GAVIN PUBLISHERS

Archives of Epidemiology

DePerrior S, et al. Arch Epidemiol 5: 148.
DOI: 10.29011/2577-2252.100048

Research Article

The Relationship between Pollen, Air Pollution and Asthma Exacerbations in Children in Allegheny County, Pennsylvania: A Case-Crossover Analysis

Sarah DePerrior[1], Judith R Rager[1], Deborah Gentile[2] Evelyn O Talbott[1]

[1]Department of Epidemiology, University of Pittsburgh Graduate School of Public Health, USA

[2]Allergy and Asthma Wellness Centers, USA

[*]**Corresponding author:** Evelyn O Talbott, Department of Epidemiology University of Pittsburgh Graduate School of Public Health, USA

Citation: DePerrior S, Rager JR, Talbott EO, Gentile D, (2021) The Relationship between Pollen, Air Pollution, and Asthma Exacerbations in Children in Allegheny County, Pennsylvania: A Case-Crossover Analysis. Arch Epidemiol 5: 148. DOI: 10.29011/2577-2252.100048

Received Date: 09 December, 2020; **Accepted Date:** 08 January, 2021; **Published Date:** 13 January, 2021

Abstract

Background: Exposures to outdoor air pollutants have been linked to asthma exacerbations in children. Few studies have examined the association between exposure to outdoor pollens and asthma outcomes in the context of its association with multiple air pollutants.

Methods: Time-stratified case-crossover design with conditional logistic regression was used to study the short-term effects of three major pollens (grass, tree, and weed) and four criteria pollutants (PM 2.5, Ozone, SO2 and NO2) on asthma Emergency Department (ED) visits in children age 5-17 reported in Allegheny County, Pennsylvania from April to October 2003-2011. Multivariable regression was conducted to investigate the effects of pollen and pollutant levels on the day of the ED visit, lags of day 1 to 5 and moving averages of day 0-2 and day 0-5.

Results: A total of 8,711 asthma ED visits were reported during the study period. In multivariable models, tree and weed pollen were significant positive predictors of asthma ED visits across multiple lags when controlling for temperature and air pollutants. Strongest effects were reported for the 3-day moving average of tree pollen (odds ratio, OR=1.02, 95% CI 1.01-1.02) and the 6-day moving average of weed pollen (OR=1.04, 95% CI 1.03-1.06). PM 2.5 and NO2 were significantly positively associated with ED visits across multiple lags, whereas SO2 was negatively associated with ED visits at several lags.

Discussion: Higher tree and weed pollen levels were associated with increased odds of asthma ED visits in children, independent of air pollution levels. Implementing methods to control allergen exposure during particular seasons may prevent adverse asthma outcomes.

Keywords: Air pollution; Asthma exacerbations; Children; Pennsylvania; Pollen

Abbreviations: ED: Emergency Department; PM: Particulate Matter; O_3: Ozone; SO_2: Sulfur Dioxide; NO_2: Nitrogen Dioxide; LUR: Land Use Regression; NLDAS: North America Land Data Assimilation System; C-CAT: Case-crossover Analysis Tool; OR: Odds Ratio; CI: Confidence Interval

Introduction

Asthma is one of the most common chronic diseases among children worldwide. It affects more than 6 million children with a prevalence of 9.4% in the United States [1]. A total of 13.8 million missed days of school were attributed to asthma in 2013, with an average of 2.6 days per child with asthma [2]. Between 2008 and 2013, the annual total cost of asthma was estimated to be over $81.9 billion in the U.S [3]. In the year of 2009, asthma exacerbations resulted in 479,000 hospitalizations and 1.9 million Emergency Department (ED) visits [4]. Common triggers for asthma exacerbation includes bacterial and viral infections, dust mites, exposure to tobacco smoke, outdoor pollens and air pollutants [5]. Air pollutants, including Particulate Matter (PM), Ozone (O_3), Sulfur dioxide (SO_2) and Nitrogen dioxide (NO_2) contribute to asthma exacerbations by affecting inflammatory pathways and immune response, remodeling airways, increasing bronchial hyperresponsiveness and oxidative airway damage [6,7].

Independent to air pollutants, tree and weed pollen appears to be the most significant predictors for ED visit due to asthma in the U.S. While grass or weed pollen was found to be associated with ED visit in Australia or Canada, suggesting regional differences should be taking into account when studying pollen exposures and asthma outcomes [8-11]. Children are at higher risk for the negative effects of outdoor pollens or air pollutants because they spend greater time outside, have developing lungs and exchange a greater volume of air than adults relative to body size [5,7,12-14]. This study aimed to examine the associations between three major outdoor pollens (grass, tree, and weed) and ED visits due to asthma in children ages 5-17 residing in Alleghany County, Pennsylvania. Furthermore, we included four major criteria pollutants (PM 2.5, ozone, SO_2 and NO_2) to examine potential confounding and effect modification between pollens and air pollutants.

Materials and Methods

Asthma Emergency Department Data

Data on Asthma ED visits were available for hospitals and hospital systems in Allegheny County, Pennsylvania for 2003-2011. Asthma ED visits were defined by primary discharge diagnosis of asthma (International Classification of Diseases, 9th revision, code 493). For the present analysis, data were restricted to children aged 5-17 who had residential zip codes in Allegheny County.

Pollen Data

Daily pollen counts for grass, tree and weed were obtained from the central pollen monitor in Allegheny County, located on the roof of Allegheny General Hospital in the North side of the City of Pittsburgh during the study period. The station was part of the National Allergy Bureau monitoring network [15]. Pollen was sampled using a Burkard Spore Trap, a volumetric air sampler that is commonly used in allergy research [16]. Daily pollen counts were in units of grains/m^3. During the study timeframe of 2003 to 2011, complete pollen counts were available for the months April through October from 2004 to 2011. For 2003, complete data was available for April through September only. Thus, daily pollen data used in this analysis comprises April 1st through September 30th 2003 and April 1st through October 31st 2004 through 2011. For days with missing pollen values, the previous available value was carried forward if there were three or fewer days with missing values. In the rare cases where there were more than three consecutive days of missing values, the remining days would be given the value from the next available day [17,18].

