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PAPER

Air pollution indicators predict outbreaks of asthma exacerbations among elementary school children: integration of daily environmental and school health surveillance systems in Pennsylvania

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Objectives of this study are to determine if a relationship exists between asthma exacerbations among elementary school children in industrialized countries (with climatic seasons) and exposure to daily air pollution with particulate matter, sulfur dioxide, nitrogen dioxide, nitrogen oxides, carbon monoxide, and ozone, when controlled for potential confounders; and, if so, to derive a statistical model that predicts variation of asthma exacerbations among elementary school children. Using an ecological study design, health records of 168 825 students from elementary schools in 49 Pennsylvania counties employing "Health eTools for Schools" were analyzed. Asthma exacerbations were recorded by nurses as treatment given during clinic visits each day. Daily air pollution measurements were obtained from the EPA's air quality monitoring sites. The distribution of asthmatic grouping for pollen and calendar seasons was developed. A Poisson regression model was used to predict the number of asthma exacerbations. The greatest occurrence of asthma exacerbations was in autumn, followed by summer, spring and winter. If the number of asthma exacerbations on a day is N and the daily mean of asthma exacerbations for the three-year period is 48, the probabilities of $N > 48$ in tree pollen and grass pollen seasons were 56.5% and 40.8%, respectively ($p < 0.001$). According to the Poisson regression, the week number and prior day CO, SO_2, NO_2, NOx, $PM_{2.5}$, and O_3 had significant effects on asthma exacerbations among students. Monitoring of air pollutants over time could be a reliable new means for predicting asthma exacerbations among elementary school children. Such predictions could help parents and school nurses implement effective precautionary measures.

Introduction

Asthma, a chronic inflammatory disease of the airways that typically starts early in life,[1] is the most common chronic childhood illness, affecting nine million individuals in the U.S. below the age of 18 years. According to the 2006 Pennsylvania BRFSS survey, asthma prevalence among children (18 years and younger) was 8.4% (approximately 231 157 children) as compared to the 9.0% overall U.S. prevalence. The lifetime asthma prevalence among children in Pennsylvania was 12.0%

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Environmental impact

The purpose of this research is to determine if a relationship exists between asthma exacerbations among elementary school children and exposure to daily air pollutants. Our study findings will be useful in emphasizing the need for reducing air pollution. Environmental health interventions can make valuable and sustainable contribution towards reducing asthma among school children and improving the well-being as well as overall performance of children in general. Many of those interventions are cost-effective and have benefits beyond improving children's health. Especially, asthma prevention and control will improve the quality of their adult life as well. Economic returns of a better respiratory health are the keys to motivate leaders in reducing air pollution. Frequent asthma exacerbations of children are also matters of deep concern to parents and will have the power to galvanize in pursuit of reducing air pollution.

(approximately 331 033 children); the national prevalence was 12.8%.[2] Based on information from school nurses, a large scale study revealed that 9.7% of elementary school students (ages 4 through 12 years) in Connecticut had asthma.[3] No previous research study of asthma prevalence was found for this particular age group in Pennsylvania. Due to the rapid development of the respiratory system early in life, children with asthma are particularly at risk of adverse health effects due to pollutant exposure.

Asthma can have a tremendous negative impact on a child's health and quality of life as well as school attendance and performance, including hospitalization, emergency room visits, difficulty sleeping, and activity restrictions.[4] Among U.S. children aged 5 to 17 years, asthma is the leading cause of school absences from a chronic illness,[5] amassing an annual loss of more than 14 million school days per year (eight days per asthmatic student).[6] Asthma accounts for more pediatric hospital admissions and emergency department (ED) visits than any other childhood disease.[7] Proportionally, asthma-related intensive care unit admissions were greatest in the Western U.S., followed by the Midwest, the Northeast, and the South.[8]

The U.S. spends $18 billion annually for asthma care.[8] This massive burden may be a result of greater exposure to air pollutants,[9–13] increased influence of other risk factors, such as infections,[14] pollen,[15–17] and obesity,[18] or improved care. In Pennsylvania, predictors of frequent asthma exacerbations were found to be (a) having Medicaid or Medical Assistance indicative of poverty, (b) lower level of education, (c) higher number of previous office or clinic visits, (d) greater number of household members, and (e) living in Philadelphia.[19] Additional as yet unidentified factors may also play a role. Factors that may contribute to seasonal patterns in asthma morbidity include changes in surface temperature, seasonal viral infections, variation in tree, grass, and weed pollen counts, and fluctuations in the amount of fungal spores and house dust mites.[20] Additionally, a higher amount of airborne water droplets may be a stimulus for bronchoconstriction. Asthmatic children frequently visit the emergency department during early mornings with high absolute humidity and a higher atmospheric temperature.[21]

Epidemiologic studies have proven that air pollution is associated with increases in asthma-related hospital admissions.[10] The aim of the current study was to determine if a relationship exists between asthma exacerbations among elementary school children and exposure to daily air pollution when controlled for potential confounders; and, if so, to derive a statistical model that predicts variation of asthma exacerbations among elementary school children based on air pollutant levels on the previous day. The current study investigated the possible relationship between the burden of asthma exacerbations among elementary school children in Pennsylvania on a particular day, as determined by school health records, and the measurements of routine air pollution indicators throughout the day: particulate matter with a diameter of <10 and <2.5 micrometers (PM_{10} and $PM_{2.5}$ respectively), sulfur dioxide (SO_2), nitrogen dioxide (NO_2), nitrogen oxides (NOx), carbon monoxide (CO), and ozone (O_3), with findings adjusted for pollen season and climatic variations. Subsequently, a statistical model was developed to estimate and predict the daily asthma burden based on air pollution measurements on the previous day.

