

# Ambient air pollution and emergency department visits for asthma in Erie County, New York 2007–2012

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## Abstract

**Purpose** 8% of the US population has asthma. Air pollution is linked to exacerbation in susceptible individuals. The objective was to identify air pollutants that increased the risk of asthma emergency department visits during a time wherein a polluting factory was criminally convicted, changing local air pollutant levels.

**Methods** An ecological time-series design used a daily count of asthma emergency visits from 2007 to 2012 as the dependent variable. Independent variables air pollutants ( $\text{NO}_2$ ,  $\text{PM}_{2.5}$ ,  $\text{CO}$ , and  $\text{O}_3$ ), controlling for meteorological conditions, were analyzed using time-series and Poisson GLM models.

**Results** 76,651 emergency asthma visits were included with an average of 35 visits per day ( $\text{SD} = 9.2$ , range 11–80) in a stationary time series. Increased visit volume in fall and spring had no associations to the air pollutants. Associations between individual air pollutants occurred in otherwise low-volume months for asthma emergency visits. The strongest relationship was an 11.6% increase in the asthma emergency visit rate during the month of June. In monthly groupings that removed most of the autumn and spring months,  $\text{O}_3$ ,

$\text{PM}_{2.5}$ ,  $\text{CO}$ , and  $\text{NO}_2$  were associated with 5, 4, 2, and 2% increases in asthma emergency visits, respectively.  $\text{CO}$  was the only pollutant with a negative association with asthma emergency visits, occurring in the month of April.

**Conclusions** Pollutants  $\text{NO}_2$ ,  $\text{PM}_{2.5}$ ,  $\text{CO}$ , and  $\text{O}_3$  were associated with increased emergency asthma visits in some, but not all months of the year. Air pollution's impact on asthma emergencies may be masked by other, more influential seasonal triggers, such as infections or allergies.

**Keywords** Air pollution · Asthma · Environmental exposures · Ambient air quality · Emergency department utilization

## Background

Over 8% of the United States population suffers from asthma (Zahran et al. 2011). Globally, the burden of asthma is projected to increase in association with residential housing quality and climate change (D'Amato et al. 2016; Masoli et al. 2004). The impact of outdoor air pollution on disability-adjusted life years worldwide has increased (Lim et al. 2012). Asthma development and exacerbation is linked to the urban environment, with closer residential exposure to air pollution from fossil fuel combustion in traffic, power plants, and industrial facilities (Guarnieri and Balmes 2014; Sacks et al. 2014).

Broadly, geographic context and ecology are linked to asthma development and outcomes, as well as several other measures of public health (Wright et al. 2008). Ambient air pollution is a key variable linked to geographic context. Criteria air pollutants are defined and regulated in the USA by the Clean Air Act, monitored and enforced by agencies such as the Environmental Protection Agency (EPA), and

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are frequently monitored in developed countries (42 USC 1977; Civic Impulse 2017). Relevant to asthma outcomes, these pollutants include particulate matter (PM) and gaseous pollutants of ozone (O<sub>3</sub>), nitrogen oxides (NO<sub>x</sub>), carbon monoxide (CO), and sulfur dioxide (SO<sub>2</sub>). Traffic-related gaseous pollutants are linked to the development of asthma in cohort studies, though this relationship is not consistently replicated across studies (Anderson et al. 2013). Long-term exposure to elevated pollutant levels restricts lung development (Gauderman et al. 2015). In previous population-level studies, there are consistent temporal patterns of short-term elevations in pollutant exposure and increased asthma emergency department (ED) visits (Choi et al. 2011; Cirera et al. 2012; Cook et al. 2011; Delfino et al. 2014; Galan et al. 2003; Halonen et al. 2010; Kloog et al. 2014; Kousha and Rowe 2014; Lavigne et al. 2012; Malig et al. 2016; Masjedi et al. 2003; Paulu and Smith 2008; Peel et al. 2005; Sacks et al. 2014; Stafoggia et al. 2013; Stieb et al. 2009; Szyszko-wicz and Kousha 2014; Tetreault et al. 2016).