Air Pollution and Meteorological Data

Daily exposure estimates by zip code for the air pollutants used in this analysis (PM 2.5, O_3 [maximum 8-hour concentrations], SO_2 and NO_2) from 2003-2011 were developed in previous research [19]. In brief, an enhanced form of Land Use Regression (LUR) and space-time co-kriging with satellite remote sensing of aerosol optical depth was used to estimate the concentrations [19]. Meteorological data were obtained from the CDC Wonder North America Land Data Assimilation System (NLDAS) Daily Air Temperatures and Heat Index (1979-2011) data request website. Daily values of maximum air temperature and maximum heat index averaged over monitoring stations for Allegheny County from 2003-2011 were used. Maximum heat index was available for days with air temperature greater than 80ºF. To account for the effects of humidity, we used a maximum apparent temperature value, which was defined as the maximum heat index when available and otherwise as average maximum temperature.

Case-Crossover Study Design

Time-stratified case-crossover analysis with conditional logistic regression was used to examine the short-term relationship between daily concentrations pollens, air pollutants and asthma ED visits. Analysis was conducted using the case-crossover Analysis Tool (C-CAT) from Apex Epidemiology Research and the New York State Department of Health [20]. C-CAT is designed for use with SAS program and creates code to conduct time-stratified case-crossover analysis. In this study, we used 28-day strata and referent periods of 7,14 and 21 days either before or after each stratum to account for day-of-the-week effects [19,21]. Thus, within one strata of 28 days, there would be three referent, or control, days for comparison. To ensure independence of events, we included a washout period of 7 days that any repeat visits for an individual over a 7-day period would be removed.

Statistical Analysis

Time series plots with 7-day moving average were used to visualize the seasonality of different pollens. Pearson correlation coefficient was used to estimate correlations between outdoor levels of pollens and air pollutants. Lagged variables for each pollen and air pollutant were created. We conducted analyses using lags of 0 (day of) through 5, as well as moving average lags over 3 days (lag 0-2) and over 6 days (lag 0-5). The averages represent cumulative exposures, including exposures on the day of the visit, as well as the preceding days. Conditional logistic regression under time-stratified case-crossover design was used to estimate the Odds Ratios (OR) of asthma ED visit and associated 95%Confidence Intervals (CI) for exposure to pollens and air pollutants. All multivariable models included apparent maximum temperature, all three pollens and all four environmental pollutants across each of the lags. We then tested the interaction terms of each pollen and air pollutant (in the format pollen*air pollutant). In order to assess whether the impacts of outdoor pollen levels differ based on sociodemographic factors, separate multivariable models were used to analyze 3-day average (average of lags 0-2) exposure stratified by gender, race/ethnicity, age group and zip code-level of poverty. Poverty data was obtained from the US Census American

Fact finder website [22] and was defined by percent of individuals living below the poverty level in each zip code: low poverty as less than 5% of individuals in poverty; moderate poverty as 5-20% of individuals living in poverty and high poverty as more than 20% of individuals living in poverty [17] Sensitivity analysis only included zip codes within the city of Pittsburgh was conducted to determine whether the use of the single pollen monitor in the city of Pittsburgh would be appropriate for county-wide analysis.

Results

A total of 8,966 asthma ED visits in children ages 5-17 were identified in April-September 2003 and April-October from 2004 to 2011. After excluding 255 recurrent events within 7 days, 8,711 asthma ED visits were included in the analysis (Table 1). Among children included in the study, 53.6% were male, 67.0% were Black and the youngest age group 5-9 years, comprised the greatest proportion of ED visits (43.5%). The majority of children were from moderate-poverty zip codes (72.1%). September had the greatest number of ED visits (22.1%), followed by October (18.8%) and May (18.3%). Distributions of pollens, air pollutants and apparent maximum temperature are shown in Table 2. The levels of tree pollen were much higher in magnitude than the levels of grass or weed pollen, with an average of 124 grains/m^3 and a maximum value of 4,152 grains/m^3. Correlations between individual pollens and air pollutants or maximum temperature were low ($r < 0.20$ for all instances, Supplemental Table 1). The 7-day moving average for pollen counts between April and October, 2005 are shown in Figure 1. Tree pollen peaked the earliest, from April through May, followed by grass around June. Weed pollen had two peaks, a smaller peak in June and then a larger one in mid-August through October. Asthma ED visits peaked in spring and fall, with lower incidence throughout the summer months (data not shown). Results for exposure to a single pollen or pollutant adjusting for 3-day average apparent maximum temperature by different lag periods and asthma ED visit are shown in Table 3. A 10 grain/m^3 increase in grass pollen was associated with a 2% decreased odds of asthma ED visit at 5-day lag. A 100 grain/m^3 increase in tree pollen at 0, 1, and 2-day lags was consistently associated with a 1% increased odds of asthma ED visit. The effect was slightly greater for the moving average lags (day 0-2 and 0-5, OR=1.02, 95% CI=1.01-1.02). Increases of 10 grains/m^3 in weed pollens at 1-day to 5-day and moving average lags were significantly associated with 2%-4% increased odds of asthma ED visits. For air pollutants, a 10 ppb increase in ozone was associated with 3%-6% increased odds of asthma ED visits at 2 and 3-day lags and both moving average lags. A 10 ppb increase in PM 2.5 was associated with a 6%-8% increased odds of asthma ED visits at 1-day to 3-day lags and 12%-16% increased odds of asthma ED visits for the two moving average lags. A 10 ppb increase in NO_2 was associated with 10%-20% increased odds of asthma ED visits at 2-day to 4-day lags and 35% increased odds of asthma ED visits for the 6-day moving average (day 0-5). Per 10 ppb increase SO_2 was associated with a 15% increased odds of asthma ED visits at 3-day lag (OR = 1.15, 95% CI 1.02-1.30).