Methods

Research design

Ecological study design was adopted in order to better understand the relationship between daily occurrence of asthma in a "whole population" of elementary school students and daily measurements of air pollution parameters.[22] In the current study, which investigates group level variables, Pennsylvania was analyzed in a cross-sectional manner, repetitively, to explore the variation in the number of asthma exacerbations in elementary schools across the entire state and its associations with average air pollutant levels for the state.[22] More specifically, air pollution variables do not have corresponding individual level values and can only be investigated at the group level (integral variables). Ecological design enabled control of individual level variability while at the same time addressing influences at the state level. In addition, this study design enabled researchers to include all the students of the enrolled elementary schools in the study sample, contrary to a study design in which each asthmatic student serves as his/her own control and excludes non-asthmatic students.[22]

Study population

School health records have been utilized for asthma tracking because school-based asthma surveillance is a reliable and cost-effective method for accessing the existing school health system infrastructure.[23] "Health eTools for Schools" (hereafter referred to as "eTools") is a Coordinated School Health (CSH) web-based software application portal developed by a private, for-profit company called InnerLink, Inc. with the utilitarian purpose of providing data for state and local health planning. Implemented in approximately 1100 schools located in districts from 49 of the 67 Pennsylvania counties, eTools is used by nurses, physical education teachers, and other staff members to routinely collect student health records, physical fitness assessments, and other types of data. From 2008 to 2010, enrolled school districts received eTools services for 168 825 elementary school students who constituted the study population. Elementary schools in North America are equivalent to primary schools in many other countries. These schools are where children receive the first stage of compulsory primary education and include pre-kindergarten through fifth grade students (ages 4 through 12 years). All eTools services for participating school districts were subsidized by the funders of eTools, the Highmark Foundation. Schools that met participation criteria were covered under the subsidy program during the three-year period and were considered for participation on a first-come, first-served basis.

At the individual level, the sole participation eligibility requirement was to be a student with a health record in an elementary school that utilized eTools. Student records from these schools were excluded if they contained incomplete or inaccurately entered health record data. In addition, no gender-, race-, ethnicity-, area-, or income-based bias existed in the enrollment of school districts, schools, or students in eTools[24] as shown in Table 1, which is approximately equal to the student distribution across all school systems in Pennsylvania.[25] Previous research determined that a school nurse was available for at least 8 hours per week in 91% of rural and 96% of urban elementary schools in Pennsylvania. Students with asthma had access to

Table 1 Demographic characteristics of students within school districts enrolled in the eTools system[a]

Demographic variable	Student category	Percentage
Gender	Males	50.80
	Females	49.20
Race	White alone	74.78
	African-American alone	8.30
	Hispanic alone	7.91
	Asian alone	1.41
	American-Indian and Alaska native	0.20
	Native Hawaiian and other Pacific Islander	0.03
	Other	3.10
	Multi-race	4.27
Socioeconomic status	Free or reduced-price lunch eligible students	38.36
	Free or reduced-price lunch ineligible students	61.64
Urban–rural distribution	Rural school students	39.22
	Suburban school students	42.65
	Urban school students	18.13

[a] Sources: (1) School District Demographic System – Map Viewer, National Center for Education Statistics, Institute of Education Sciences, 2012 (ref. 25); (2) eTools Schools Demographic Characteristics, Highmark Foundation.[24]

inhalers at the school health office in 91% of rural and 93% of urban elementary schools.[26] In general, the nurses in rural schools served schools several miles apart from one another and therefore were more likely to assign other school staff members nursing functions when the nurse was not present at the school.[27] A staff member who knew how to treat asthma attacks was always available in 84% of urban schools and in 81% of rural schools.[26] However, nurses did not record treatments carried out in their absence. All of the above factors are important with respect to the generalizability of study results to elementary school students at the state level or outside of Pennsylvania.[22]

Data collection

Within the 49 Pennsylvania counties, 168 825 records of elementary school students were identified. Data on asthma were originally noted in records maintained by school nurses as the type of treatment given to a student on a particular day. Treatment options for school health nurses were based on the prescribed medication provided for the student. For the purposes of this study, having asthma was defined as "any case managed with antiasthmatic medications." Antiasthmatic medications refer to medications that treat or prevent asthma attacks (*e.g.*, bronchodilators, inhaled corticosteroids). Some children were prescribed only one drug category, while others were prescribed drugs from both categories and, sometimes, even more. Therefore, separation of different categories of antiasthmatic drugs was judged to be very unlikely to contribute to the findings of this study. In fact, school nurses recorded the trade names of all the medications administered, which were later categorized into functional groups (*i.e.*, antiasthmatics, analgesics, *etc.*). It was assumed that the treatment option noted by a school nurse correctly represented the disease.

