ORIGINAL ARTICLE

Effects of daily variation in outdoor particulates and ambient acid species in normal and asthmatic children

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Background: Evidence suggests that the respiratory health of children may be adversely affected by daily variation in outdoor pollutants, particularly ozone and particulates. However, data from the UK are sparse and the contribution of different particulate fractions and acid species, together with the identification of those individuals most at risk, are not clear.
Methods: One hundred and sixty two 9 year old children were enrolled from two inner city locations and recorded daily symptoms and twice daily peak expiratory flow (PEF) over 8 week periods in the winter and summer. Their results were analysed with daily pollutant levels at appropriate lags using regression models which corrected for trends, weather, pollen, and autocorrelation.
Results: Pollutant levels were generally low, especially in the summer. Multiple statistically significant associations were noted between health outcomes and pollutant concentrations, but no consistent patterns in identified effects were apparent between pollutants, lags, direction of observed effect, or location. There was no evidence to suggest that subgroups with atopy or pre-existing wheeze are more sensitive to pollutant effects.
Conclusion: These data do not suggest that adverse health outcomes are associated with daily variation in health effects. No evidence was found to indicate that particulates or individual acid and anion species are more closely related to adverse health outcomes than other pollutants.

Air pollution is generally recognised to affect human health, even below current regional standards.[1] In children, short term falls in lung function and increases in respiratory symptoms have been related to daily variations in pollutant levels, including the mass concentration of particulates.[2 3] Children with pre-existing respiratory disease may be more sensitive to such effects,[4 5] although this observation may not translate simply to "asthma severity".[6] However, a recent European multicentre study of asthmatic children (Pollutant Effects on Asthmatic Children in Europe (PEACE)) failed to detect any consistent association between air pollutants and short term health effects, despite the wide range of climatic conditions and pollutant mixes encountered across the sites.[7]

The characteristics of particles responsible for their specific health effects are not known. Measures of particle acidity have been shown to produce similar health outcome relationships to particle mass measures.[8] One study has suggested that hospital admissions may be most closely related to particle acidity, sulphate content (SO_4^{2-}) and small size,[9] but other studies report adverse effects of particulates in the absence of significant acidity.[3] Levels of individual acid and anion species, including nitrate (NO_3^-), nitric acid (HNO_3), and ammonium (NH_4^+), have also shown significant, albeit small, relationships with short term adverse respiratory health outcomes.[10]

This study aimed to characterise potential short term adverse respiratory effects of outdoor air pollutants on UK urban primary school children with and without chronic respiratory symptoms or an atopic phenotype. In addition, the study considered whether any such effects were more closely related to $PM_{2.5}$ than to PM_{10} (mass concentration of particulates with mean aerodynamic diameter $<2.5\,\mu m$ and $10\,\mu m$, respectively) and to concentrations of individual acid and anion species than to particulate mass measures.

METHODS

A time series "panel" study design was used[11] with two 8 week monitoring periods representing winter (13 January–10 March 1997) and summer (19 May–14 July 1997) conditions. Subjects were recruited from five primary schools in two urban locations—Birmingham, a major city in the English Midlands, and Sandwell, a large urban area contiguous with Birmingham—which were analysed separately. The schools selected were close to major motorways and congested city arterial roads. Study approval was obtained from the East Birmingham research and ethics committee.

Panel recruitment and monitoring

The panel comprised 9 year old children enrolled during September 1996. After giving written consent, parents completed a questionnaire detailing their child's respiratory symptoms, atopic illnesses, and relevant housing factors. Subjects were divided into subgroups on the basis of reported wheezing in the previous 12 months in the absence of a respiratory tract infection. Baseline spirometric tests and skin testing to common allergens (cat, dog, grass, trees, house dust mite, and cockroach) were performed. Children were considered atopic on the basis of at least one positive skin test (mean weal diameter at least 3 mm greater than negative control).

Children and teachers were instructed in peak expiratory flow (PEF) measurement and all subjects were issued with a PEF meter (Vitalograph Ltd, UK). The highest of three PEF readings at morning registration (08.45–09.00 hours) and at the end of the school day (15.30–15.45 hours) were recorded. At weekends parents were asked to ensure a reading at breakfast time and in mid-afternoon. Subjects were required to record medication taken each day and to respond to the following five questions:

- "Did you cough today?"
- "Were you ill today?"
- "Were you short of breath (SOB) today?"
- "Did you wake up last night with a cough or wheeze?"
- "Did you wheeze today?"