Total Asthma Emergency Department (ED) visit (N= 8,711)		
Characteristic	**n**	**%**
Gender		
Female	4040	46.38
Male	4671	53.62
Race/ethnicity		
White	2677	30.73
Black	5833	66.96
Other	96	1.10
Missing	105	1.21
Age Group		
5 to 9	3790	43.51
10 to 13	2909	33.39
14 to 17	2012	23.10
Poverty (zip code level)		
Low (<5%)	505	5.80
Moderate (5-20%)	6283	72.13
High (>20%)	1923	22.08
Month		
April	1366	15.68
May	1592	18.28
June	860	9.87
July	583	6.69
August	744	8.54
September	1927	22.12
October	1639	18.82

Table 1: Characteristics of children with asthma Emergency Department (ED) visits, Allegheny County, 2003-2011.

Exposures	Mean	SD	Minimum	25th	Median	75th	Maximum
Grass (grains/m³)	7.55	17.43	1	1	1	4	160
Tree (grains/m³)	123.87	378.10	1	1	1	54	4152
Weed (grains/m³)	14.18	26.76	1	1	6	14	371
PM 2.5 (µg/m³)	14.65	7.68	2.88	9.04	12.96	18.19	54.32
O_3* (ppb)	45.87	14.72	2.22	36.11	46.20	55.30	120.07
SO_2 (ppb)	5.91	2.42	1.77	4.15	5.38	7.32	19.17
NO_2 (ppb)	10.10	4.03	0.45	7.18	9.76	12.51	29.11
Apparent Maximum Temperature (F)	73.82	12.64	28.51	65.48	75.06	83.12	115.99
PM - Particulate Matter; O_3 - Ozone; SO_2 - Sulfur dioxide; NO_2 - Nitrogen dioxide; SD - Standard Deviation *Maximum 8-hour concentrations							

Table 2: Distribution of pollens, air pollutants and apparent maximum temperature, 2003-2011.

	Apparent Maximum Temperature	Grass	Tree	Weed	PM2.5	O_3	SO_2	NO_2
Grass	0.11	1	-0.02	-0.05	0.08	0.17	0.06	-0.02
	<.0001		<.0001	<.0001	<.0001	<.0001	<.0001	<.0001
Tree		-0.02	1	-0.15	-0.11	0.07	0.04	0.05
		<.0001		<.0001	<.0001	<.0001	<.0001	<.0001
Weed			-0.15	1	0.14	0.08	0.02	-0.04
			<.0001		<.0001	<.0001	<.0001	<.0001
PM2.5				0.14	1	0.61	0.55	0.33
				<.0001		<.0001	<.0001	<.0001
O_3					0.61	1	0.36	0.16
					<.0001		<.0001	<.0001
SO_2						0.36	1	0.46
						<.0001		<.0001
NO_2							0.46	1
							<.0001	
Apparent Maximum Temperature								0.08
								<.0001
PM - particulate matter; O_3 - Ozone; SO_2 - Sulfur dioxide; NO_2 - Nitrogen dioxide								

Supplemental Table 1: Pearson correlation coefficients between pollens, air pollutants, and apparent maximum temperature.