Data analyzed for this study were provided by InnerLink, Inc. which had custodial responsibility under a common Statement of Understanding and Service Level Agreement with all participating school systems. Data pertaining to total use of antiasthmatic medications at the school level were unavailable. The school year in Pennsylvania usually begins in August, ends in June, and typically includes an extended winter break. Therefore, surveillance data were commonly unavailable for the last three weeks of June, all of July, the first three weeks of August, and the second half of December every year. The selected schools were scattered throughout the state except for some counties in the northeast and southeast regions where eTools is not available (Fig. 1). The daily mean of asthma exacerbations for the period of three years was used to negate the effect of year-to-year variations in the number of participating schools in Pennsylvania.

Pennsylvania State regulations require a child of school age who desires to possess and self-administer an asthma inhaler in a school setting to demonstrate the capability to self-administer medication using an inhaler and to do so responsibly.[28] While technically allowed on an individual basis at any age, asthma medication self-administration is less likely to occur among elementary students due to the regulatory stipulation of developmentally appropriate restrictions.[29] Hence, only data from elementary school students' records were included in this study. To safeguard student rights, all U.S. school districts, including those in Pennsylvania, must collect and maintain all student academic and health records in accordance with provisions of the federal Family Educational Rights and Privacy Act (FERPA).[30]

Hourly data on seven air pollutants collected at EPA measurement stations all over the state, 48 stations on average per day with 908 readings per day, were downloaded from the EPA website (http://www.epa.gov/ttn/airs/airsaqs/detaildata/downloadaqsdata.htm). These were obtained for school days only, although the data are available for all days throughout the period 2008–2010. EPA air pollution monitoring stations across the state utilize the same units of measurement: the units of SO_2 and NO_2 were in parts per billion (ppb); the units of CO, O_3, and NOx were in parts per million (ppm), and the units of $PM_{2.5}$ and PM_{10} were in micrograms per cubic meter (μg m^{-3}). On average, 46 stations measured pollutants every day (Fig. 2). Available EPA data contained no missing values.

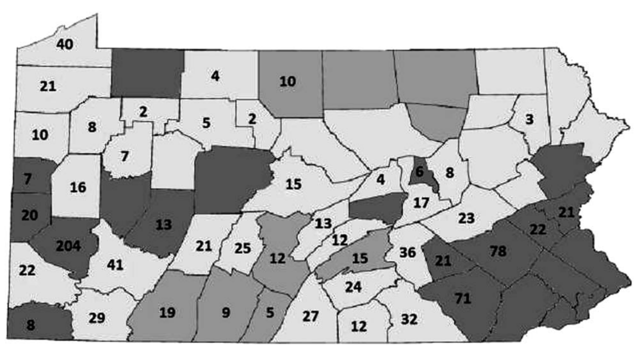

Fig. 1 Distribution of eTools-enrolled schools in Pennsylvania and air quality by county. Numbers indicate the sum of eTools-enrolled schools in each county. Dark grey = very unhealthy or hazardous air quality (AQI > 200). Medium grey = unhealthy air quality (AQI 151-200). Light grey = unhealthy for sensitive groups (AQI 101-150). None of the counties in Pennsylvania has moderate or good air quality (AQI < 101).