During the present study period, an industry in a densely populated area of Erie County, New York, was found guilty in court of violating several facets of the Clean Air Act by failing to install, report, and address appropriate pollution controls (United States v Tonawanda Coke Corporation 2013). The factory was located in the most concentrated area (over sixty) of air polluting permitted sources in New York State (Toxic Release Inventory Explorer 2015). Pollutants 1,3-butadiene, acetaldehyde, acrolein, benzene, carbon tetrachloride, and formaldehyde were well above recommended levels at ambient air quality monitors in proximity to the factory (New York State Department of Environmental Conservation 2009). The most notable air pollutant reductions after the regulatory and enforcement actions were in relation to benzene. However, these volatile pollutants interact to form other compounds (such as ground level ozone) rapidly and were not directly measured daily during the 5-year study period (2007–2012), thus limiting the ability to link short-term temporal changes in the direct emissions to health outcomes and temporal patterns of asthma ED visits. Given the nature of multi-pollutant mixtures that interact rapidly to form one another, criteria pollutants provided the most frequently measured proxy of overall pollution exposure during the study window.

The Environmental Protection Agency factory raid in December of 2009, subsequent state-level environmental protection regulatory activity, conviction in 2013, and associated decrease in ambient pollutants created a unique natural experiment (United States v Tonawanda Coke Corporation 2013). Grassroots organizations and local stakeholders indicated that the regulatory and enforcement actions motivated neighboring industries to review and reduce overall emissions and air pollution. The purpose of this research was to investigate the ecological county-wide relationship

of air pollutant levels (NO<sub>2</sub>, PM<sub>2.5</sub>, CO, and O<sub>3</sub>) and asthma ED visits in an urban setting over a period of time in which a major industrial facility was cited, and later convicted, for violations of the United States Clean Air Act (Anderson et al. 2013; Gauderman et al. 2015; Wright et al. 2008).

## Materials and methods

### Design

This study utilized a retrospective time-series ecological design at the county level. A count of the ED visits for each day in the time-series was the unit of analysis. The study was based on community-based participatory action principles.

### Setting

This study took place in Erie County, New York, from 2007 to 2012.

### Exposure assessment

Daily concentrations of air pollutants were obtained from the EPA's air quality system ambient air monitoring repository (United States Environmental Protection Agency 2017). We included 24 h averages of CO (ppm), NO<sub>2</sub> (ppb), and 8-h maximum of O<sub>3</sub> (ppb) from the monitor with the least amount of missing data as most representative of average population exposures (Darrow et al. 2011). Because PM<sub>2.5</sub> (µg/m<sup>3</sup>) was highly correlated among monitors, the overall mean for 5 monitors' 24 average value of PM<sub>2.5</sub> (µg/m<sup>3</sup>) was used. 24-h averages are justified in this type of study design (Darrow et al. 2011). We excluded sulfur dioxide for anticipated associations with spacial heterogeneity due to plume formation and touchdowns characteristic of coal-fired power plant emissions (Strickland et al. 2010).

### ED visits

All ED visits for asthma (ICD-9 codes 493.00–493.92) were extracted from the SPARCS (Statewide Planning and Research Cooperative System) identifiable dataset for hospitals from 2007 to 2012 (New York State Department of Health 2015). We included both inpatient ED visits (an ED visit that led to a hospital admission) and outpatient ED visits (an ED visit that led to a disposition to home, community or other non-hospital setting). A visit was added to the daily counts of ED visits if any one of the first three ICD codes indicated asthma.

## Weather

Daily average temperatures, average wind speed, and relative humidity were obtained from the National Weather Service data from the Greater Buffalo International Airport monitor.

## Analysis

Data were examined with descriptive statistics, estimates of auto-correlations with time-series, cross-correlations among days and pollutant monitors, and Pearson product moment correlations among pollutants. We tested for trend using both the Augmented Dickey–Fuller (ADF) unit root and the Kwiatkowski–Phillips–Schmidt–Shin (KPSS) test. We split the daily data into two equal groups, before and after January 1, 2010, to conduct an unadjusted test of mean difference in ED visits and pollutants before and after the regulatory activity. We conducted initial single-pollutant models in a Poisson generalized linear model (GLM) following methods from previously published studies (Darrow et al. 2014; Peel et al. 2005; Strickland et al. 2010). We utilized the 3-day moving average pollutant concentration [the average of concentrations today (lag 0), yesterday (lag 1), and 2 days ago (lag 2)]. Meteorological variables were entered using cubic polynomials for 3-day moving averages. Seasonality was adjusted by using cubic splines with 1 knot per month (placed on 15th of each month) (Darrow et al. 2014; Peel et al. 2005). An indicator term was used for each day of week and season. Utilizing a novel method, we selected empirically based pseudo-seasons by (1) adding monthly interactive terms with each individual pollutant to determine if the association changed by month of the year, (2) grouping months with similar empirical estimates, (3) refitting the Poisson GLM model and testing for differences among the groups, and (4) iteratively adjusting if we found there were no significant differences among groups (by combining these groups). With the potential for substantial variation in the number of asthma ED visits and association with pollutants by month of the year even within seasons, conventional conceptual definitions of season (e.g. autumn, winter) may not have grouped months with similar pollutant–asthma ED visit associations together. Thus, we utilized an empirical data-driven approach to group months with similar interactions together. The residuals were tested to confirm temporal dependence was removed from the model using the Ljung–Box test.