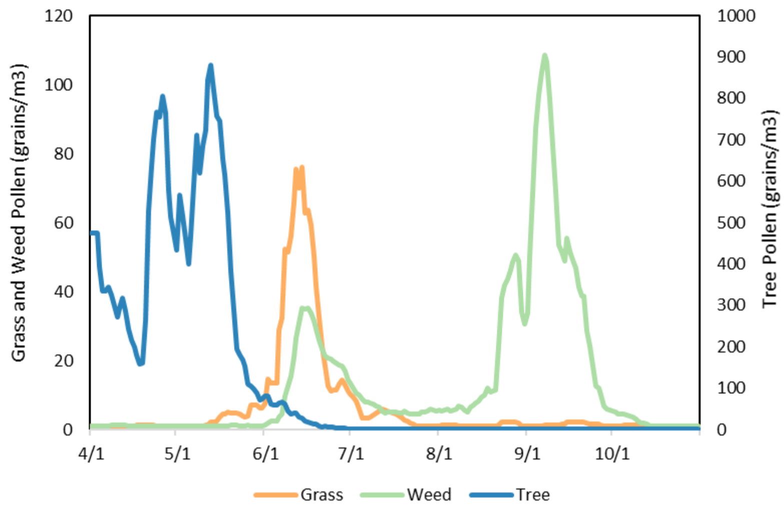


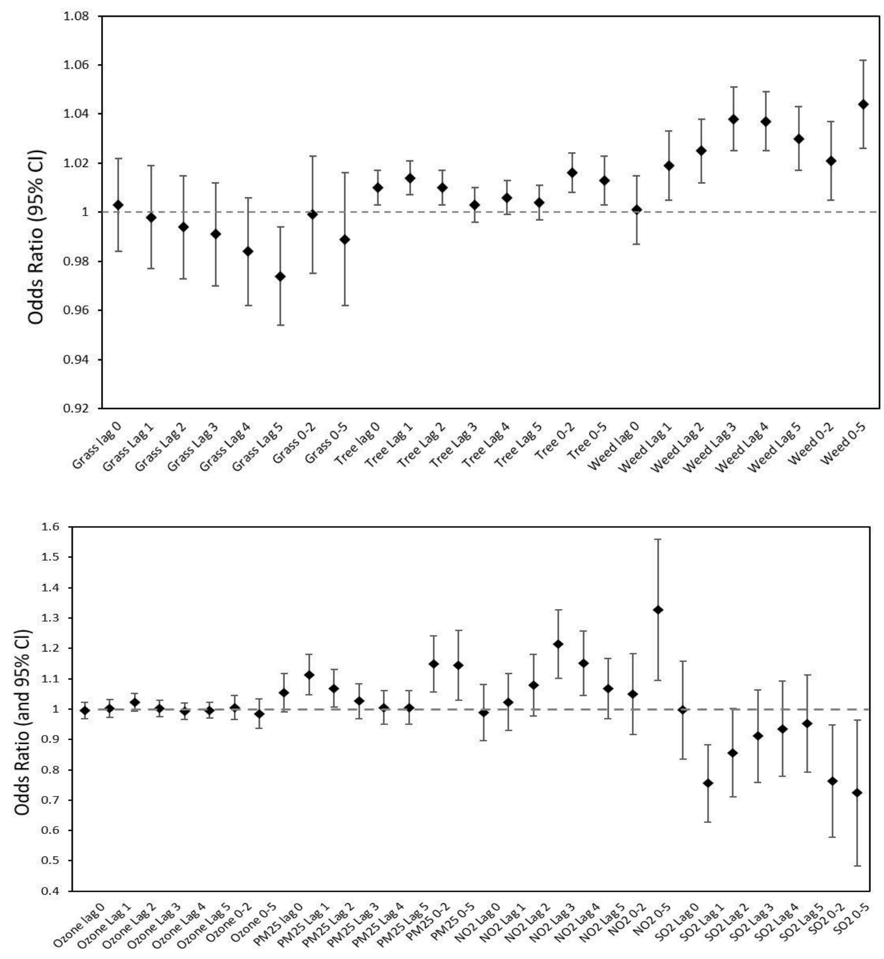
Figure 1: Time series plots for grass, weed and tree pollen counts, April-October 2005, 7-day moving average.

	Grass (per 10 grains/ m^3)	Tree (per 100 grains/ m^3)	Weed (per 10 grains/ m^3)	Ozone (per 10 ppb)	PM 2.5 (per 10 ppb)	NO_2 (per 10 ppb)	SO_2 (per 10 ppb)
Day of lag	**Odds Ratio (95% Confidence Interval)**						
0	1.00 (0.98-1.02)	**1.01 (1.00-1.02)**†	1.00 (0.99-1.01)	1.01(0.99-1.03)	1.04 (0.99-1.08)	1.03 (0.96-1.10)	1.06 (0.94-1.19)
Lag 1	1.00 (0.98-1.02)	**1.01 (1.01-1.02)**†	**1.02 (1.00-1.03)***	1.02 (0.99-1.04)	**1.06 (1.02-1.11)**†	1.02 (0.95-1.09)	0.90 (0.79-1.02)
Lag 2	1.00 (0.98-1.02)	**1.01 (1.00-1.02)**†	**1.03 (1.01-1.04)**†	**1.04 (1.02-1.07)**†	**1.08 (1.04-1.13)**†	**1.10 (1.02-1.18)***	1.06 (0.93-1.20)
Lag 3	1.00 (0.98-1.02)	1.00 (0.99-1.01)	**1.04 (1.02-1.05)**†	**1.03 (1.01-1.05)***	**1.07 (1.03-1.11)**†	**1.20 (1.12-1.29)**†	**1.15 (1.02-1.30)***
Lag 4	0.99 (0.97-1.01)	1.01 (0.99-1.01)	**1.04 (1.02-1.05)**†	1.01 (0.99-1.04)	1.03 (0.99-1.07)	**1.12 (1.05-1.20)**†	1.08 (0.96-1.22)
Lag 5	**0.98 (0.96-0.99)***	1.00 (0.99-1.01)	**1.03 (1.02-1.04)**†	1.01 (0.99-1.03)	1.01 (0.98-1.05)	1.05 (0.98-1.13)	1.03 (0.91-1.15)
3-Day Avg	1.00 (0.97-1.02)	**1.02 (1.01-1.02)**†	**1.02 (1.00-1.04)***	**1.04 (1.01-1.07)***	**1.12 (1.05-1.19)**†	1.09 (0.99-1.20)	1.01 (0.85-1.20)
6-Day Avg	0.99 (0.96-1.01)	**1.02 (1.01-1.02)**†	**1.04 (1.02-1.06)**†	**1.06 (1.02-1.10)**†	**1.16 (1.08-1.25)**†	**1.35 (1.18-1.54)**†	1.17 (0.93-1.47)
All models adjusting for 3-day average apparent maximum temperature. *P<0.05; †P<0.01 PM - Particulate Matter; O_3 - Ozone; SO_2 - Sulfur dioxide; NO_2 - Nitrogen dioxide							

Table 3: Exposure to single pollen or pollutant and asthma Emergency Department (ED) visit.

Results for full models including apparent maximum temperature, all three pollens and four air pollutants by day of lag are shown in Figure 2 and Supplemental Table 2. Independent of air pollutants and two other pollens, grass pollen was associated with a 3% decreased odds of asthma ED visits at 5-day lag. Tree pollen was associated with a 1% to 2% increased odds of asthma ED visits at the day of exposure, at 1 and 2-day lag and 3-day and 6-day moving averages. Weed pollen was significantly associated with 2% to 4% increased odds of asthma ED visits for all lags and averages. Independent of pollens, PM 2.5 was associated with 7%-11% increased odds of asthma ED visits at 1 and 2-day lags, and 14%-15% increased odds of asthma ED visits for the two moving average lags. NO_2 was associated with 15%-21% increased odds of asthma ED visits at lag day of 3 and 4, and 35% increased odds of asthma ED visits for the 6-day moving average. SO_2 was associated with 24%-28% decreased odds of asthma ED visits for both moving averages. Ozone was not significantly associated with asthma ED visit at any lag. We obtained similar results in the sensitivity analysis of when limited the residency of zip codes within the city of Pittsburgh (Supplemental Table 3). We did not find significant interactions between any given pollen and air pollutant on asthma ED visit (P>0.05 for all instances).

