–0.97
Low	1.10	1.07–1.13	1.00	0.98–1.03	1.18	1.16–1.21	0.99	0.97–1.01	1.10	1.08–1.12	0.95	0.94–0.97

^a Adjusted for 3-day moving average temperature, 3-day moving average relative humidity, holiday indicator and school-in-session indicator, ozone same day, PM_{2.5} same day, tree pollen 3-day average, grass pollen 3-day average, weed pollen 3-day average, ragweed 3-day average.

^b Interquartile range increases are the respective multiplier of the given lag period for ozone, PM_{2.5} and tree pollen in calculating the risk ratio. Due to narrow interquartile ranges, a 10-unit increase is used for grass pollen, weed pollen and ragweed.

^c Socioeconomic status is categorized into high < 5% living in poverty, moderate 5–20% living in poverty, and low > 20% living in poverty

^d Values in bold are statistically significantly different and assessed at a significance level of 5%.

Our study relied on pollen from one of two monitoring stations in the state of New Jersey (AAAAI, 2012). This one station served as representative for the whole state (Dvorin et al., 2001; Im and Schneider, 2005). If more geographically diverse stations were available there would be more confidence in daily exposure assessment since not every child throughout the state would be experiencing an identical pollen exposure profile. However, as New Jersey is a small state, 70 km in width and 170 km in length, with little variability in mean temperature especially in the urban population hubs, and with little difference in exposure to sunlight, pollen peak differences would be minimal (Office of the NJ State Climatologist, 2013). Additionally, the control of temperature in all analyses should minimize the impact of pollen misclassification, as differences in pollen peaks may be associated with temperature.

The case-crossover design creates a ratio of case day versus control day exposure to estimate the relative difference in exposures. If pollen exposures are consistently over- or under-estimated proportionately, effect estimates would be unbiased by pollen exposure misclassification. However this may not be the case during times closest to and during pollen peak periods. Examining 3-day and 5-day moving averages of pollen values and categorizing values into high vs. low days should limit the impact of any pollen misclassification on effect estimates.

Different categorizations in calculating effect measures were explored. We examined relative risks using IQR or 10 grain increases and also a high vs. low binary categorization based on existing standards. Where sufficient data variability was available – ozone, PM_{2.5} and tree pollen – we examined effect estimates using quintiles. Positive associations between ozone and pediatric asthma ED visits were seen below the 75 ppb standard, suggesting that our understanding of respiratory health risk and ozone levels may need to be re-examined. Also a high association with tree pollen and pediatric asthma ED visits starting from a low quintile range and a subsequent dose-response was observed.

The burden of pediatric asthma is disproportionately distributed by gender, race, ethnicity and SES (Bacon et al., 2009; Canino et al., 2009; Gupta et al., 2009; Hackbarth et al., 2011; Liu and Pearlman, 2009). Race and ethnicity have been shown to modify the associations of nitrogen dioxide and childhood asthma hospitalizations suggesting that exposure to particulate matter and respiratory outcomes may be affected by race and ethnicity (Grineski et al., 2010; Nachman and Parker, 2012). When we stratified by gender, race, ethnicity and SES; ozone had a larger effect estimate among non-Hispanics than Hispanics; however Hispanics may be more impacted by PM_{2.5}. Stratification indicated that ozone and PM_{2.5} may have a differential impact of pediatric ED asthma visits by race and ethnicity, yet the mechanisms of these impacts need to be further examined. None of the exposures resulted in different effect measures when stratified on our measure of SES. A study of the association of air-quality and pediatric asthma-related ED visits did find a real increase in relative risk among children living in a zip code with a high percentage of children living below the poverty level (Babin et al., 2007). Our census tract, area-based measure of SES – percentage of population living below the poverty level – may not be capturing a vulnerable risk group.

5. Conclusions

In our large, state-wide, study of the associations of pediatric asthma ED visits and ozone, PM_{2.5}, tree, grass, weed pollen and ragweed, we used a time-stratified case-crossover analysis with bi-directional control sampling. We found positive associations with ozone, PM_{2.5}, tree pollen and weed pollen. Ragweed had a negative association, while the association with grass pollen was

minimal. The most clinically relevant days for ozone and PM_{2.5} were found to be the day of the ED visits, while the association with tree and weed pollen appear to be sustained across lags with an effect 5 days prior to the asthma ED event.