We conducted sensitivity analyses testing the same model by transforming the pollutant by using cubic time, quarterly (four per year) knots, and monthly knots. Conceptually, adding knots can be compared to adding a joint where fitted curves are allowed flexibility to bend into a sequential fitted curve of a different shape or direction for a smoother, flexible, non-linear pattern. Due to the results of the sensitivity

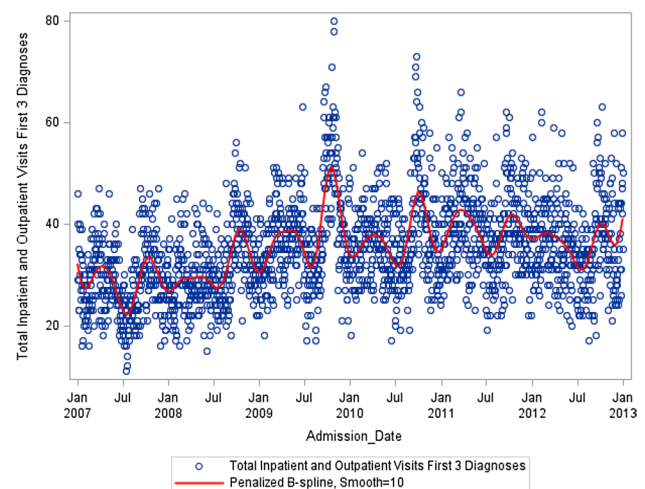
analysis, we did not proceed to a multi-pollutant model. Data analyses were conducted using SAS (Version 9.1), STATA (Version 14.2), with supplementary testing in MATLAB.

## Results

### Descriptive and pollutant correlations

A total of 76,651 ED asthma visits spanning 2192 days were analyzed. There was an average of 35 visits per day ( $SD = 9.2$ ) with a range from 11 to 80. Figure 1 is a scatterplot of the daily number of ED asthma for each day of the study period. A penalized b-spline was fitted to visualize the underlying trend, and spikes in visits each fall (September–October) and spring (March) were evident. The average number of daily visits was highest in October ( $M = 42.4$ ,  $SD = 10.3$ ) and lowest in July ( $M = 29.2$ ,  $SD = 7.1$ ). The asthma ED visit time series was stationary, indicating no overall increasing or decreasing trend over the study period (augmented Dickey–Fuller unit root test  $p < 0.05$ ). The majority (62%) of the outpatient ED visits and a substantive amount (20%) of the inpatient ED visits had the first diagnosis code as a symptoms or ill-defined condition, such as shortness of breath, wheeze, or cough, with a second or third diagnosis of asthma. By volume, working-aged women (18–64) constituted the largest group of ED users for asthma (Supplemental Figure 5), demonstrating a disparity. Temporal trends for ED asthma visits in school-aged boys and girls were similar. Using a cut-point of January 1, 2010, there were approximately five more visits per day during the second half of the study.

Table 1 lists the descriptive statistics for each pollutant and meteorological variable. Average pollutant levels in



**Fig. 1** Daily counts of emergency department visits Erie County, New York (January 1, 2007–December 31, 2012)

**Table 1** Descriptive statistics for pollutant and meteorologic variables 2007–2012

	Mean	SD	Range	IQR	Missing days (%)
Carbon monoxide ppm	0.32	0.13	0.25–1.07	0.075	2.42
Nitrogen dioxide (ppb)	13.7	12.5	0–45.5	9.24	9.26
PM <sub>2.5</sub> (µg/m <sup>3</sup> )	10.3	9.1	0–44.7	6.20	0.73
Ozone (ppb)	0.039	0.013	0.008–0.088	0.017	0.91
Average temperature	49.7	18.5	3–85	31.0	0
Average wind speed	9.64	8.90	1.3–31.9	5.4	0
Relative humidity	71.56	12.01	32.7–99.7	16.5	0