In the secondary analysis, we conducted separate multivariable analysis stratified by gender, race/ethnicity, age group and zip code-level of poverty for the 3-day moving average models. In this analysis, the associations between tree or weed pollens and asthma ED visits were more pronounced in male, Black or other race/ethnicity, age group 5-9 or 10-13 and moderate poverty (Table 4). The association between PM2.5 and asthma ED visits were more pronounced in Black, age group 5-9 and 10-13, low and high poverty.



All models included all pollens, all air pollutants, and 3-day average apparent maximum temperature.

Figure 2: Multivariable analysis on exposure to pollens or pollutants and asthma Emergency Department (ED) visit (odds ratio and 95% confidence interval) by day of lag.

	Lag Day 0	Lag Day 1	Lag Day 2	Lag Day 3	Lag Day 4	Lag Day 5	Average Lag Day 0-2	Average Lag Day 0-5
Parameter	**Odds Ratio (95% Confidence Interval)**							
Grass	1.00 (0.98-1.02)	1.00 (0.98-1.02)	0.99 (0.97-1.02)	0.99 (0.97-1.01)	0.98 (0.96-1.01)	**0.97 (0.95-0.99)***	1.00 (0.98-1.02)	0.99 (0.96-1.02)
Tree	**1.01 (1.00-1.02)†**	**1.01 (1.01-1.02)†**	**1.01 (1.00-1.02)†**	1.00 (0.99-1.01)	1.01 (0.99-1.01)	1.00 (0.99-1.01)	**1.02 (1.01-1.02)†**	**1.01 (1.00-1.02)***
Weed	1.00 (0.99-1.02)	**1.02 (1.01-1.03)†**	**1.03 (1.01-1.04)†**	**1.04 (1.03-1.05)†**	**1.04 (1.02-1.05)†**	**1.03 (1.02-1.04)†**	**1.02 (1.00-1.04)***	**1.04 (1.03-1.06)†**
Ozone	1.00 (0.97-1.02)	1.00 (0.97-1.03)	1.02 (0.99-1.05)	1.00 (0.98-1.03)	0.99 (0.97-1.02)	1.00 (0.97-1.02)	1.01 (0.97-1.05)	0.99 (0.94-1.03)
PM 2.5	1.05 (0.99-1.12)	**1.11 (1.05-1.18)†**	**1.07 (1.01-1.13)***	1.03 (0.97-1.08)	1.01 (0.95-1.06)	1.01 (0.95-1.06)	**1.15 (1.06-1.24)†**	**1.14 (1.04-1.26)†**
NO_2	0.99 (0.90-1.08)	1.02 (0.94-1.12)	1.08 (0.99-1.18)	**1.21 (1.11-1.33)†**	**1.15 (1.05-1.26)†**	1.07 (0.98-1.17)	1.05 (0.93-1.18)	**1.33 (1.13-1.56)†**
SO_2	1.00 (0.86-1.16)	**0.76 (0.65-0.88)†**	0.86 (0.73-1.00)	0.91 (0.78-1.06)	0.94 (0.80-1.09)	0.95 (0.82-1.11)	**0.76 (0.61-0.95)***	**0.72 (0.54-0.96)***

All models adjusting for other pollens or air pollutants and 3-day average apparent maximum temperature.
*P<0.05; †P<0.01
PM - particulate matter; O_3 – ozone; SO_2 - sulfur dioxide; NO_2 - nitrogen dioxide

Supplemental Table 2: Exposure to pollens or pollutants and asthma Emergency Department (ED) visit by Day of Lag.

	Lag Day 0	Lag Day 1	Lag Day 2	Lag Day 3	Lag Day 4	Lag Day 5	3-Day Average	6-Day Average
Parameter	**Odds Ratio (95% Confidence Interval)**							
Grass	1.00 (0.97-1.02)	0.99 (0.97-1.02)	1.00 (0.97-1.02)	1.00 (0.97-1.02)	0.99 (0.97-1.02)	0.98 (0.95-1.00)	1.00 (0.97-1.03)	0.99 (0.96-1.03)
Tree	1.01 (1.00-1.02)	**1.02 (1.01-1.02)†**	**1.01 (1.00-1.02)†**	1.01 (0.99-1.02)	**1.01 (1.00-1.02)***	1.00 (0.99-1.01)	**1.02 (1.01-1.03)†**	**1.02 (1.01-1.03)†**
Weed	0.99 (0.98-1.01)	**1.02 (1.00-1.04)***	**1.03 (1.01-1.05)†**	**1.04 (1.02-1.05)†**	**1.03 (1.02-1.05)†**	**1.03 (1.01-1.04)†**	**1.02 (1.00-1.04)***	**1.04 (1.02-1.07)†**
O_3	1.01 (0.98-1.05)	0.99 (0.96-1.03)	1.01 (0.98-1.05)	0.99 (0.96-1.03)	0.99 (0.96-1.03)	1.00 (0.96-1.03)	1.01 (0.96-1.06)	0.98 (0.93-1.05)
PM 2.5	1.00 (0.93-1.08)	**1.14 (1.06-1.22)†**	**1.09 (1.01-1.17)***	1.06 (0.99-1.13)	1.02 (0.96-1.10)	1.02 (0.95-1.09)	**1.15 (1.04-1.26)†**	**1.18 (1.05-1.33)†**
NO_2	1.02 (0.92-1.13)	1.03 (0.93-1.14)	1.06 (0.96-1.18)	**1.19 (1.07-1.32)**	1.11 (0.99-1.23)	1.01 (0.91-1.12)	1.06 (0.92-1.22)	**1.25 (1.03-1.51)***
SO_2	0.85 (0.70-1.04)	**0.61 (0.50-0.75)†**	0.83 (0.68-1.02)	0.90 (0.74-1.10)	0.97 (0.79-1.18)	0.96 (0.78-1.18)	**0.57 (0.43-0.76)†**	**0.58 (0.39-0.84)†**

All models included all pollens, all air pollutants, and 3-day average apparent maximum temperature.
*P<0.05; †P<0.01
PM - particulate matter; O_3 – ozone; SO_2 - sulfur dioxide; NO_2 - nitrogen dioxide

Supplemental Table 3: Exposure to pollens or pollutants and asthma Emergency Department (ED) visit by Day of Lag, limited to zip codes within the City of Pittsburgh.