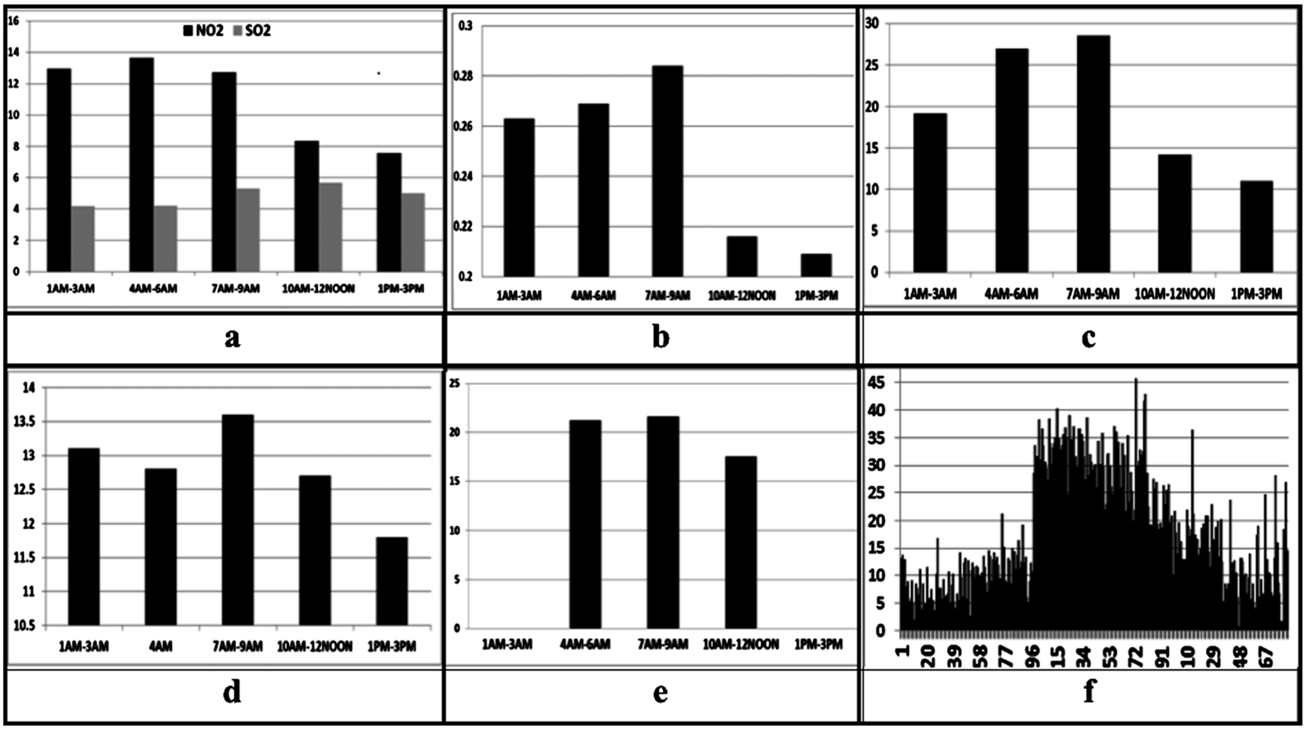

Fig. 2 Mean NO_2 (2a), SO_2 (2a), CO (2b), NOx (2c), $PM_{2.5}$ (2d), and PM_{10}* (2e) concentrations for three-hour periods before school hours and during school hours (1 AM to 3 PM), as well as variation of daily mean of O_3 concentration** throughout the year (2f), 2008–2010$^{¥}$. *PM_{10} data were not available for 1 AM to 3 AM and 1 PM to 3 PM time intervals. **The horizontal axis of (2f) (ozone) is the "school day of the year" (varies between 1 and 284). $^{¥}$The unit of NO_2 and SO_2 was parts per billion (ppb), while the unit of CO, NOx, and O_3 was parts per million (ppm). The unit of $PM_{2.5}$ and PM_{10} was micrograms per cubic meter (μg m^{-3}).

To adhere to ecological study design, the average over all monitoring stations was used as was the average over all schools for asthma data. The relationship between air pollutants and asthma exacerbations was controlled for potential confounders: pollen season (an asthma trigger) and the date of the year (a proxy composite measure of climatic variations). As pollen seasons have an identical pattern across years according to information obtained from the www.pollen.com website, March–July (3rd to 7th month) was considered "tree pollen season" and August–October (8th to 10th month) was considered "grass pollen season." The remaining months were considered "no pollen season."[31]

Analysis

A Poisson regression model was developed to explain the predictors' effects (including air pollutant concentrations and pollen levels) on the number of asthma exacerbations on the next day. The initial Poisson regression model is a function of a set of predictors:

If "X" is a (k + 1)-dimensional vector consisting of "k" independent predictor variables (*e.g.*, CO, SO_2, and NO_2) concatenated to some constant, then the model takes the following form: $\log_e(E(C|X)) = a + bX$, where a and X belong to R^k; b belongs to R; "e" is 2.718 approximately; and "C" is the daily count of asthma exacerbations. Hence, the predicted value of the associated Poisson distribution is given as $E(C|x) = e^{a+bx}$.

A Poisson regression, repeated measure approach (*i.e.*, Generalized Estimating Equation, SAS-9.31 Genmod procedure) was used in order to include three exposure measures over the three years, where the repeated subject was the "same day of year." Poisson regression allows the rate of asthmatic students in pre-kindergarten through fifth grade (ages 4–12 years) to depend on numerical and non-numerical predictors through a nonlinear link function (log function) with Poisson response probability distribution, and it also facilitates analysis of correlated data arising from repeated measurements when the measurements are assumed to be multivariate normal.

Modeling predictors were air pollutant levels (*e.g.*, overall daily mean of each pollutant), an environmental-related variable (*e.g.*, "pollen season"), and time-related variables (*e.g.*, "week number" and "month number"). The week number varied from 1 to 52, while the month number varied from 1 to 12. For assessing model goodness of fit, the Pearson Scale was used to maintain the over-dispersion. The model fit was established *via* backward stepwise selection. The independent variables and their interactions were kept within the model if they reached significant probability ($p < 0.05$).