New Jersey's small geographic size and high population density create an environment in which populated areas are exposed to local and regional sources of pollution. (Lioy and Georgopoulos, 2011). Efforts to reduce the impact of harmful air pollutants in New Jersey have been successful, yet the impact of ozone and PM_{2.5} could be further reduced with tightened standards (Lioy and Georgopoulos, 2011). The association between pollen levels and allergic respiratory diseases, such as asthma are important as levels of airborne allergenic pollen may be increasing (Ziello et al., 2012). Pediatric asthma risk is complex and multifactorial. The health and economic burden of pediatric asthma underscores the importance of understanding the complex risk patterns and factors (Bahadori et al., 2009).

Competing interest

The authors declared that they have no competing interests. All authors have made substantive contributions to this study. JG assisted in the development of the protocol, performed data analysis and drafted the manuscript. LB provided pollen data and substantively edited the manuscript. JF conceptualized and substantively designed the protocol, assisted with data analysis and edited the manuscript. All authors have read and approved this version of the manuscript.

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Appendix A. Supplementary material

Supplementary data associated with this article can be found in the online version at <http://dx.doi.org/10.1016/j.envres.2014.03.035>.

References

- AAAAI (2012). National Allergy Bureau. Retrieved 2012, 2012, from <http://www.aaaai.org/global/nab-pollen-counts.aspx>.
- Anderson, W., et al., 2001. Asthma admissions and thunderstorms: a study of pollen, fungal spores, rainfall, and ozone. *QJM* 94, 429–433.
- Babin, S.M., et al., 2007. Pediatric patient asthma-related emergency department visits and admissions in Washington, DC, from 2001 to 2004, and associations with air quality, socio-economic status and age group. *Environ. Health* 6, 9.
- Bacon, S.L., et al., 2009. Individual-level socioeconomic status is associated with worse asthma morbidity in patients with asthma. *Respir. Res.* 10, 125.
- Bahadori, K., et al., 2009. Economic burden of asthma: a systematic review. *BMC Pulm. Med.* 9, 24.
- Barnett, A.G., et al., 2005. Air pollution and child respiratory health: a case-crossover study in Australia and New Zealand. *Am. J. Respir. Crit. Care Med.* 171, 1272–1278.
- Barnig, C., Casset, A., 2012. Respiratory allergens and asthma exacerbation. *Rev. Mal. Respir.* 29, 810–819.
- Bielory, L., et al., 2012. Climate change and allergic disease. *Curr. Allergy Asthma Rep.* 12, 485–494.
- Blando, J., et al., 2012. Anthropogenic climate change and allergic diseases. *Atmosphere* 3, 200–212.