SD standard deviation, IQR interquartile range

**Table 2** Pearson correlation coefficients among pollutants

	1	2	3	4
1. Ozone	–	0.03	– 0.04	0.47***
2. Nitrogen dioxide		–	0.28***	0.38***
3. Carbon monoxide			–	0.25***
4. Fine particulate matter				–

\*\*\*  $p < 0.001$

this study were well below national ambient air quality standards. The pollutants were positively and statistically significantly correlated with one another, except ozone with the other gaseous pollutants (NO<sub>2</sub> and CO) (Table 2). The same pollutant measured at different monitors within the county was strongly correlated for PM<sub>2.5</sub> at five monitoring sites ( $r = 0.90$ – $0.97$ ), moderately correlated for NO<sub>2</sub> ( $r = 0.78$ ), and poorly correlated for the two CO ( $r = 0.19$ ) monitors as one monitor (the one chosen for this study) was located adjacent to a major highway. Supplemental Figures 1–4 are scatterplots with a penalized  $b$ -spline to visualize the trend of the daily 24 h average levels of PM<sub>2.5</sub>, NO<sub>2</sub>, and CO, as well as the 8-h maximum values for O<sub>3</sub>. The ADF test ( $p < 0.05$ ) and the KPSS test of both the entire series and subsamples divided before and after the cut point of January 1, 2010 ( $p > 0.05$ ) indicated stationarity. Using a cut-point of January 1, 2010, to group the first and second half of the study period, respectively, daily levels of NO<sub>2</sub> and PM<sub>2.5</sub> were lower, CO was higher, and O<sub>3</sub> remained the same in the second half of the study period (Supplemental Table 1). Cross-correlation analyses demonstrated that all pollutants were most correlated on lag 0, indicating dispersion within 1 day across the different monitoring sites (Supplemental Figure 5).

## NO<sub>2</sub>

Nitrogen dioxide models are listed in Table 3, with resulting Rate Ratios, Poisson GLM final model, and Poisson GLM preliminary monthly interaction term. The month of June was statistically different from any other month, with the strongest interaction term, and is listed as monthly group 1. A 9.24-ppb increase in NO<sub>2</sub> is associated with an 11.6% increase in the asthma ED visit rate during the month of June. As outlined in the methods section of this paper, months were grouped by empirical similarities in their pollutant–ED visit interaction term rather than by traditionally conceptualized seasons. Thus, the second pseudo-season, or monthly group 2, included January–March and July–October which is conceptually coherent with winter and summer weather seasons, where general ED volume for asthma is lower. During these months, a 9.24-ppb increase in NO<sub>2</sub> is associated with a 3.3% increase in the volume of asthma ED visits. Finally, the interaction of NO<sub>2</sub> and the weather transition seasons of April, May, November, and December were empirically similar and represented in monthly group 3. No association was found between NO<sub>2</sub> and asthma ED visits during this pseudo-season group.

## PM<sub>2.5</sub>

Table 4 lists the results for fine particulate matter. The monthly interaction terms were utilized to empirically group February, March, June, July, and August together. A 6.2-µg/m<sup>3</sup> increase in PM<sub>2.5</sub> during these months increased the rate of asthma ED visits by 4.4%. January, April, May, September, October, November, and December were grouped, with no observed associations to levels of PM<sub>2.5</sub>.

## O<sub>3</sub>

The results for ozone can be found on Supplemental Table 2. The monthly interaction terms were utilized to empirically group June, July, August, February, and March into a single group. Overall, a one IQR increase in ozone (0.017 ppm) resulted in a 4.7% increase in asthma ED visits during these months. April, May, September, and December were placed into the second group. No association between ozone and asthma ED visits was observed during this time. Finally, October and November were placed in the third group, wherein there was also no observed association between ozone and asthma ED visits.

