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The effect of air pollution on inner-city children with asthma

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The effect of air pollution on inner-city children with asthma. K.M. Mortimer, L.M. Neas, D.W. Dockery, S. Redline, I.B. Tager. ©ERS Journals Ltd 2002.

ABSTRACT: The effect of daily ambient air pollution was examined within a cohort of 846 asthmatic children residing in eight urban areas of the USA, using data from the National Cooperative Inner-City Asthma Study.

Daily air pollution concentrations were extracted from the Aerometric Information Retrieval System database from the Environment Protection Agency in the USA. Mixed linear models and generalized estimating equation models were used to evaluate the effects of several air pollutants (ozone, sulphur dioxide (SO_2), nitrogen dioxide (NO_2) and particles with a 50% cut-off aerodynamic diameter of 10 μm (PM_{10}) on peak expiratory flow rate (PEFR) and symptoms in 846 children with a history of asthma (ages 4–9 yrs).

None of the pollutants were associated with evening PEFR or symptom reports. Only ozone was associated with declines in morning % PEFR (0.59% decline (95% confidence interval (CI) 0.13–1.05%) per interquartile range (IQR) increase in 5-day average ozone). In single pollutant models, each pollutant was associated with an increased incidence of morning symptoms: (odds ratio (OR)=1.16 (95% CI 1.02–1.30) per IQR increase in 4-day average ozone, OR=1.32 (95% CI 1.03–1.70) per IQR increase in 2-day average SO_2, OR=1.48 (95% CI 1.02–2.16) per IQR increase in 6-day average NO_2 and OR=1.26 (95% CI 1.0–1.59) per IQR increase in 2-day average PM_{10}.

This longitudinal analysis supports previous time-series findings that at levels below current USA air-quality standards, summer-air pollution is significantly related to symptoms and decreased pulmonary function among children with asthma.

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Much of the evidence for the effect of air pollution on respiratory health [1–8] is based on time-series analyses of repeated measurements in closed cohorts, which create a daily summary of responses across all study individuals. Fluctuations in this summary measure are evaluated relative to daily fluctuations in air pollution. Therefore, these approaches are not well suited to investigations of individual-level factors related to heterogeneity of response. Time-series analyses require that the distribution of individual-level factors in the study population remain stable over time [9] or that data on changes in these characteristics are included in the model. This limits their usefulness in studying populations which do not remain fixed during the study period.

Longitudinal analysis techniques such as mixed linear models and generalized estimating equations provide a more statistically powerful alternative by incorporating individual level outcomes and covariates. They permit estimation of individual mean effects and individual change over time as well as population mean effects over the entire study period. These methods require no assumptions about stability of population characteristics over time and subjects with incomplete data can be included in the analysis [10]. Therefore these methods are well-suited for epidemiological studies.

These methods were used to evaluate air pollution-related health effects in a large cohort of inner-city children with asthma. Individual-level risk factors that modified the response to ozone in this cohort have been reported previously [11]. In particular, it was found that asthmatic children born prematurely (<37 weeks) or with a low birth weight (<2.5 kg) had a significantly greater response to increases in ozone. This study compares these results to time-series and other analyses and presents multipollutant models.

Design and methods

Cohort identification

The cohort was obtained from the National Cooperative Inner-City Asthma Study (NCICAS), a multicentre study of asthmatic children in eight urban areas in the USA. Although NCICAS examined a wide range of risk factors for asthma morbidity, including access to healthcare, psychosocial problems, and the home environment, this report is limited to the association with urban air pollution. The design and methods have been reported previously [12]. Briefly, children and their parents were recruited from emergency departments and primary care clinics in eight urban areas: Bronx and East Harlem, NY; Baltimore, MD; Washington, DC; Detroit, MI; Cleveland, OH; Chicago, IL; and St. Louis, MO. Children were 4–9 yrs old and resided in inner-city neighbourhoods in which the income of $\geqslant$30% of residents was below the federal poverty level. Study children had either: 1) parental report of physician-diagnosed asthma and symptoms in the past 12 months or 2) respiratory symptoms consistent with asthma, such as cough, wheezing or shortness of breath, that lasted >6 weeks during the previous year, together with increased symptoms with exercise or cold air exposure or a family history of asthma. The protocol included an in-person baseline interview, a home survey, three brief telephone follow-up interviews at three-month intervals, and two-week peak expiratory flow rate (PEFR) and symptom diaries after the baseline interview and prior to each follow-up interview. To reduce confounding by temperature and seasonal infectious disease, this analysis is restricted to those children who returned at least one diary during June–August of 1993.