- Boutin-Forzano, S., et al., 2004. Visits to the emergency room for asthma attacks and short-term variations in air pollution. A case-crossover study. *Respiration* 71, 134–137.
- Cakmak, S., et al., 2012. Does air pollution increase the effect of aeroallergens on hospitalization for asthma? *J. Allergy Clin. Immunol.* 129, 228–231.
- Canino, G., et al., 2009. Addressing asthma health disparities: a multilevel challenge. *J. Allergy Clin. Immunol.* 123, 1209–1219.
- Carracedo-Martinez, E., et al., 2010. Case-crossover analysis of air pollution health effects: a systematic review of methodology and application. *Environ. Health Perspect.* 118, 1173–1182.
- Centers for Disease Control (CDC), 2012. Asthma's impact on the nation. National Asthma Control Program (NACP) Atlanta.
- Dales, R.E., et al., 2008. Tree pollen and hospitalization for asthma in urban Canada. *Int. Arch. Allergy Immunol.* 146, 241–247.
- Dapul-Hidalgo, G., Bielory, L., 2012. Climate change and allergic diseases. *Ann. Allergy Asthma Immunol.* 109, 166–172.
- Darrow, L.A., et al., 2012. Ambient pollen concentrations and emergency department visits for asthma and wheeze. *J. Allergy Clin. Immunol.* 130, 630–638 (e4).
- DellaValle, C.T., et al., 2012. Effects of ambient pollen concentrations on frequency and severity of asthma symptoms among asthmatic children. *Epidemiology* 23, 55–63.
- Dvorin, D.J., et al., 2001. A comparative, volumetric survey of airborne pollen in Philadelphia, Pennsylvania (1991–1997) and Cherry Hill, New Jersey (1995–1997). *Ann. Allergy Asthma Immunol.* 87, 394–404.
- D'Amato, G., Cecchi, L., 2008. Effects of climate change on environmental factors in respiratory allergic diseases. *Clin. Exp. Allergy* 38, 1264–1274.
- D'Amato, G., et al., 2001. The role of outdoor air pollution and climatic changes on the rising trends in respiratory allergy. *Respir. Med.* 95, 606–611.
- D'Amato, G., et al., 2010. Urban air pollution and climate change as environmental risk factors of respiratory allergy: an update. *J. Investig. Allergol. Clin. Immunol.* 20, 95–102 (quiz following 102).
- Eaton, D.K., et al., 2010. Youth risk behavior surveillance – United States, 2009. *MMWR Surveill. Summ.* 59, 1–142.
- Erbas, B., et al., 2005. Air pollution and childhood asthma emergency hospital admissions: estimating intra-city regional variations. *Int. J. Environ. Health Res.* 15, 11–20.
- Fung, K.Y., et al., 2003. Comparison of time series and case-crossover analyses of air pollution and hospital admission data. *Int. J. Epidemiol.* 32, 1064–1070.
- Galan, I., et al., 2003. Short-term effects of air pollution on daily asthma emergency room admissions. *Eur. Respir. J.* 22, 802–808.
- Giovannini, M., et al., 2010. Hospital admissions for respiratory conditions in children and outdoor air pollution in Southwest Milan, Italy. *Acta Paediatr.* 99, 1180–1185.
- Grineski, S.E., et al., 2010. Children's asthma hospitalizations and relative risk due to nitrogen dioxide (NO₂): effect modification by race, ethnicity, and insurance status. *Environ. Res.* 110, 178–188.
- Gupta, R.S., et al., 2009. Eliminating asthma disparities: is there evidence of progress? *Curr. Opin. Pulm. Med.* 15, 72–78.
- Hackbarth, A.D., et al., 2011. Racial and ethnic disparities in hospital care resulting from air pollution in excess of federal standards. *Soc. Sci. Med.* 73, 1163–1168.
- Heguy, L., et al., 2008. Associations between grass and weed pollen and emergency department visits for asthma among children in Montreal. *Environ. Res.* 106, 203–211.
- Im, W., Schneider, D., 2005. Effect of weed pollen on children's hospital admissions for asthma during the fall season. *Arch. Environ. Occup. Health* 60, 257–265.
- Jalaludin, B., et al., 2008. Air pollution and ED visits for asthma in Australian children: a case-crossover analysis. *Int. Arch. Occup. Environ. Health* 81, 967–974.
- Ji, M., et al., 2011. Meta-analysis of the association between short-term exposure to ambient ozone and respiratory hospital admissions. *Environ. Res. Lett.*, 6.
- Johnson, P.R., Graham, J.J., 2005. Fine particulate matter national ambient air quality standards: public health impact on populations in the northeastern United States. *Environ. Health Perspect.* 113, 1140–1147.
- Johnston, S.L., et al., 1996. The relationship between upper respiratory infections and hospital admissions for asthma: a time-trend analysis. *Am. J. Respir. Crit. Care Med.* 154, 654–660.
- Li, S., et al., 2011. Association of daily asthma emergency department visits and hospital admissions with ambient air pollutants among the pediatric Medicaid population in Detroit: time-series and time-stratified case-crossover analyses with threshold effects. *Environ. Res.*
- Lierl, M.B., Hornung, R.W., 2003. Relationship of outdoor air quality to pediatric asthma exacerbations. *Ann. Allergy Asthma Immunol.* 90, 28–33.
- Lioy, P.J., Georgopoulos, P.G., 2011. New Jersey: a case study of the reduction in urban and suburban air pollution from the 1950s to 2010. *Environ. Health Perspect.*
- Liu, S.Y., Pearlman, D.N., 2009. Hospital readmissions for childhood asthma: the role of individual and neighborhood factors. *Public Health Rep.* 124, 65–78.