The model variables were established *via* backward selection by initially entering the seven variables—PM_{10}, $PM_{2.5}$, CO, NOx, NO_2, SO_2, and O_3—based on scaled deviance criterion (*i.e.*, the closer a criterion was to "1" the greater was the likelihood of model selection). Then, variables with non-significant effects were excluded. After that, variable interactions were entered one by one to the model, keeping only those that had significant p-values ($p < 0.05$). The Wald statistic was used in the Genmod procedure type-3 to assess parameter significance. In order to assess statistical significance of the seven explanatory variables at the 0.05 confidence level (or less), 284 clusters (with only three clusters having

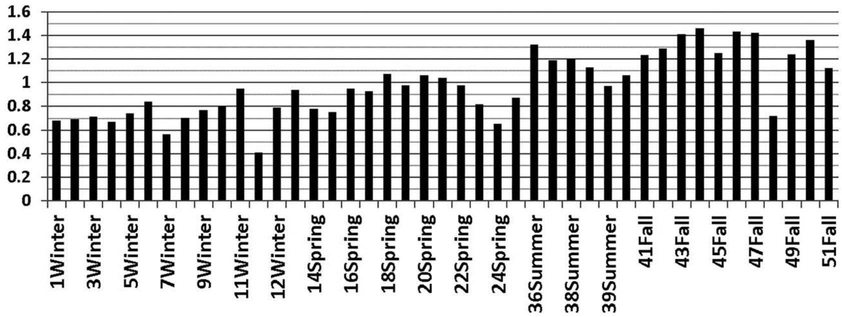

Fig. 3 Antiasthmatic use among elementary school students, 2008–2010: ratio of weekly mean to annual mean for the three year period. *No data available for the period between 25th and 34th weeks of the year due to summer vacation; no data available for the last (52nd) week of the year due to winter break.

missing values) were used for this model after excluding weekends, holidays, winter break, and summer vacation. Having a considerably larger number of clusters (284 repeated subjects) in this study than the required number (40 clusters) reduced the type-1 error.[32] The quasi-likelihood information model criterion (QIC), which is available as part of the Genmod procedure of SAS 9.3, was used to choose the best correlation structure matrix and also to select the best subset of covariates (*i.e.*, smallest QIC implies best structure matrix).

The model was fit with a scaling factor specified to adjust for the over-dispersion. The scale parameter (3.5484) was estimated by the square root of Pearson's Chi-square divided by the degree of freedom. Using Pearson's Chi-square, the scaled deviance was made close to 1 (1.0238). The model was adjusted for over-dispersion so that any inference will not be questionable.

Fig. 3 presents the ratio of weekly mean to annual mean of antiasthmatic medication use among elementary school students over the three years. In order to minimize the effect of the increase in asthma reporting over time, the ratio of weekly mean of asthma exacerbations to the annual average was used instead of the absolute number of asthma exacerbations per week. This served to minimize the impact of distortion caused by the annual variation in the number of schools using eTools on the weekly pattern of asthma exacerbation occurrences.

Two cross-tabulation tables were developed to check the conditional probability of days with higher and lower numbers of asthma exacerbations in different seasons (Table 3: pollen seasons and Table 4: calendar seasons). The first group represents days of asthma cases <48 and the second group represents days of asthma cases ≥48. The value (48) is the daily mean of asthma exacerbations for the period 2008–2010. Chi-square statistics were used to test significant differences.

Human subjects' approval statement

This study was approved by the Indiana University Bloomington Institutional Review Board.

Results

The mean number of asthma exacerbations per day was 48 for the 2008–2010 time period. A gradual increase of asthma exacerbations was observed from 2008 to 2010, both in elementary schools and in schools with higher grades (Table 2). This is partially explained by the increase in the number of schools participating in the asthma surveillance system. The total number of schools (elementary, middle, and high) increased from 2008 to 2009, with a slight decrease from 2009 to 2010. However, an increase from 9.2% to 17.5% (90%) in the percentage of all

Table 2 Visits to school health nurses due to asthma as reported by school nurses in Pennsylvania elementary schools, 2008–2010

Year	Number of elementary schools in eTools	Annual asthma visits	Average of asthma visits on one school day	Number of asthma visits per 100 schools on one school day
2008	471	4332	22	5
2009	675	8921	47	7
2010	621	14 178	70	11

Table 3 Daily mean of asthma exacerbations by pollen season and by calendar season[a]

Overall mean and median of asthma exacerbations, 2008–2010				
N	Mean	Median	95% confidence interval	
570	48	45	45	50
Daily mean of asthma exacerbations by pollen seasons				
Pollen season	*n*	Mean	95% confidence interval	
Tree pollen	200	54	51	58
Grass pollen	206	47	43	52
No pollen	165	40	36	43
Daily mean of asthma exacerbations by calendar season				
Calendar season	*n*	Mean	95% confidence interval	
Fall	179	56	53	59
Winter	169	38	34	41
Spring	165	48	43	52
Summer	58	52	44	60

[a] Note: classifying pollen season was based on "month number" conditions: if "month number" = 3, 4, 5, 6, or 7, then pollen season = "Tree Pollen"; if "month number" = 8, 9, or 10, then pollen season = "Grass Pollen"; if "month number" = 1, 2, 11, or 12, then pollen season = "No Pollen."