Exposure measures

Air pollutant concentrations were obtained from the Aerometric Information Retrieval System of the Environmental Protection Agency in the USA. Daily pollutant metrics were calculated by averaging hourly readings for selected periods, based on peak occurrences, which are noted in the section on each pollutant. Multiday metrics were calculated by averaging these daily metrics. Children within the same urban area were assigned common daily and multiday values for each pollutant, calculated by averaging the pollutant concentrations from all monitors in the corresponding county. Single and multipollutant models are presented. Pollutants are often highly correlated, and consequently this report focuses on ozone as a good marker for summer air pollution in the NCICAS cities. Weather data were obtained from local airports.

Outcome measures

Children were trained in the use of a mini-Wright peak flow meter (Clement Clarke, Columbus, OH, USA). PEFR and symptoms (cough, chest tightness, wheeze) were reported in the morning upon rising, and before bedtime, prior to use of any inhaled medications. The maximum of three manoeuvres, performed while standing, was recorded. NCICAS was not an intervention and parents were not instructed on the interpretation of PEFR. Values <70 or >450 L·min^{-1} (0.4% and 2.5% of readings, respectively) were considered to be implausible (*e.g.* errors in transcription) and were deleted.

Three outcome measures were evaluated separately for morning and evening: 1) daily per cent change from the diary-specific median PEFR; 2) the incidence of $\geqslant$10% decline from the diary-specific median PEFR; 3) the incidence of any symptom. Changes in PEFR (rather than mean levels) and incidence (rather than prevalence) were evaluated to focus on the impact of air-pollution level on changes in morbidity.

Statistical methods

The per cent change in PEFR was analysed using linear mixed effect models (SAS Proc Mixed [13]), while the incidence of symptoms and incidence of a 10% decline in median PEFR were modelled with generalized estimating equations, using a logistic link. Change-in-estimate criteria and likelihood ratio tests were used to determine the choice of covariates, with an alpha level of 0.05. Akaike's Information Criteria (AIC) was used to evaluate the best correlation structure and to determine if a covariate should be entered as a fixed or random effect. Models with the AIC closest to zero were considered to best fit the data. Standard errors were insensitive to the use of several covariance structures, therefore results from models assuming the most simple structure (independence) were reported.

Lagged air pollution effects were evaluated using moving averages, unrestricted distributed lags, and polynomial distributed lags. Within-model lag-specific estimates were combined to create a cumulative effect over a specified interval and estimates were then compared across models.

Results

Approximately 60% of the children returned a diary for each of the four visits. From June–August of 1993, 846 children returned at least one diary, for a total of 910 diaries. Their characteristics were similar to the entire NCICAS cohort (n=1528), although children who reported $\geqslant$2 asthma medications in the previous three months (an indicator of asthma severity) were more likely to have returned diaries (table 1). Each diary contributed up to 14 days of readings (11,622 child days). Completeness of diary readings was unrelated to pollution levels during the diary period.

Pollutant and temperature distributions are presented in figure 1. Across all urban areas, the 8-h average ozone (10:00–18:00 h) was 48 parts per billion (ppb), and <5% of days exceeded the proposed USA

Table 1. – Demographic characteristics of National Cooperative Inner-city Asthma Study (NCICAS) children who returned at least one diary between June 1–August 31, 1993

Patient characteristics	Total	Bronx	East Harlem	Baltimore	Washington DC	Detroit	Cleveland	Chicago	St. Louis
Subjects n	846	143	104	111	92	84	56	138	118
Diaries n	910	151	113	128	99	88	61	141	129
Male %	63	60	61	63	72	63	66	59	62
Black %	71	23	37	90	99	94	98	65	97
Hispanic %	19	66	51	1	0	0	0	27	0
Severe[#] %	48	57	42	51	45	49	38	52	42
Morning PEFR $L \cdot min^{-1}$ mean±SD	206±72.7	217±71.1	211±68.5	206±79.3	205±67.1	190±66.9	193±76.8	206±72.0	205±75.6
10% decline in morning PEFR[¶]	14.1	13.4	12.8	13.8	12.7	13.8	13.2	14.8	16.9
Any morning symptom[¶]	11.6	11.9	12.1	11.0	10.0	10.5	10.0	11.3	14.2