- Mahbub, P., et al., 2011. Prediction model of the buildup of volatile organic compounds on urban roads. *Environ. Sci. Technol.* 45, 4453–4459.
- Mar, T.F., Koenig, J.Q., 2009. Relationship between visits to emergency departments for asthma and ozone exposure in greater Seattle, Washington. *Ann. Allergy Asthma Immunol.* 103, 474–479.
- McMillan, N.J., et al., 2010. Combining numerical model output and particulate data using Bayesian space-time modeling. *Environmetrics* 21, 48–65.
- Mohr, L.B., et al., 2008. Influence of season and temperature on the relationship of elemental carbon air pollution to pediatric asthma emergency room visits. *J. Asthma* 45, 936–943.
- Moodley, K.G., et al., 2011. Passive monitoring of nitrogen dioxide in urban air: a case study of Durban metropolis, South Africa. *J. Environ. Manage.* 92, 2145–2150.
- NJ DEP, 2013a. Attainment area status. Bureau of Air Quality Planning, Trenton, NJ.
- NJ DEP, 2013b. Welcome to New Jersey's Air Monitoring Web Site!, Trenton, NJ, USA.
- Nachman, K.E., Parker, J.D., 2012. Exposures to fine particulate air pollution and respiratory outcomes in adults using two national datasets: a cross-sectional study. *Environ. Health* 11, 25.
- Navidi, W., 1998. Bidirectional case-crossover designs for exposures with time trends. *Biometrics* 54, 596–605.
- Navidi, W., et al., 1999. Statistical methods for epidemiologic studies of the health effects of air pollution. *Res. Rep. Health Eff. Inst.* 1–50 (discussion 51–6).
- New Jersey Department of Health and Senior Services, 2013. New Jersey Asthma Strategic Plan 2008–2013, Trenton, NJ.
- Newhouse, C.P., Levett, E., 2004. Correlation of environmental factors with asthma and rhinitis symptoms in Tulsa, OK. *Ann. Allergy Asthma Immunol.* 92, 356–366.
- Office of the NJ State Climatologist, 2013. Monthly Climate Maps, Piscataway, NJ.
- PHASE, 2007. Technical Background Report: Case-Crossover Analysis of Acute Health Effects and Ambient Air Quality for Environmental Public Health Tracking. NYSDOH, pp. 1–65.
- Peel, J.L., et al., 2005. Ambient air pollution and respiratory emergency department visits. *Epidemiology* 16, 164–174.
- Pereira, G., et al., 2009. Residential traffic exposure and children's emergency department presentation for asthma: a spatial study. *Int. J. Health Geogr.* 8, 63.
- Pereira, G., et al., 2010. A case-crossover analysis of traffic-related air pollution and emergency department presentations for asthma in Perth, Western Australia. *Med. J. Aust.* 193, 511–514.
- Port, A., et al., 2006. Aeroallergen prevalence in the northern New Jersey–New York City metropolitan area: a 15-year summary. *Ann. Allergy Asthma Immunol.* 96, 687–691.
- Riedl, M., Diaz-Sanchez, D., 2005. Biology of diesel exhaust effects on respiratory function. *J. Allergy Clin. Immunol.* 115, 221–228 (quiz 229).
- Salvi, S., 2007. Health effects of ambient air pollution in children. *Paediatr. Respir. Rev.* 8, 275–280.
- Samoli, E., et al., 2011. Acute effects of air pollution on pediatric asthma exacerbation: evidence of association and effect modification. *Environ. Res.* 111, 418–424.
- Seaton, A., et al., 1995. Particulate air pollution and acute health effects. *Lancet* 345, 176–178.
- Sheppard, L., et al., 1999. Effects of ambient air pollution on nonelderly asthma hospital admissions in Seattle, Washington, 1987–1994. *Epidemiology* 10, 23–30.
- Silverman, R.A., Ito, K., 2010. Age-related association of fine particles and ozone with severe acute asthma in New York City. *J. Allergy Clin. Immunol.* 125, 367–373 (e5).
- Statistical Analysis Software (SAS) Institute Inc., 2002–2008, Cary, NC.
- Strickland, M.J., et al., 2010. Short-term associations between ambient air pollutants and pediatric asthma emergency department visits. *Am. J. Respir. Crit. Care Med.* 182, 307–316.
- Szyszkowicz, M., 2008. Ambient air pollution and daily emergency department visits for asthma in Edmonton, Canada. *Int. J. Occup. Med. Environ. Health* 21, 25–30.
- Tobias, A., et al., 2003. Short term effects of airborne pollen concentrations on asthma epidemic. *Thorax* 58, 708–710.
- Tolbert, P.E., et al., 2000. Air quality and pediatric emergency room visits for asthma in Atlanta, Georgia, USA. *Am. J. Epidemiol.* 151, 798–810.
- US EPA, 2011. National Ambient Air Quality Standards (NAAQS), Washington, DC, USA.
- US EPA, 2012. Fused Discrete Air Quality Surfaces, Washington, DC, USA.
- Villeneuve, P.J., et al., 2007. Outdoor air pollution and emergency department visits for asthma among children and adults: a case-crossover study in northern Alberta, Canada. *Environ. Health* 6, 40.
- Zeka, A., et al., 2005. Short term effects of particulate matter on cause specific mortality: effects of lags and modification by city characteristics. *Occup. Environ. Med.* 62, 718–725.
- Ziello, C., et al., 2012. Changes to airborne pollen counts across Europe. *PLoS One* 7, e34076.
- Ziska, L., et al., 2011. Recent warming by latitude associated with increased length of ragweed pollen season in central North America. *Proc. Natl. Acad. Sci. USA* 108, 4248–4251.