## CO

Supplemental Table 3 displays the results for CO. Monthly group 1 that consisted of January, March, October, November, and December and demonstrated no relationship with

**Table 3** Nitrogen dioxide to asthma emergency department visits rate ratios, Poisson GLM final model, and Poisson GLM preliminary monthly interaction term

	Rate ratio for monthly groupings		Final model		Preliminary monthly interaction model		
	Rate ratio	95% CI	Estimate	95% CI	Interaction	Estimate	95% CI
Monthly Group 1	1.12	1.05–1.18	0.012***	0.006 to 0.018			
Monthly Group 2	1.02	1.01–1.03	0.004*	0.000 <sup>a</sup> to 0.007	June*NO <sub>2</sub>	0.014**	0.004 to 0.023
					July*NO <sub>2</sub>	0.006	– 0.004 to 0.016
					February*NO <sub>2</sub>	0.005*	.000 <sup>a</sup> to 0.010
					September*NO <sub>2</sub>	0.005	– 0.001 to 0.011
					August*NO <sub>2</sub>	0.004	– 0.007 to 0.014
					January*NO <sub>2</sub>	0.003	– 0.002 to 0.008
					October*NO <sub>2</sub>	0.003	– 0.002 to 0.008
					March*NO <sub>2</sub>	0.003	– 0.002 to 0.008
Monthly Group 3	1.00	0.97–1.04	0.001	– 0.003 to 0.004	May*NO <sub>2</sub>	0.001	– 0.005 to 0.007
					April*NO <sub>2</sub>	– 0.000 <sup>b</sup>	– 0.005 to 0.005
					November*NO <sub>2</sub>	– 0.001	– 0.006 to 0.004
					December*NO <sub>2</sub>	– 0.001	– 0.007 to 0.005
Intercept			2.686***	1.385 to 3.987			
Lag1			0.078***	0.033 to 0.122			
Lag2			0.072**	0.028 to 0.117			

Final model adjusted for temperature, wind speed, and relative humidity

GLM generalized linear model

\*  $p < 0.05$ , \*\*  $p < 0.01$ , \*\*\*  $p < 0.001$

<sup>a</sup>Actual value greater than zero, rounded to 3 decimal places

<sup>b</sup>Actual value less than zero, rounded

<sup>c</sup>Actual number less than 1.00, rounded

ambient CO. Monthly group 2 included February, June, July, August, and September. Asthma ED visits in this pseudo-season grouping demonstrated a 1.6% increase for every 0.075 ppm increase in ambient CO. April was the only month in Group 3 and demonstrated a decreased rate in asthma ED visits with increased ambient CO.

For the single-pollutant models, the Ljung–Box test up to six lags were non-significant ( $p = 0.447$ – $0.688$ ), indicating we had adequately controlled for temporal dependence in the Poisson GLM model with two log lags added, along with the other weather and time covariates listed in the methods section.

### Sensitivity analysis and multi-pollutant model

The sensitivity analysis was conducted by testing the same model unadjusted and by transforming the pollutant by using cubic time, quarterly (four per year) knots, and monthly knots. The best model (using monthly knots) was selected using the Akaike information criterion (AIC). The relationships of PM<sub>2.5</sub> and ED asthma visits

remained consistent. CO did not reach significance with time constraints, and the magnitude and significance of NO<sub>2</sub> and ozone were reduced the more closely time was constrained. Given the substantial differences among the months, and evidence of unmeasured confounding and difficulty ascertaining adequate knots and degrees of freedom to capture the true underlying relationships and need to constrain monthly variability, a multi-pollutant model was not attempted, nor were subgroup analyses conducted. Multi-pollutant models are often not supported due to strong correlations between pollutants (Woodruff et al. 2009) which have demonstrated attenuated effects (Strickland et al. 2016).

### Community-based participatory research

An infographic was created and disseminated by local community groups with a focus on the education regarding the fall epidemic of asthma exacerbations and disparity for working-aged women.



**Table 4** Fine particulate matter to asthma emergency department visits rate ratios, and Poisson GLM final model, and Poisson GLM preliminary monthly interaction term