[#]: reported at least 2 classes of medicines at baseline; [¶]: incidence·100 child-$days^{-1}$. PEFR: peak expiratory flow rate.

standard of 80 ppb (157 $\mu g \cdot m^{-3}$) [14]. The effect estimates were scaled to a 15 ppb increase in ozone (the approximate interquartile range, table 2). The average intradiary range in daily ozone was 48 ppb.

Models for all three outcomes included fixed effects for an ozone metric, indicators for diary number (*i.e.* baseline, 3 or 6-month diary), day of study (starting June 1, 1993), rain in the past 24 h, urban area, and a linear term for 12-h average wet-bulb temperature. Including the temperature term in the model increased the magnitude of the ozone coefficient by >30%, suggesting it was a strong confounder. Nonlinear terms for temperature had little effect on the magnitude or precision of the ozone coefficient. Modelling urban area as a fixed rather than random effect provided a better fit and did not influence the ozone estimate, nor did including a term for day of week. Daily medication use and time-activity information were not available for inclusion in the models.

No association was seen between single or multiday ozone metrics and any evening outcome measure (table 2). The effect of ozone on morning outcomes increased over several days and the strongest association was seen for multiday moving averages.

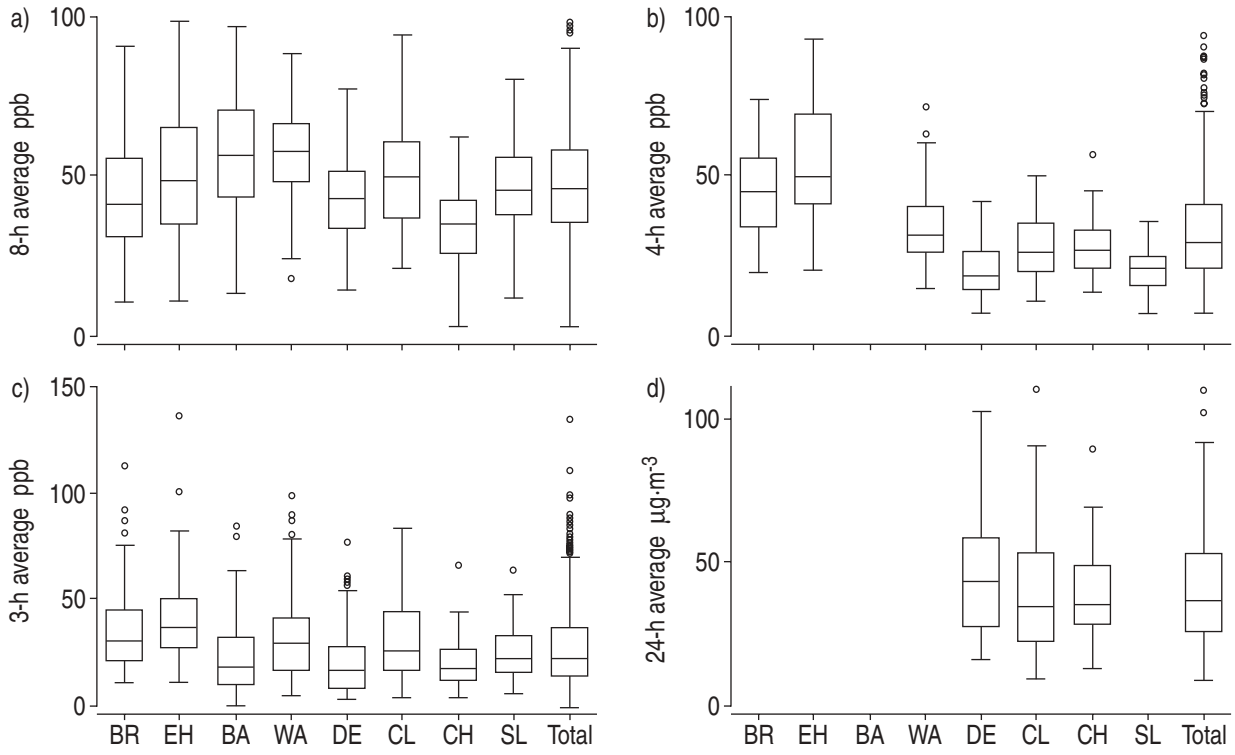

Fig. 1. – Pollutants shown by urban area a) ozone, b) nitrogen dioxide, c) sulphur dioxide and d) particles with a 50% cut-off aerodynamic diameter of 10 µm. Boxes extend from the 25th to 75th percentile (Interquartile range (IQR)). The lines extend to lower and upper adjacent values, defined as three halves of the IQR. Circles represent days more extreme than the adjacent values. BR: Bronx; EH: East Harlem; BA: Baltimore; WA: Washington; DE: Detroit; CL: Cleveland; CH: Chicago; SL: St Louis; ppb: parts per billion.

Table 2. – Effect of a 15 parts per billion increase in ambient ozone concentration on peak expiratory flow rate (PEFR) and asthma symptoms in 8 urban areas of the National Cooperative Inner-city Asthma Study (NCICAS) June 1–August 31, 1993

Measures	PEFR[#] % change (95% CI)	Incidence of ⩾10% decline in PEFR[#]	Incidence of symptoms[#]
Morning measures			
Lag 1	-0.06 (-0.38–0.26)	1.04 (0.97–1.12)	1.03 (0.94–1.12)