Supplemental Table 1. OR and 95% CI of high versus low pollen categories for each quintile of ozone and PM_{2.5}

	Tree 3-day (Ref=1000)		Grass 3-day (Ref=30)		Weed 3-day (Ref=30)		Ragweed 3-day (Ref=30)	
	OR	95% CI	OR	95%CI	OR	95% CI	OR	95% CI
Ozone Same-day ^{ppb}								
Q1 (8.38 -35.83)	0.87	0.30-2.55	0.65	0.54-0.78	1.78	1.48-2.15	1.28	0.73-2.23
Q2 (35.84 - 42.47)	2.95	2.34-3.71	1.10	0.65-1.87	2.50	1.59-3.93	1.09	0.65-1.82
Q3 (42.48 - 48.18)	1.90	1.53-2.36	1.05	0.72-1.54	1.03	0.54-1.94	1.06	0.75-1.49
Q4 (48.19 - 55.73)	1.45	1.13-1.85	1.16	0.59-2.29	1.16	0.56-2.42	0.81	0.55-1.17
Q5 (55.74 - 96.12)	1.30	0.84-2.03	0.60	0.31-1.16	1.39	0.74-2.62	0.62	0.51-0.74
PM _{2.5} Same Day ^{µg/m3}								
Q1 (0.53 - 6.05)	2.13	1.75-2.61	0.81	0.55-1.19	1.08	0.71-1.64	0.43	0.26-0.69
Q2 (6.06 - 8.45)	1.67	1.32-2.11	0.75	0.53-1.04	1.11	0.74-1.68	0.78	0.58-1.07
Q3 (8.46 - 11.43)	1.44	1.12-1.85	0.96	0.66-1.38	1.68	1.18-2.39	0.73	0.53-1.01
Q4 (11.44 - 16.84)	1.64	1.17-2.31	0.52	0.35-0.77	1.68	1.10-2.56	0.83	0.53-1.30
Q5 (16.85 - 47.21)	0.81	0.35-1.90	0.78	0.59-1.03	1.03	0.76-1.39	0.56	0.35-0.88

Supplemental Table 2. OR and 95% CI of each quintile of ozone and PM_{2.5} for high and low categories of pollen

	Tree 3-day				Grass 3-day				Weed 3-day				Ragweed 3-day			
	High		Low		High		Low		High		Low		High		Low	
	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
Ozone Same-day ^{ppb}																
Q1 (8.38 -35.83)	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Q2 (35.84 - 42.47)	0.86	0.71-1.05	0.96	0.90-1.02	0.85	0.30-2.42	0.97	0.92-1.02	1.24	0.81-1.91	0.92	0.87-0.98	0.99	0.77-1.26	0.97	0.91-1.03
Q3 (42.48 - 48.18)	0.85	0.70-1.05	1.11	1.04-1.19	0.71	0.18-2.84	1.07	1.01-1.13	2.64	1.76-3.96	0.98	0.93-1.05	1.07	0.81-1.40	1.07	1.00-1.13
Q4 (48.19 - 55.73)	0.78	0.62-0.98	1.11	1.04-1.19	0.65	0.15-2.86	1.06	1.00-1.12	2.70	1.74-4.19	0.98	0.92-1.05	0.80	0.60-1.06	1.06	1.00-1.13
Q5 (55.74 - 96.12)	0.90	0.66-1.23	1.19	1.11-1.27	0.72	0.23-2.25	1.10	1.03-1.17	3.81	2.41-6.02	1.06	0.99-1.13	0.96	0.72-1.28	1.10	1.03-1.18
PM _{2.5} Same Day ^{µg/m³}																
Q1 (0.53 - 6.05)	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Q2 (6.06 - 8.45)	0.90	0.79-1.01	1.01	0.95-1.07	0.53	0.21-1.31	1.01	0.96-1.06	1.57	1.14-2.17	0.97	0.92-1.02	1.14	0.88-1.47	1.00	0.94-1.05
Q3 (8.46 - 11.43)	0.92	0.81-1.05	1.01	0.95-1.07	0.54	0.21-1.43	1.02	0.97-1.08	1.53	1.11-2.12	0.94	0.89-1.00	1.01	0.79-1.31	1.00	0.95-1.06
Q4 (11.44 - 16.84)	1.00	0.86-1.17	1.01	0.95-1.07	0.64	0.23-1.77	1.03	0.98-1.09	2.32	1.61-3.34	0.97	0.92-1.03	1.01	0.76-1.34	1.01	0.96-1.07
Q5 (16.85 - 47.21)	1.04	0.71-1.51	1.06	0.99-1.12	0.62	0.19-2.04	1.06	1.00-1.12	2.51	1.73-3.64	1.02	0.96-1.08	1.42	1.06-1.89	1.04	0.98-1.11