Table 4 Distribution of days with low and high rates of asthma exacerbations by pollen season[a] and calendar season[b]

Category of days by the number of exacerbations		Pollen season[a] Tree pollen	Grass pollen	No pollen	Total
Exacerbations < 48 (below mean)	Frequency	87	122	105	314
	Column %	43.5	59.2	63.6	55.0
Exacerbations ≥ 48 (above mean)	Frequency	113	84	60	257
	Column %	56.5	40.8	36.4	45.0
Total	Frequency	200	206	165	571
	Row %	35.0	36.1	28.9	100

Category of days by the number of exacerbations		Calendar season[b] Fall	Spring	Summer	Winter	Total
Exacerbations < 48 (below mean)	Frequency	72	98	29	115	314
	Column %	40.2	59.4	50.0	68.05	55.0
Exacerbations ≥ 48 (above mean)	Frequency	107	67	29	54	257
	Column %	59.8	40.61	50.0	31.95	45.0
Total	Frequency	179	165	58	169	571
	Row %	31.4	28.9	10.2	29.6	100

[a] Chi-square = 0.0002. [b] Chi-square < 0.0001.

Table 5 Modeling the probability of the number of asthma exacerbations among elementary school students on a particular day based on seven pollutant parameters by Poisson regression and empirical standard error estimates[a]

Parameter	Estimate	Standard error	Wald 95% confidence limits		Pr > ChiSq
Intercept	3.3974	0.0778	3.245	3.5498	<0.0001
Week#	0.0075	0.0016	0.0043	0.0107	<0.0001
$CO^* O_3$	0.0451	0.007	0.0314	0.0588	<0.0001
NOx	0.0108	0.0037	0.0036	0.0181	0.0035
$SO_2^* NO_2$	−0.0044	0.001	−0.0063	−0.0026	<0.0001
$PM_{2.5}$	0.0096	0.0044	0.001	0.0182	0.0284

[a] Note: Week# = week number in the calendar year (starting from the first week in January), varies from 1 to 52. O_3 = mean O_3 concentration of the previous day, in parts per million (ppm), SO_2 = mean SO_2 concentration of the previous day, in parts per billion (ppb), NO_2 = mean NO_2 concentration of the previous day, in parts per billion (ppb), NOx = mean NOx concentration of the previous day, in parts per million (ppm), CO = mean CO concentration of the previous day, in parts per million (ppm), $PM_{2.5}$ = mean $PM_{2.5}$ concentration of the previous day, in micrograms per cubic meter (μg m^{-3}). *This sign denotes interaction (*e.g.*, the interaction effect of CO and O_3).

schools (pre-kindergarten through grade 12) that reported at least one asthma exacerbation and a boost from 5 to 11 (120%) in the number of asthma exacerbations reported per 100 schools partially explained the real increase in asthma prevalence among school children because those particular increases are not influenced by an increase in the number of schools participating in the asthma surveillance system under conditions of minimal bias in eTools enrollment. Reported exacerbations may, however, be influenced by increased diligence of school nurses since any surveillance system takes a few years to reach the full functional capacity. Geographical differences in new school enrolment may also have influenced these increases of 90% and 120%.

Use of antiasthmatics among school children as reported by school nurses has an almost identical pattern in each year, 2008–2010 (Fig. 1). The ratio of weekly mean to annual mean was calculated for each week to minimize the effect of the continuous increase in school asthma surveillance system participation on the observed pattern of weekly reporting over years. The peak of antiasthmatic use usually fell between September and November (fall), while the lowest use of antiasthmatics was reported in winter (Fig. 2). Table 3 shows the distribution of asthmatic daily mean for pollen and calendar seasons. Table 4 shows the distribution of asthmatic grouping for pollen and calendar seasons: the probability of asthma exacerbations ≥48 given that the tree pollen season comprises 56.5% of the year and the probability of asthma exacerbations ≥48 given that the grass pollen season comprises 40.78%.

According to the Poisson regression model, week number within the calendar year, NOx, SO_2, NO_2, $PM_{2.5}$, CO, and O_3 levels on the previous day were all found to have significant effects on the occurrence of asthma exacerbations among elementary school students. The variables PM_{10}, pollen season, and calendar season had no significant effect within the Poisson model and, therefore, were excluded. Month number was also excluded to enhance model goodness of fit. According to the criteria for assessing goodness of fit, the scaled deviance criterion for the selected model below was 1.023 with a scaled Pearson value of 1.000 (Table 5).