Lag 2	-0.13 (-0.40–0.15)	1.04 (0.98–1.11)	1.10 (1.02–1.19)
Lag 3	-0.32 (-0.59–-0.05)	1.04 (0.97–1.10)	1.01 (0.94–1.09)
Lag 4	-0.22 (-0.48–0.05)	1.09 (1.02–1.16)	1.09 (1.01–1.17)
Lag 5	-0.22 (-0.49–0.05)	1.03 (0.97–1.10)	0.99 (0.92–1.07)
Lag 6	0.07 (-0.20–0.33)	0.97 (0.91–1.03)	0.97 (0.90–1.04)
Average, lag 1–5	-0.59 (-1.05–-0.13)	1.14 (1.02–1.27)	
Average, lag 1–4			1.16 (1.02–1.30)
Evening measures			
Average, lag 0–4	-0.05 (-0.51–0.41)	1.00 (0.89–1.13)	
Average, lag 0–3			1.02 (0.88–1.18)

Data are presented as odds ratio with 95% confidence intervals in parentheses unless otherwise stated. [#]: Adjusted for day of study, previous 12-h mean wet-bulb temperature, urban area, diary number, rain in the past 24 h, with an independence covariance structure.

A 15 ppb increase in 5-day moving average ozone was associated with a 0.59% decline in morning PEFR (95% CI 0.13–1.05) and with the incidence of a ⩾10% decline in morning PEFR (OR=1.14, 95% CI 1.02–1.27). The incidence of morning symptoms was most strongly associated with a 4-day moving average (OR=1.16, 95% CI 1.02–1.30.) The effect of the corresponding multiday lags on each evening outcome is presented for comparison purposes (*i.e.* average of lag 0–4 for evening measures can be compared to the average of lag 1–5 for morning measures).

For morning PEFR, cumulative effects from unrestricted lag, second degree polynomial distributed lag, and moving average models were nearly identical (cumulative declines=0.54%, 0.51%, and 0.59%). Unrestricted lag models suggested that the ozone exposures from 3–5 days prior have a greater impact on morning %PEFR than more immediate exposures. The 5-day average (lags 1–5) showed a slightly greater effect than a 3-day average (lags 3–5) or 4-day average (lags 2–5) (data not shown), despite the fact that the estimates from models using lags 1 and 2 suggested little increased risk. For morning symptoms, unrestricted lag, polynomial distributed lag, and moving average models yielded similar cumulative estimates (OR=1.13, 1.14, 1.14, respectively).

Excluding days when ozone was >80 ppb (proposed US Federal Standard) provided estimates which were nearly identical findings to those obtained using all of the days (0.70% decline in PEFR (95% CI 0.12–1.29%), OR=1.15 (95% CI 0.99–1.33) for a 10% decline in morning PEFR, OR=1.17 (95% CI 1.01–1.35) for the incidence of morning symptoms).