	Rate ratio for monthly groupings		Final model		Preliminary monthly interaction model		
	Rate ratio	95% CI	Estimate	95% CI	Interaction	Estimate	95% CI
Monthly Group 1	1.04	1.02–1.06	0.007***	0.004 to 0.010	March*PM 2.5	0.010**	0.004–0.017
					June*PM 2.5	0.008**	0.003–0.013
					February*PM 2.5	0.008*	0.001–0.016
					July*PM 2.5	0.007**	0.002–0.011
					August*PM 2.5	0.006*	0.001–0.011
Monthly Group 2	0.99	0.96–1.02	– 0.001	– 0.004 to 0.002	January*PM 2.5	0.00 <sup>a</sup>	– 0.00 <sup>b</sup> to 0.01
					May*PM 2.5	0.00 <sup>a</sup>	– .00 <sup>b</sup> to .00 <sup>a</sup>
					April*PM 2.5	0.00 <sup>a</sup>	– .00 <sup>b</sup> to 0.01
					December*PM 2.5	– 0.00 <sup>b</sup>	– 0.01 to 0.01
					September*PM 2.5	– 0.00 <sup>b</sup>	– .00 <sup>b</sup> to .00 <sup>a</sup>
					October*PM 2.5	– 0.00 <sup>b</sup>	– 0.01 to .00 <sup>a</sup>
					November*PM 2.5	– 0.00 <sup>b</sup>	–0.01 to .00 <sup>a</sup>
Intercept			2.949***	1.732–4.166			
Lag 1			0.066***	0.024–0.108			
Lag 2			0.068**	0.026–0.110			

GLM generalized linear model

\*  $p < 0.05$ , \*\*  $p < 0.01$ , \*\*\*  $p < 0.001$

<sup>a</sup>Actual value greater than zero, rounded

<sup>b</sup>Actual value less than zero, rounded. Final model adjusted for temperature, wind speed, and relative humidity

## Discussion

### Main findings

The purpose of this study was to identify criteria air pollutants that increased the risk of an ED visit for asthma in Erie County, New York, from 2007 to 2012. We found that the overall 6-year trend in asthma ED visits was grossly unchanged and associated with increases in air pollution only during specific months and monthly groupings. These monthly groupings tended to include most summer and winter months together and were selected because the statistical interaction for the months were very similar when testing the pollutant to emergency department visits relationships. This research adds to the body of evidence in three important ways: (1) we studied a time period that included a unique natural experiment of an EPA raid and state environment agency action on a polluting factory; (2) we utilized a novel operational definition of an asthma ED visit and seasonal groupings; (3) we found that specific months and monthly groupings provided the highest risk for a pollutant-associated ED asthma visit.

### Description of the ED visit time series

The time-series (statistically stationary) indicated that the changes in industrial emissions did not produce a signal in asthma ED visits that could be grossly detected at the ecological, county-level over the 6-year period. In unadjusted testing of the average daily visits, by two groups of days before and after January 1, 2010 (the EPA raid occurred in December of 2009 with follow-up regulatory activity in January), there were approximately five more asthma ED visits in the second half of the study. There are several unmeasured plausible explanations for this increase, such as traffic-related pollution, changes in cigarette smoke exposure or healthcare access, changes in medical coding, or population shifts in those diagnosed with asthma over time. The temporal fluctuations in our data, with a fall asthma exacerbation epidemic that corresponds with rhinovirus and back-to-school season, spring allergy, and RSV infection seasons are similar to previous study (Johnston et al. 2006; Johnston and Sears 2006; Moineddin et al. 2008). Respiratory infection is the most common reason for asthma exacerbation and may both mask and increase susceptibility to the impact of

ambient air pollution (Linaker et al. 2000). Previous studies have documented that the adult exacerbations are delayed until after a spike in children is observed, suggesting children spread fall infections to adults and the magnitude of the fall epidemic was declining (Johnston et al. 2006; Johnston and Sears 2006). Our study, completed a decade later, is contrary to this prediction and does not demonstrate a decline in fall asthma exacerbations (particularly in 2009), but provides supporting evidence that adult women are the demographic that strongly influence or determine the population pattern (Moineddin et al. 2008). In particular, the volume of ED asthma visits by working-aged women reveals the need to include focused interventions, often directed at children, towards this demographic.

### Methodologic approach

In this present study, we utilized a novel methodologic approach to include the first three billing codes to define an asthma ED visit. Asthma is typically defined as the first billing code in ecological studies with similar design to the present study, which would have included less than half (30,531) of the total visits utilized for this present study. The majority of the outpatient ED visits (visits that did not lead to hospitalization) were characterized by an initial diagnosis code of an ill-defined condition or symptom such as cough, wheeze, chest pain, or shortness of breath. Our method is justified because asthma may be exacerbated by another condition, such as infection, and using the primary billing code would exclude such visits. Because the primary purpose of emergency care is to stabilize the acute, presenting condition, there may be medical-legal reasons to code the visit as a symptom-based encounter. Our method enables greater sensitivity, but may sacrifice specificity in capturing asthma ED visits. Because the operational definition of ED asthma visit used in our study did include potentially non-related visits, such as sprains and fractures with a secondary diagnosis of asthma, further work is warranted to refine the first code used to enhance specificity.