The following formula was derived from the GEE findings above:

$$\log(E(\mathrm{AsEx})) = 3.397 + 0.008\,(\mathrm{Week\#}) + 0.011(\mathrm{NOx}) - 0.004\,(SO_2{*}NO_2) + 0.011(PM_{2.5}) + 0.045\,(CO{*}O_3)$$

AsEx = number of asthma exacerbations predicted for the day.

$$E(\mathrm{AsEx}) = e^{[3.397+0.008\,(\mathrm{Week\#})+0.011(\mathrm{NOx})-0.004\,(SO_2{*}NO_2)+0.011(PM_{2.5})+0.045\,(CO{*}O_3)]}$$

Discussion

Routinely measured and publicly available air pollutant indicators provide a good estimate and a reliable tool for forecasting asthma burden on the school health system the next day. For instance, the output from the Poisson regression analysis above is based on three years of surveillance of asthma exacerbations and does not restrict the utilization of the above equation beyond interpolation. Furthermore, the extrapolation for forecasting is also realistic given the current analysis based on the average of asthma exacerbations for the 2008–2010 time period. Therefore, it is possible to recommend that an asthmatic student should take necessary precautions to prevent or control a possible asthma exacerbation if there is a higher probability forecast of having asthma exacerbations on the particular day based on levels of seven air pollutants from the previous day, depending on the pollen season and the date of the year. For example, if the number of asthma exacerbations within the surveillance system for the next day is calculated as 72, based on levels of air pollutants, pollen season, and date of the year, it will be a high risk day because the predictive number (*i.e.*, 72) is greater than the mean number of exacerbations (*i.e.*, 48).

Measurements of pollutant parameters used in this study are recorded daily and hourly in multiple monitoring sites in all states. The current study revealed that the computation of the combined effect of those main air pollutants is effective in predicting asthma exacerbations because it provides a representation of overall air pollution when controlled for pollen and date of the year. In addition, the formula can be updated annually or quarterly with new data from air quality monitoring sites and school health records.

The causal effects of various air pollutants on causing respiratory symptoms resulting in asthma exacerbations are diverse. PM has components, such as elemental carbon, that are associated with respiratory health effects in children.[12] As the size of $PM_{2.5}$ is very small, it penetrates most deeply into the lungs. Children are exposed to air pollution in the form of PM from school bus exhaust and that of other vehicles. Air pollution inside a school bus cabin can be greater than roadway concentrations, depending on individual vehicle characteristics.[33]

In many studies, NO_2 was highly correlated with asthma attacks.[34,35] The U.S. Environmental Protection Agency (EPA) states that annual average NO_2 levels of 0.053 ppm (parts per million) or higher are considered a risk factor for respiratory diseases.[36] O_3 is also associated with asthma exacerbations.[11] In some instances, assessment of several air pollutant effects on asthma revealed O_3 to be the only pollutant associated with increased hospital admissions.[37] SO_2 is also a potential asthmagen. The EPA considers 24 hour average SO_2 levels of 0.14 ppm or higher to be a risk factor for respiratory diseases.[36] Experimental studies have revealed that SO_2 levels above 0.10 ppm caused bronchoconstriction or reductions in lung function in asthmatics.[38,39] CO interferes with the blood's ability to carry oxygen to the body's tissues and results in numerous adverse health effects. Both SO_2 and CO are also associated with asthma admissions among younger children.[40]

Although some studies generated controversial findings,[34,35] many have demonstrated that air-borne pollen plays an important role in triggering asthma attacks.[15,16] Several types of pollen are found to play a role in causing asthmatic attacks with grass pollen having a more significant effect in triggering asthma attacks.[15] Thunderstorms are known to break up pollen grains and release starch granules of a respirable size.[17] During the spring and early summer in Pennsylvania, tree pollens (*e.g.*, Cypress, Elm, Ash, Birch, Hickory, Maple, Oak, Poplar, Sycamore, and Walnut) are most likely to cause asthma symptoms. During the late summer and fall, grass pollens (*e.g.*, Bluegrass, Bermuda grass, Orchard grass, Red top grass, Sweet vernal grass, and Timothy grass) are more likely to trigger asthma symptoms. In addition, weed pollens, such as ragweed, also play a role in triggering asthma exacerbations during fall.[31]

Attempts have been made to predict the number of asthma exacerbations using meteorological variables. Previous studies of asthma in children have shown that the greatest number of exacerbations occurred in the fall[41–43] or summer.[44] Four decades ago, Jaklin *et al.*[45] showed that cold and dry air in winter as well as hot and dry air in summer were associated with an increased incidence of upper airway inflammation. Makra *et al.*[46] showed that temperature and relative humidity can be used to predict the number of asthma exacerbations. From the summer to early autumn period, the total number of respiratory disease occurrences increased proportionally with temperature. Additionally, hospital admissions were predicted by low relative humidity. Atmospheric variables in the winter months were not predictive of the number of hospitalized patients.[46]

By accurately predicting the variation in asthma exacerbations, the school health system can reallocate both the human and physical resources needed to execute extra precautionary measures that either prevent asthma attacks or identify and quickly treat attacks should they occur. Symptoms of mild asthmatics are relatively easy to control and they will rarely suffer from exacerbations, control of which may be very poor. Similarly, moderate to severe asthmatics require more intensive treatments to control their symptoms, leading to good symptom control.[47] Therefore, prediction of asthma outbreaks is important for diagnosed asthmatic children as their household members can take more preventive measures to avoid asthma exacerbations, regardless of the disease severity. In addition, being informed of the greater possibility of an asthma outbreak on a particular day or week, school nurses and teachers will be able to pay more attention to early identification of asthma exacerbations among children.