The consistency of urban area-specific estimates was evaluated by adding an "ozone by urban area" interaction term to each model. Interaction terms were null. In fact, with the exception of the Baltimore centre, the estimates for morning %PEFR were strikingly similar across urban areas (table 3). In all areas except St. Louis, the increase in ozone was associated with an increase in the incidence of morning symptoms.

The number of ozone monitors per urban area ranged from 1–13. Analyses were repeated using the average of readings from up to the three closest monitors to the centre of the child's zipcode [15], and

Table 3. – Estimated effect of a 15 parts per billion increase in ambient ozone on peak expiratory flow rate (PEFR) and asthma symptoms for each National Cooperative Inner-city Asthma Study (NCICAS) urban area

Urban area	Morning % PEFR % change[#,¶]	Incidence of ⩾10% decline in morning PEFR[#,¶]	Incidence of morning symptoms[#,¶]
Bronx	-0.69 (-1.54–0.15)	1.10 (0.90–1.34)	1.23 (0.98–1.54)
East Harlem	-0.73 (-1.63–0.17)	1.15 (0.90–1.48)	1.22 (0.97–1.53)
Baltimore	0.24 (-0.95–1.43)	1.37 (1.09–1.72)	1.19 (0.89–1.60)
Washington, D.C	-0.54 (-2.02–0.93)	0.95 (0.68–1.33)	1.11 (0.72–1.72)
Detroit	-0.75 (-2.36–0.86)	1.24 (0.91–1.68)	1.72 (1.12–2.64)
Cleveland	-0.62 (-2.23–0.99)	1.31 (0.87–1.97)	1.20 (0.81–1.79)
Chicago	-0.62 (-2.41–1.16)	1.18 (0.77–1.80)	1.09 (0.69–1.72)
St. Louis	-0.86 (-2.10–0.38)	0.99 (0.73–1.34)	0.82 (0.59–1.14)
All urban areas	-0.59 (-1.05–-0.13)	1.14 (1.02–1.27)	1.16 (1.02–1.30)

Data are presented as odds ratio with 95% confidence intervals in parentheses unless otherwise stated. [#]: Models include day of study, previous 12-h mean temperature, urban area, diary number, rain in the past 24 h, ozone and "ozone by urban area" interaction term, with an independence covariance structure; [¶]: 5-day average ozone for %PEF and 10% declines in PEF, 4-day average ozone for symptoms.

the findings were similar (0.50% decline in %PEFR and symptom OR=1.15.)

Co-pollutants

Sulphur dioxide (SO_2), nitrogen dioxide (NO_2), and particles with a 50% cut-off aerodynamic diameter of 10 μm (PM10) were evaluated using models similar to the ozone models described earlier. Estimates for evening effects were null (data not shown). Only morning %PEFR and symptom incidence findings are presented (table 4).

Daily SO_2 data were available for all eight urban areas, with an average intradiary range of 53 ppb. The correlation between 8-h ozone and 3-h mean (08:00–11:00 h) SO_2 was 0.29. Single-pollutant models suggest that single and multiday lags of SO_2 had little effect on morning %PEFR (data not shown). The greatest effect on morning symptoms was seen for a 2-day moving average lag (table 4). Results were similar for 3 and 4-day moving averages. When 5-day average ozone and 2-day average SO_2 were entered in a model simultaneously, there was essentially no impact on the estimate for SO_2 while the estimate for ozone decreased slightly.

Daily NO_2 was available in seven urban areas (nearly 10,000 child days), with an average intradiary range of 32 ppb. The correlation between 8-h mean ozone and 4-h NO_2 (06:00–10:00 h) was 0.27. NO_2 was not associated with declines in %PEFR and the greatest effect on morning symptoms was for a 6-day moving average. Joint modelling of NO_2 and ozone slightly reduced the estimates for each pollutant.