Methodologically, many studies have controlled for seasonal epidemics and an anticipated difference in the effect of pollutants by stratifying analysis by warm and cold season or traditional conceptualizations of autumn, spring, winter, and summer (Delfino et al. 2014; Kloog et al. 2014; Kousha and Rowe 2014; Sacks et al. 2014; Stieb et al. 2009). Additional seasonal control may be achieved by using a case-crossover design. In this present study, we focused on month-by-pollutant interactions to allow novel empirical monthly groupings into pseudo-seasons for times of year when the pollutant–visit interaction were similar. The data-driven method to group months by empirical similarities, rather than traditionally conceptualized seasons, enabled a more nuanced understanding of high-risk times for ambient

air pollution and asthma. We found specific months (such as June), or monthly groupings, provided the highest risk for a pollutant-influenced asthma ED visit. Our results support previous studies that pollutants in warm season are associated with greater ED asthma visit risk, despite that overall asthma ED visits peak in the autumn. This is conceptually coherent with increased exposure during the warm season, when individuals are more likely to be outdoors and/or have windows open to allow for indoor and outdoor air exchange. These results can assist practitioners to target risk communication for avoiding pollutants to high-risk times or seasons. However, further research is needed to elucidate if these observed relationships are due to uncontrolled confounding or model misspecification (Alhanti et al. 2016; Darrow et al. 2014; Lavigne et al. 2012; Szyszkowicz and Kousha 2014).

### Pollutant by month and monthly grouping associations

In our present study, we observed positive and statistically significant associations between NO<sub>2</sub>, PM<sub>2.5</sub>, O<sub>3</sub>, CO, and ED asthma visits with different patterns of monthly interactions. CO was the only pollutant with higher measures in the second half of the study, and the only pollutant with a negative association to asthma ED visits (and even then only in the month of April). All pollutants' associations were positive and statistically significant in the month of June. The strongest association was NO<sub>2</sub> in June, linked to a 12% increase in asthma ED visits. For PM<sub>2.5</sub> and O<sub>3</sub>, there were similar associations in the winter months of February and March along with the summer months of June, July, and August. Empirically grouping these months together for their similar interactions as summer/winter representation, there were significant relationships with PM<sub>2.5</sub> and O<sub>3</sub>, respectively, with asthma ED visits. Perhaps because of the stronger magnitude of the relationship between NO<sub>2</sub> and asthma ED visits, the monthly grouping that demonstrated a relationship to asthma ED visits extended to include January and October. Consistently, no relationship between the pollutants of NO<sub>2</sub>, PM<sub>2.5</sub>, and O<sub>3</sub> and asthma ED visits were observed in the spring months of April/May, nor late autumn months of November/December. CO demonstrated the weakest and least consistent relationship among the pollutants, with notable spikes on the visual inspection of the time-series in the second half of the study. Closer to the factory site that had been the focus of regulatory activity, additional pollutants, such as formaldehyde, had also demonstrated increases in the later years of the study period and were attributed to field observations of increased diesel truck traffic (New York State Department of Environmental Conservation 2016). Based on the overall ED visit pattern, it is plausible that seasonal respiratory infections and allergy season, along with low-risk times of year for O<sub>3</sub> formation,

masked the potential relationships of pollutants to asthma ED visits.

Ecological studies utilizing exposure data from centrally located stationary monitors contribute knowledge to temporal patterns of exposure to inform policy and future intervention. However, this type of study does not establish causation of a single person's asthma attack or ED visit (Strickland et al. 2011). Individual air pollutants measured by central, stationary monitors are often highly correlated, may be released by the same or similar source, may act as proxies for one another, and chemically interact to form one another. Because people inhale a mix of pollutants in their natural environments, studies of single pollutants are thought to misclassify exposure (Gass et al. 2015; Szyszkowicz and Kousha 2014). While some dual or multi-pollutant models have demonstrated a stronger magnitude of effect on health outcomes, (Kousha and Castner 2016; Szyszkowicz and Kousha 2014) evidence in asthma-specific studies remain mixed and inconsistent (Gass et al. 2015; Tolbert et al. 2000).