From the perspective of the health care professional, the level of control may be more relevant because the aim of treatment is to relieve symptoms and reduce the effect of asthma on patient functioning. A large-scale study conducted in the U.S. revealed that 40% of asthma patients reported night waking, 30% perceived poor control, 22% missed daily activities, and 8% overused reliever medications in the past month, while 24% of those with four control problems required hospitalization during the past year.[4] Therefore, the level of control is obviously not optimal for many asthmatics. Being informed of a possible asthma outbreak due to changes in air pollutants, when adjusted for pollen and date of the year, doctors and nurses in emergency rooms or in private practice can take extra precautions and utilize resources more efficiently to serve an increased number of asthma patients.

Past studies have found that an emergency response plan was available for medical emergencies in 91% of rural and 94% of urban schools in Pennsylvania, and a rapid response system that linked the school to emergency health care services was available in two-thirds of schools.[26] Therefore, with accurate prediction of asthma exacerbations, the school health system can play a major role by effectively reallocating both human and physical response resources as well as by alerting teachers and asthmatic children to take extra precautions against asthma attacks very early. It also enables them to identify and quickly treat those attacks that do occur. Mass media and local media can also play an important role in this effort. Results of the current study can be used to inform similar programming at the national level and in other states. Routine integration of health measures with environmental indicators in states across the country will be helpful for predicting the extent of various health problems and helpful for more efficient management of physical and human resources.

Limitations

Apart from decreased accuracy that results from using group averages and ignoring individual level variations, a risk is present for "ecological fallacy": the erroneous interpretation that specific asthmatic children in the group share the characteristics of the study sample.[22] However, it is possible to interpret that asthmatic children of elementary school age in Pennsylvania have a higher (or lower or average) risk on a particular day. In addition, there is a possibility that other asthma triggers apart from adjusted confounders (pollen season and date of the year), such as respiratory infections, may confound the relationship between pollutants and asthma exacerbations.

Asthma surveillance in schools is not being conducted during winter breaks, summer vacations, weekends, and school holidays. The possibility that some students in the study population self-administer medications at school was difficult to exclude.[29] Some students who experienced a worsening of symptoms at night or early in the morning did not attend school; so their asthma exacerbations were not included in school health records. In addition, some cases of asthma exacerbations, which were treated by other staff because a school nurse was not there, could have been missed. However, it is unlikely that the underestimation of the actual number of asthma exacerbations would have influenced the results of the model.

The number of schools using eTools during 2007 was relatively low; therefore, student data from that year were not included in some of the analyses. The number of schools using eTools changed each year with some schools dropping off and others joining, causing fluctuations in the total number of available student data records. Additionally, each year some students left their school or school district. Nevertheless, the total number of student data strings provided for any one year was sufficiently robust, as was the number of data strings available for multi-year comparisons, to generate reliable results.

Several other limitations are noted. A variable that incorporated lag time between symptoms and environmental effects was not included when the association between the combined effect of the independent variables on a particular day and the occurrence of asthma exacerbations on the next day was considered. Furthermore, it was impossible to include lag time for the effect of the interactions between pollutant variables, which are also predictive of asthma exacerbations, and distinguish new patients from the repeated treatment of asthma exacerbations in the same child. Because the frequency of exacerbations depended on asthma triggers, such as air pollution, only the number of asthma exacerbations per day was incorporated, and the number of new patients per day was not.

As the role of socioeconomic factors[3] and climate[46] in the occurrence of asthma exacerbations is well known, the findings of this study can only be generalized to other industrialized countries with a similar seasonal pattern of climate. In addition, the findings cannot be generalized beyond the elementary school age group because the effect of asthma triggers differs with age.[3] Finally, the confounding effect of ground weather factors on the relationship between air pollution (in combination with pollen) and asthma exacerbations cannot be excluded. To address this possibility, another study will be conducted, utilizing the same student data, to evaluate the influence of air pollution and pollen in combination with ground weather factors on asthma exacerbations.

Conclusion

Monitoring of air pollutants (PM_{10}, $PM_{2.5}$, CO, NOx, NO_2, SO_2, and O_3) over time can serve as a reliable new means for predicting variation in asthma exacerbations among elementary school children when controlled for pollen season and date of the year; therefore, this study with its novel approach constitutes transformative research.[48] The new mathematical model derived from statistical integration of routine environmental observations and school health records may be used to scrutinize the complexity of asthma as a dynamic outcome determined by multiple environmental parameters. Assessing the risk of future asthma outbreaks is also possible based on analysis of air pollution fluctuations.

Declaration of interest

The authors report no conflicts of interest in relation to the current study.

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