Daily PM10 was measured only in Chicago, Cleveland and Detroit (>3,000 child days,) with an average intradiary range of 53 $\mu g \cdot m^{-3}$. The correlation between 24-h average PM10 and 8-h average ozone was 0.51. Although there were no statistically significant effects of PM10 on morning %PEFR, estimates were negative and of similar magnitude to those found for ozone (0.89% decline per 25 $\mu g \cdot m^{-3}$ increase in 6-day moving average, 95% CI -0.54–2.31% decline). Significant effects on evening %PEFR were found only at much greater lags (8 days). None of the lags of PM10 were associated with the incidence of evening symptoms. In a single-pollutant model, the strongest association with morning symptoms was seen for a 2-day average. Entering PM10 and ozone in the model simultaneously resulted in a slight reduction in the PM10 estimate, but a larger reduction in the ozone estimate and wider confidence intervals (table 4).

Each individual pollutant was associated significantly with an increase in the incidence of morning symptoms. Multiday lags with the strongest associations in each of the single-pollutant models were simultaneously entered into a model. When restricted to the seven urban areas with complete data for ozone, SO_2 and NO_2, only SO_2 remained significantly associated with morning symptoms. Models with all four pollutants were restricted to the three urban areas with complete data. Estimates for most pollutants were positive, however the confidence intervals were wide due to the substantially smaller sample size and colinearity among pollutants.

Discussion

This study provides evidence of measurable negative respiratory health effects in children from eight inner-city communities in northeastern and midwestern USA. Direct comparisons to estimates reported in other studies are difficult, due to variations in outcome measures, analytical techniques and exposure definitions. A time-series analysis of 61 asthmatic children [8] in the Netherlands reported results corresponding to a 0.4% decline in PEFR and OR=1.03 per 15 ppb of ozone. Similarly, a summer camp study of asthmatic children in Connecticut [16] observed effects comparable to a 0.5% decline in PEFR per 15 ppb increase in ozone, despite much higher average ozone concentrations. Smaller effects were found among a group of 71 asthmatic children in

Table 4. – Single and multipollutant models for the incidence of morning asthma symptoms National Cooperative Inner-city Asthma Study (NCICAS)

Model[#]	Ozone Average of lag 1–5	SO_2 Average of lag 1–2	NO_2 Average of lag 1–6	PM10 Average of lag 1–2
All 8 urban areas				
Single pollutant	1.16 (1.02–1.30)	1.19 (1.06–1.35)		
Ozone+SO_2	1.11 (0.97–1.27)	1.18 (1.05–1.33)		
7 urban areas[¶]				
Single pollutant	1.12 (0.97–1.30)	1.22 (1.07–1.40)	1.48 (1.02–2.16)	
Ozone+NO_2	1.07 (0.92–1.26)		1.40 (0.93–2.09)	
Ozone+SO_2+NO_2	1.06 (0.90–1.25)	1.19 (1.04–1.37)	1.31 (0.87–2.09)	
3 urban areas[+]				
Single pollutant	1.10 (0.78–1.55)	1.32 (1.03–1.70)	1.70 (0.77–3.74)	1.26 (1.00–1.59)
Ozone+PM10	1.04 (0.70–1.55)			1.25 (0.97–1.61)
Ozone+SO_2 +NO_2+PM10	1.00 (0.75–1.34)	1.23 (0.94–1.62)	1.45 (0.63–3.34)	1.14 (0.80–1.48)

Data are presented as odds ratio with 95% confidence intervals in parentheses. [#]: Adjusted for day of study, previous 12-h mean temperature, urban area, diary number, rain in the past 24 h, with an independence covariance structure; [¶]: NO_2 data were not available in Baltimore; [+]: Daily PM10 were collected in Chicago, Cleveland and Detroit. For the odds ratio estimates are rescaled to an interquartile range change (20 ppb for SO_2 and NO_2, 20 $\mu g \cdot m^{-3}$ for particles with a 50% cut-off aerodynamic diameter of 10 μm (PM10), 15 ppb for ozone). SO_2: sulphur dioxide; NO_2: nitrogen dioxide.

Mexico City [3], with no effect on PEFR and OR=1.03 for symptoms per 15 ppb increase in ozone. In each of these studies, effects were found over shorter intervals (0–2 day lags) than in the NCICAS population (4–5 day moving average). In contrast to other findings [1, 3, 17], current day effects were not found in the NCICAS cohort. Instead, the strongest associations were seen with multiday moving averages. Other studies have also reported larger estimates from moving day average exposures than those based on single-day exposures [18, 19, 20]. The Pollution Effects on Asthmatic Children in Europe (PEACE) study [21] did not see an effect of winter pollutants and presented data based on shorter lags. These differences, as well as possible differences in population characteristics that modify the response to pollution may account for the contradictory results [10]. Findings in these USA inner-city asthmatic children are comparable to findings reported elsewhere, suggesting the magnitude of the air pollution-related effect on asthma morbidity is not substantially greater in this population in relation to more socioeconomically diverse groups of asthmatic children. The baseline risk for asthma morbidity may be higher in these communities and, therefore air pollution may contribute substantially to the burden of asthma morbidity.