	Grass	Tree	Weed	O_3	PM2.5	NO_2	SO_2
	(per 10 grains/m^3)	(per 100 grains/m^3)	(per 10 grains/m^3)	(per 10 ppb)	(per 10 µg/m3)	(per 10 ppb)	(per 10 ppb)
Characteristic	**Odds Ratio (95% Confidence Interval)**						
Gender							
Female	1.01 (0.97-1.05)	1.01 (0.99-1.03)	1.02 (0.99-1.05)	1.00 (0.94-1.06)	**1.18(1.05-1.33)**†	1.08 (0.90-1.29)	**0.68(0.48-0.96)***
Male	0.99 (0.96-1.03)	**1.02(1.01-1.03)**†	1.02 (0.99-1.04)	1.01 (0.96-1.06)	**1.13(1.02-1.30)***	1.03 (0.88-1.21)	0.83 (0.62-1.10)
Race/Ethnicity							
White	1.00 (0.96-1.04)	1.01 (0.99-1.02)	1.01 (0.98-1.04)	1.02 (0.96-1.09)	1.09 (0.96-1.23)	1.16 (0.94-1.43)	0.95 (0.67-1.34)
Black	1.00 (0.97-1.03)	**1.02(1.01-1.03)**†	1.02 (1.00-1.04)	1.00 (0.95-1.05)	**1.17(1.05-1.30)**†	0.99 (0.85-1.16)	**0.69(0.52-0.93)***
Other	0.92 (0.70-1.21)	1.01 (0.95-1.06)	**1.12 1.01-1.24)***	0.97 (0.74-1.27)	1.34 (0.76-2.34)	0.99 (0.43-2.29)	0.38 (0.08-1.85)
Age Group							
5 to 9	0.99 (0.95-1.02)	**1.02(1.01-1.03)**†	**1.03(1.00-1.05)***	1.01 (0.95-1.07)	**1.15(1.03-1.29)***	0.98 (0.82-1.17)	0.79 (0.57-1.09)
10 to 13	1.03 (0.99-1.08)	**1.02(1.01-1.04)**†	1.00 (0.97-1.03)	0.97 (0.90-1.04)	**1.21(1.05-1.40)**†	1.17 (0.94-1.46)	0.71 (0.48-1.05)
14 to 17	0.98 (0.94-1.03)	1.00 (0.98-1.02)	1.03 (0.99-1.07)	1.05 (0.97-1.14)	1.07 (0.92-1.26)	1.04 (0.81-1.32)	0.77 (0.50-1.21)
Zip Code Poverty							
Low	1.05 (0.95-1.15)	1.00 (0.98-1.03)	1.00 (0.95-1.06)	0.96 (0.84-1.11)	**1.32(1.00-1.73)***	1.03 (0.56-1.86)	0.77 (0.34-1.77)
Medium	1.00 (0.97-1.03)	**1.02(1.01-1.03)**†	**1.02(1.00-1.04)***	1.01 (0.97-1.06)	1.09 (0.99-1.19)	1.11 (0.96-1.28)	**0.69(0.53-0.91)**†
High	1.00 (0.95-1.05)	1.01 (0.99-1.03)	1.02 (0.99-1.05)	1.00 (0.92-1.09)	**1.30(1.10-1.53)**†	0.91 (0.72-1.16)	0.91(0.60-1.39)

All models adjusting for other pollens or air pollutants, and 3-day average apparent maximum temperature.
*P<0.05; †P<0.01
Table Abbreviations: PM - particulate matter; O_3 - Ozone; SO_2 - Sulfur dioxide; NO_2 - Nitrogen dioxide

Table 4: Exposure to pollens or pollutants and asthma Emergency Department (ED) visits, stratified by patients' characteristics, 3-day average.

Discussion

In this case-crossover analysis, we found that exposure to higher levels of tree or weed pollen was significantly associated with increased odds of asthma ED visit across multiple lags among children aged 5-17 years residing in Allegheny County, Pennsylvania. This association was independent of levels of air pollutants. Moreover, exposure to higher levels of PM2.5 and NO_2 was associated with increased odds of asthma ED visit, with more pronounced effect seen when averaged across multiple preceding days.

Other studies conducted in the mid-Atlantic region of the U.S. have shown similar findings, though there is some variation in which individual pollens are identified as most significant. A case-control study in New Jersey reported that tree pollen and weed pollen were significant predictors of asthma exacerbations, with greatest magnitude of effects at 3-day and 5-day average lags [17]. In this study, grass pollen was generally not a significant predictor, and ragweed, when considered as distinct from other weeds, was negatively associated with asthma exacerbations [17]. Another study conducted in the Washington DC area, which focused primarily on the effects of pollutants but also examined pollens, reported that a 100 grain/m^3 increase in tree pollen was associated with 1.8% increased risk of asthma ED visits in children aged 5-12 years when controlling for PM 2.5 and ozone, a result similar in magnitude to our work [23]. This study did not find significant effects of weed or grass pollen within their population [23]. A study out of Philadelphia, PA demonstrated a clear exposure-response pattern between tree pollen and asthma exacerbations, whereby risk increased consistently with increasing level of pollen [24]. They also demonstrated significant effects of weed pollens excluding ragweed, though this did not follow a clear exposure-response pattern across increasing levels of pollen [24]. Meta-analysis conducted in 2017 identified grass pollen as a significant predictor of asthma ED visits, though authors noted differences by region, with tree and weed pollen identified as key triggers across multiple studies in the US [8].