The relationship of pollutants CO and NO<sub>2</sub> with asthma exacerbations in our study was consistent with previous studies (except for the negative relationship for CO in April), and is highly influenced by traffic patterns, which is difficult to separate from industry activity in ecological study (Darrow et al. 2011). CO demonstrated special heterogeneity and increases over time in our examination of correlations among county monitors, and additional study at finer geographic resolution is warranted. PM<sub>2.5</sub> demonstrated the most consistent association with asthma ED visits, regardless of how time was constrained in sensitivity analyses of the model. This is expected as PM<sub>2.5</sub> was the only pollutant that we averaged over several area monitors, because the values were highly correlated. PM<sub>2.5</sub> can travel long distances and may represent pollution that may originate outside of the county, with wide dispersion and less potential heterogeneity than the gaseous pollutants. As expected, the relationship of O<sub>3</sub>, formed by sunlight, was strongest in the warmer months. O<sub>3</sub> also has germicidal properties, and the interaction of respiratory infection and air pollutants requires further study.

Our data did not support proceeding to a multi-pollutant model. Multi-pollutant models are theoretically enticing, but individual pollutant effects are reasonable as previous studies have often demonstrated a single-pollutant, rather than a synergistic or multiplicative effect (Gass et al. 2015). In addition, single-pollutant models are coherent for translation to regulatory policy to establish acceptable standards of pollutant levels (Di et al. 2017).

It is particularly noteworthy that the associations with air pollutants were observed during times of overall low asthma ED volume. The results were not consistent in our sensitivity analysis using quarterly and monthly knots, indicating the temporal trend between month and season overshadows

the potential associations between the asthma ER visits and pollutants.

### Contextualized in evidence of biological plausibility and policy

The mechanistic pathway and biological plausibility for how low levels of air pollution cause asthma exacerbations for those with genetic predisposition include cellular damage caused by oxidative stress, airway remodeling, immune response with inflammatory pathways, and increased sensitization to subsequent allergens and infectious agents (Guarnieri and Balmes 2014). More research is needed to evaluate the most relevant exposure measure in ecological studies, such as peak exposure (daily maximum measure) or a 24-h average (Darrow et al. 2011).

Our findings have policy implications. The enforcement actions by the federal and state environmental agencies led to a reduction in hydrocarbon emissions, such as benzene, a potent precursor that combines with nitrogen oxides to form ground level ozone (New York State Department of Environmental Conservation 2009). The American Thoracic Society (ATS) has recommended more stringent guidelines for ozone and particulate matter to further lower the pollutant threshold levels (Cromar et al. 2016). This study adds evidence to also use more stringent controls for pollutants NO<sub>2</sub>, PM<sub>2.5</sub>, and O<sub>3</sub> associated with ED asthma use. According to the ATS online tool, available at <http://www.healthoftheair.org>, if the metropolitan area in this study (Buffalo–Niagara region) were to reduce ozone to recommended ATS levels, the region would experience 35 fewer overall annual deaths and 66,380 fewer adverse health events such as an emergency department visit for asthma.

### Conclusion

In conclusion, we did not identify a change in ED asthma utilization as a result of air pollution decline over the full 6-year study period. The association of air pollution with ED visits for asthma may be masked by other, more influential triggers with marked temporal monthly or multi-month patterns. NO<sub>2</sub> in June demonstrated the strongest relationship, associated with a 12% increase in asthma ED visits. Several summer and winter months, when grouped together, demonstrated that O<sub>3</sub>, PM<sub>2.5</sub>, CO, and NO<sub>2</sub> were associated with 5, 4, 2, and 2% increases in asthma emergency visits, respectively. We used a novel approach to define high-risk months and air pollutants for a more nuanced understanding of the pollutant–asthma ED relationships by particular times of year. Our study informs future work to identify individualized susceptibility to air pollution triggers, applications to more closely monitor symptoms at high-risk times, public



health prevention at the beginning of the school year, and healthcare operations to prepare for high-volume spikes.

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**Author contributions** JC and YY contributed to the concept, design and analysis of the data. LG contributed to the analysis and interpretation of the data. JC drafted the paper and all authors contributed to the revision and final approval.

#### Compliance with ethical standards

**Ethical approval** Relevant ethical approval was obtained from the New York State Data Protection Review Board (#1403-05) and the University at Buffalo's Institutional Review Board.

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