Small declines in PEFR may be of questionable clinical significance. There were, however, significant associations with the incidence of $\geqslant 10\%$ declines in PEFR and symptoms that clearly have clinical importance to asthma morbidity [22]. The consistency of these effects suggests that despite known limitations [23], the peak flow data effectively captured important decrements in pulmonary function. Nondifferential misclassification of outcome and exposure data may have contributed to an underestimate of the effects. Also, a report published previously [10] has identified subgroups with more clinically important responses to air pollution. Future analyses of the health effects of air pollution would benefit from the inclusion of individual-level risk factors, which can greatly modify the size of the health effect.

The effects on PEFR and symptoms were limited primarily to morning measures. Morning values are better indicators of asthmatics who are susceptible to airway narrowing [24], and, therefore, focusing on morning measures may identify children at greater risk for adverse health outcomes. The most severe bronchoconstriction occurs in the morning, when measurable differences between and within individuals may be greatest. Alternatively, the lack of association with evening measures may be due to the use of asthma medication during the day, which may attenuate the association with air pollution and daily peak flow and symptom reports [1, 25]. The lack of evening effects may reflect misclassification due to an inability to adjust for time the child spent outdoors or exercising, both of which affect respiratory dose [26]. Controlling for these factors may improve the estimates [4].

Only three of the urban areas had daily PM10 monitors, making the sample size too small to allow for unambiguous assessment of multipollutant models. In these three cities, however, a stronger association was seen for PM10 than ozone, and, as others have reported PM10 was more strongly associated with asthma symptoms rather than PEFR [3]. Delfino *et al.* [1] reported that 8-h maximum PM10 was more highly associated with morbidity than the 24-h PM10 measurements. It was not possible to test that hypothesis with existing monitoring data.

Biological mechanisms for delayed effects on pulmonary function include increased bronchial reactivity secondary to airway inflammation associated with irritant exposures. Animal and chamber studies suggest that exposure to air pollution may augment airway cellular infiltration and cellular activation, enhance release of cytotoxic inflammatory mediators, alter membrane permeability, and alter mucociliary clearance [27–29]. Given the lengthy lag times for ozone, PM10 and NO_2 effects, ambient pollutants may not only be acting as a direct trigger of asthma attacks, but may also act indirectly as a primer for a subsequent antigen exposure [30, 31]. While ozone was most influential on PEFR, NO_2 had the strongest effect on symptoms. NO_2 may be a better marker for the summer-pollutant mix in these cities, largely east of the Mississippi, in that it is related to the photochemistry of ozone and the emissions of hydrocarbons that accompany particle pollutants released from automobiles.

These findings are not likely to be confounded by asthma risk factors such as allergen sensitization and housing characteristics since they do not vary within the two-week monitoring interval. Medication or air conditioner use and exposure to tobacco smoke may vary daily, however, those data were not available. The similarity of the quantitative group mean estimates to those from time-series analyses discussed earlier, however, suggests that confounding does not explain the results.

In conclusion, summer-time air pollution is associated with increased asthma morbidity and decreased pulmonary function among inner-city children with asthma in the USA. These findings from generalized estimating equations and mixed models support previously published reports from time-series analysis, and those reported from less urban populations. The impact of pollution was not immediate, but developed over several days, with the largest effects seen on morning outcomes. Nitrogen dioxide, sulphur dioxide, and particles with a 50% cut-off aerodynamic diameter of 10 μm were associated with increases in symptoms, with nitrogen dioxide exhibiting the strongest influence. Ozone was most influential on peak expiratory flow rate. Adverse respiratory effects were observed in all cities, at levels below proposed USA air quality standards.

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necessarily represent the official views of the Environmental Protection Agency (EPA). The research described in this article has been subject to EPA's peer and administrative review and it has been approved for publication.

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