Our study expanded on this previous work by considering the effects of NO_2 and SO_2 in addition to PM 2.5 and ozone. PM 2.5 and ozone have generally been included in pollen analyses, but other pollutants were not consistently considered. Because previous research on pollutants in Allegheny County demonstrated health effects of NO_2 and SO_2 on asthma ED visits in children [19], we included these two air pollutants in this analysis. Particulate matter, ozone and NO_2 are primary components of air pollution in urban areas, with SO_2 also abundant in industrial areas such as Southwest Pennsylvania, making each important to consider [31]. Our research was further strengthened by 9 years of asthma ED data. Because pollen research is generally limited to only the warm season of the year when outdoor pollen is circulating, studies using 1-2 years of asthma ED visits may be limited by relatively low numbers of events [25]. This work was also strengthened by the inclusion of all major hospitals in the Allegheny county, thus improving the generalizability of the findings, as well as our assessment of differential effects of pollen by sociodemographic factors including race and poverty level.

For both pollens and pollutants within our multivariable models, the 3-day and 6-day moving averages resulted in the strongest effects. This type of dose-response relationship has been noted in other research on both pollens and pollutants and suggests that exposure to cumulated airway irritants over a series of days can contribute to a heightened allergic response [23,26,27]. This finding has also been supported by inhaled allergen challenge studies, which have demonstrated dose-response relationships between cumulative allergen exposure and both eosinophilic inflammation and reduced forced expiratory volume [28,29]. Furthermore, airway eosinophil levels have been shown to remain elevated 48 hours after allergen exposure, indicating the persistent inflammatory effects of such exposures [29]. The strength of the multi-day averages as predictors across studies suggests the potential utility of this type of measure for informing public health guidelines and reporting [24].

This study did not find significant interactions between the effects of pollens and pollutants on asthma ED visits. However, some studies have suggested that pollutants such as ozone may act synergistically with pollens to increase allergenicity and trigger stronger inflammatory response [30-32]. Ozone has been shown to increase inflammation in the airways and thus have a priming effect in the airways, increasing susceptibility to allergens [31,33].

Health effects of pollen on asthma may differ by sociodemographic factors. We reported that the effects of tree pollen to be slightly stronger among male and Black children, as well as in younger age groups. There is evidence that school-age children experience greater effects of elevated pollen compared with very young children or older teens, possibly due to physiological differences and time spent outdoors [23]. Similarly boys may have greater risks of pollen-associated asthma exacerbations as compared to girls [17,34]. Racial disparities in asthma prevalence and outcomes are known to exist and previous research has established that Black children are more likely than White children to have both allergic sensitization and asthma [35]. Notably, these differences generally persist after adjusting for socioeconomic status [36]. Some research has demonstrated differential effects of certain pollens by race [24], though this is not consistent across studies [17] Neighborhood-level effects have also been documented, suggesting that children in higher poverty neighborhoods may be at greater risk of allergen-associated asthma exacerbations [18,23]. Here we did not find this consistent pattern of effects when stratifying by the zip code-level poverty indicator. However, this type of measure cannot capture individual-level variations, and thus an individual-level proxy for socioeconomic status, such as insurance type, might add more precision. Further research is needed to better understand which factors drive these differences in disease process and outcomes so that interventions can be targeted to address health disparities in allergies and asthma.

It is important to note the ecological context and limitations of this research. First, use of one pollen monitor to represent exposures across the county may not have adequately represented the more fine-level variations in pollen levels nor well represent individual exposures. Nonetheless, sensitivity analysis suggested that one central monitor could adequately represent levels across the county and these population-level findings can serve to guide public health recommendations. Second, meteorological factors that may affect pollen levels and distributions, such as wind and electrical storms, were not available in this study. Third, variations in housing quality and exposure to indoor allergens and smoke also play an important role in asthma outcomes and should be further considered within the context of outdoor environmental exposures [37]. Finally, although case-crossover design is able to control for potential person-level confounders that are stable over time, such as age, gender, and genetic predisposition, potential confounding by time-varying factors such as seasonal patterns or more long-term trends like decreases in pollution over years may exist.

Conclusion

In summary, increased environmental levels of tree and weed pollen were significantly associated with increased odds of asthma ED visits in children residing in Allegheny County, Pennsylvania. This association was independent of the effect of increased levels of air pollutants. Our findings suggest that exposure to pollens may contribute to the burden of asthma in children. Implementing methods to limit allergen exposure during particular seasons may prevent adverse asthma outcomes.

Acknowledgements

We would like to acknowledge Asha Patel, MS for performing the pollen counts. We also wish to acknowledge Dr. Yueh-Ying Han, Research Associate Professor, Department of Pediatrics, University of Pittsburgh School of Medicine, for her help in biostatistical interpretation of this data.

Funding

Pennsylvania Department of Health through a contract with the University of Pittsburgh (CDC Environmental Public Heath Tracking Program): Contract #5U38EH00952-05, 2016. This work has also been supported by The Heinz Endowments Grants E6450, E6462 and E7476.

References

1. Asthma Facts. American College of Allergy, Asthma & Immunology.
2. Zahran HS, Bailey CM, Damon SA, Garbe PL, Breysse PN (2018) Vital Signs: Asthma in Children - United States, 2001-2016. MMWR Morb Mortal Wkly Rep 67: 149-155.
3. Nurmagambetov T, Kuwahara R, Garbe P (2018) The Economic Burden of Asthma in the United States, 2008-2013. Ann Am Thorac Soc 15: 348-356.
4. Asthma's impact on the nation : data from the CDC National Asthma Control Program. 2019.
5. Castillo JR, Peters SP, Busse WW (2017) Asthma Exacerbations: Pathogenesis, Prevention, and Treatment. J Allergy Clin Immunol Pract 5: 918-927.
6. Gowers AM, Cullinan P, Ayres JG, Anderson HR, Strachan DP, et al. (2012) Does outdoor air pollution induce new cases of asthma? Biological plausibility and evidence; a review. Respirology 17: 887-898.
7. Guarnieri M, Balmes JR (2014) Outdoor air pollution and asthma. Lancet 383: 1581-1592.
8. Erbas B, Jazayeri M, Lambert KA, Katelaris CH, Prendergast LA, et al. (2018) Outdoor pollen is a trigger of child and adolescent asthma emergency department presentations: A systematic review and meta-analysis. Allergy 73: 1632-1641.
9. Heguy L, Garneau M, Goldberg MS, Raphoz M, Guay F, et al. (2008) Associations between grass and weed pollen and emergency department visits for asthma among children in Montreal. Environ Res 106: 203-211.
10. Zhong W, Levin L, Reponen T, Hershey GK, Adhikari A, et al. (2006) Analysis of short-term influences of ambient aeroallergens on pediatric asthma hospital visits. Sci Total Environ 370: 330-336.
11. 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.
12. Miller MD, Marty MA (2010) Impact of environmental chemicals on lung development. Environ Health Perspect 118: 1155-1164.
13. Salvi S (2007) Health effects of ambient air pollution in children. Paediatr Respir Rev 8: 275-280.
14. Thomas M (2006) Allergic rhinitis: evidence for impact on asthma. BMC Pulm Med 6 Suppl 1: S4.
15. National Allergy Bureau (2019) American Academy of Allergy Asthma & Immunology.
16. Levetin E. Use of the Burkard Spore Trap. American Academy of Allergy Asthma & Immunology.
17. Gleason JA, Bielory L, Fagliano JA (2014) Associations between ozone, PM2.5, and four pollen types on emergency department pediatric asthma events during the warm season in New Jersey: a case-crossover study. Environ Res 132: 421-429.
18. Goodman JE, Loftus CT, Liu X, Zu K (2017) Impact of respiratory infections, outdoor pollen, and socioeconomic status on associations between air pollutants and pediatric asthma hospital admissions. PLoS One 12: e0180522.
19. Talbott EO, Bilonick R, Sharma RK, Rager J, Duan E (2016) Relationship between Air Pollution and Asthma with other Acute Respiratory Hospitalizations/Emergency Department Visits in Pennsylvania.
20. Abraham JH, Bateson TF (2006) Case-Crossover Analysis Tool (C-Cat) Beta Version 1.1 User's Manual. New York: Apex Epidemiology Research, LLC
21. Glad JA, Brink LL, Talbott EO (2012) The relationship of ambient ozone and PM(2.5) levels and asthma emergency department visits: possible influence of gender and ethnicity. Arch Environ Occup Health 67: 103-108.
22. American Fact Finder. (2019) United States Census Bureau.
23. Babin SM, Burkom HS, Holtry RS, et al. (2007) Pediatric patient asthma-related emergency department visits and admissions in Washington, DC, from 2001-2004, and associations with air quality, socio-economic status and age group. Environ Health 6: 9.
24. De Roos AJ, Kenyon CC, Zhao Y, Moore K, Melly S, et al. (2020) Ambient daily pollen levels in association with asthma exacerbation among children in Philadelphia, Pennsylvania. Environ Int 145: 106138.
25. Lierl MB, Hornung RW (2003) Relationship of outdoor air quality to pediatric asthma exacerbations. Ann Allergy Asthma Immunol 90: 28-33.
26. Darrow LA, Hess J, Rogers CA, Tolbert PE, Klein M, et al. (2012) Ambient pollen concentrations and emergency department visits for asthma and wheeze. J Allergy Clin Immunol 130: 630-638.
27. Erbas B, Akram M, Dharmage SC, Tham R, Dennekemp M, et al. (2012) The role of seasonal grass pollen on childhood asthma emergency department presentations. Clin Exp Allergy 42: 799-805.
28. Ørby PV, Bønløkke JH, Bibby BM, Peter R, Hertel O, et al. (2019) Dose-response curves for co-exposure inhalation challenges with ozone and pollen allergen. Eur Respir J 54: 1801208.
29. Jarjour NN, Calhoun WJ, Kelly EA, Gleich GJ, Schwartz LB, et al. (1997) The immediate and late allergic response to segmental bronchopulmonary provocation in asthma. Am J Respir Crit Care Med 155: 1515-1521.
30. Frank U, Ernst D (2016) Effects of NO_2 and Ozone on Pollen Allergenicity. Front Plant Sci 7: 91.
31. D'Amato G, Bergmann KC, Cecchi L, Annesi- Maesano I, et al. (2014) Climate change and air pollution: Effects on pollen allergy and other allergic respiratory diseases. Allergo J Int 23: 17-23.

32. Holz O, Mucke M, Paasch K, Bohme S, Timm P, et al. (2002) Repeated ozone exposures enhance bronchial allergen responses in subjects with rhinitis or asthma. Clin Exp Allergy 32: 681-689.

33. Dales RE, Cakmak S, Judek S, Dann T, Coates F, et al. (2004) Influence of outdoor aeroallergens on hospitalization for asthma in Canada. J Allergy Clin Immunol 113: 303-306.

34. Shrestha SK, Katelaris C, Dharmage SC, Burton P, Vicendese D, et al. (2018) High ambient levels of grass, weed and other pollen are associated with asthma admissions in children and adolescents: A large 5-year case-crossover study. Clin Exp Allergy 48: 1421-1428.

35. Sitarik A, Havstad S, Kim H, Zoratti EM, Ownby D, et al. (2020) Racial disparities in allergic outcomes persist to age 10 years in black and white children. Ann Allergy Asthma Immunol 124: 342-349.

36. Jones BL (2020) We continue to fail black children with asthma and allergic disease. Ann Allergy Asthma Immunol 124: 305-306.

37. Kanchongkittiphon W, Gaffin JM, Phipatanakul W (2014) The indoor environment and inner-city childhood asthma. Asian Pac J Allergy Immunol 32: 103-110.