Diary cards were issued and collected weekly and inspected immediately for errors or omissions. Data were entered onto a

Table 1 Characteristics of the 162 panel members (all aged 9 years by September 1996), of whom 39 (24%) were defined as having suffered recent wheezing on the basis of a parental report on questionnaire

	Birmingham children (n=104)	Sandwell children (n=58)	Subgroup with recent wheezing (n=39)	Subgroup without recent wheezing (n=123)
Sex				
Girls	52 (50%)	24 (41%)	14 (36%)	62 (50%)
Boys	52 (50%)	34 (59%)	25 (64%)	61 (50%)
Ethnicity*				
ISC	9 (9%)	2 (3%)	4 (10%)	7 (6%)
Black	7 (7%)	2 (3%)	4 (10%)	5 (4%)
White	88 (85%)	51 (88%)	30 (77%)	109 (89%)
Other	0 (0%)	1 (2%)	0 (0%)	1 (1%)
Parental report of respiratory symptoms				
Wheezing ever	34 (33%)	23 (40%)	34 (87%)	23 (19%)
Wheezing in past 12 months	23 (22%)	16 (28%)	39 (100%)	0 (0%)
Diagnosed asthma	24 (23%)	20 (34%)	28 (72%)	16 (13%)
Nocturnal cough in past 12 months	27 (26%)	20 (34%)	21 (54%)	26 (21%)
Housing factors				
⩾1 household smoker	53 (51%)	27 (47%)	17 (44%)	63 (52%)
Furry pets	72(69%)	35 (60%)	23 (59%)	84 (69%)
Gas cooking	85 (82%)	37 (64%)	31 (79%)	91 (75%)
Gas fire use	74 (71%)	40 (69%)	27 (69%)	87 (71%)
Damp housing (reported)	14 (13%)	6 (10%)	9 (23%)	11 (9%)
Baseline investigations				
Atopic (⩾1 positive skin test)	27 (26%)	23 (40%)	19 (49%)	31 (25%)
Mean (SD) % predicted FEV_1	98 (12.5)	98 (10.5)	96 (14.2)	99 (12.5)
Mean (SD) % predicted FVC	89 (13.3)	89 (13.8)	86 (15.4)	90 (12.8)

ISC=Indian subcontinent.
*Total less than 162 as no response given in two cases.

spreadsheet by optical character recognition scanning (DRS Infotech, Milton Keynes, UK). Prior to analysis, PEF recordings were corrected for non-linear errors of the meters using an equation derived from the response of a sample of meters to a servo-controlled pump.[12]

Environmental monitoring

The five schools were near existing background urban air pollution monitoring stations, either as part of the National Automatic Urban and Rural Network or provided by local government. These stations measure nitrogen oxides (NO_x, NO, NO_2), sulphur dioxide (SO_2), ozone, carbon monoxide (CO), and PM_{10} as hourly averages. Measurements of PM_{10} and $PM_{2.5}$ used TEOM instruments equipped with 2.5 μm cyclone inserts operated at 50°C.[13] At two sites denuders enabled measurement of ammonia (NH_3) and acid gases (SO_2, hydrochloric acid (HCl), and HNO_3), chloride (Cl^-), NO_3^-, and NH_4^+.[14 15] Measurements of SO_4^{2-}, NO_3^-, and Cl^- were made by standard ion chromatographic methods, and of aerosol strong acid (H^+) by aqueous extraction and determination of pH according to the method of Koutrakis and coworkers.[16] The samples were collected daily and stored under refrigeration for batch analysis.

The University of Birmingham Weather Service and the Pollen Research Unit, Worcester provided daily maximum, mean and minimum temperatures, mean relative humidity, barometric pressure, wind speed, and summer pollen counts.

Statistical analysis

Analysis of data followed the methodology developed for the PEACE study.[17] Subjects who failed to record data on more than 22 days in each period (40%) were excluded because of inadequate data collection. The first two days of all PEF records were ignored to reduce potential training effects, and each subject's PEF record was transformed into daily deviations from their individual mean PEF for morning and afternoon separately. PEF data were analysed as the daily mean of individual deviations (ΔPEF), weighted according to the number of reporting children that day. Symptom data were analysed as the daily proportion of subjects reporting each symptom (% prevalent symptoms) or reporting a new episode of each symptom (% incident symptoms). For each day the denominator was defined as the number of children recording both morning and afternoon PEF.

Putative associations between environmental variables and health outcomes were initially explored using bivariate correlation (Pearson's correlation coefficient, r) and considered lags of 0–3 days and a 7 day prior mean. Final results were calculated using a linear regression approach for ΔPEF and logistic regression for symptoms. Final effect estimates were then derived from β (regression) coefficients in models accounting for relevant confounding factors. For each outcome, terms correcting for trend, weather elements, autocorrelation within the model residuals, and a dummy variable indicating school-days (versus weekends and holidays) were included. For ΔPEF, linear and square root trend terms were considered for inclusion to adjust for lung growth and potential training effects. For symptoms, linear, quadratic and higher order polynomial trend terms were considered.[17] Weather and summer pollen variables were considered for inclusion at the lag resulting in the strongest association to the health outcome. The a priori hypothesis required linear trend, a temperature term, and a term correcting for first order autocorrelation to be included. Other trend and weather terms were included on the basis of examining the residual variance and goodness of fit (r^2) statistics. Terms correcting for higher order autocorrelation were included on the basis of visually examining the autocorrelation and partial autocorrelation functions of the model residuals. For comparability, both Birmingham and Sandwell models were required to contain the same terms, albeit at different lags for weather variables. Pooled results for the entire panel could then be derived for ΔPEF and symptom outcomes by combing the effect estimate from each location after weighting by the inverse of its variance.

In addition to considering each panel as a whole, subgroups based on atopic status and a history of recent wheezing were analysed with the main pollutants of interest using the models identified for the whole panel to determine whether these children were at increased risk of adverse health effects.[18] In

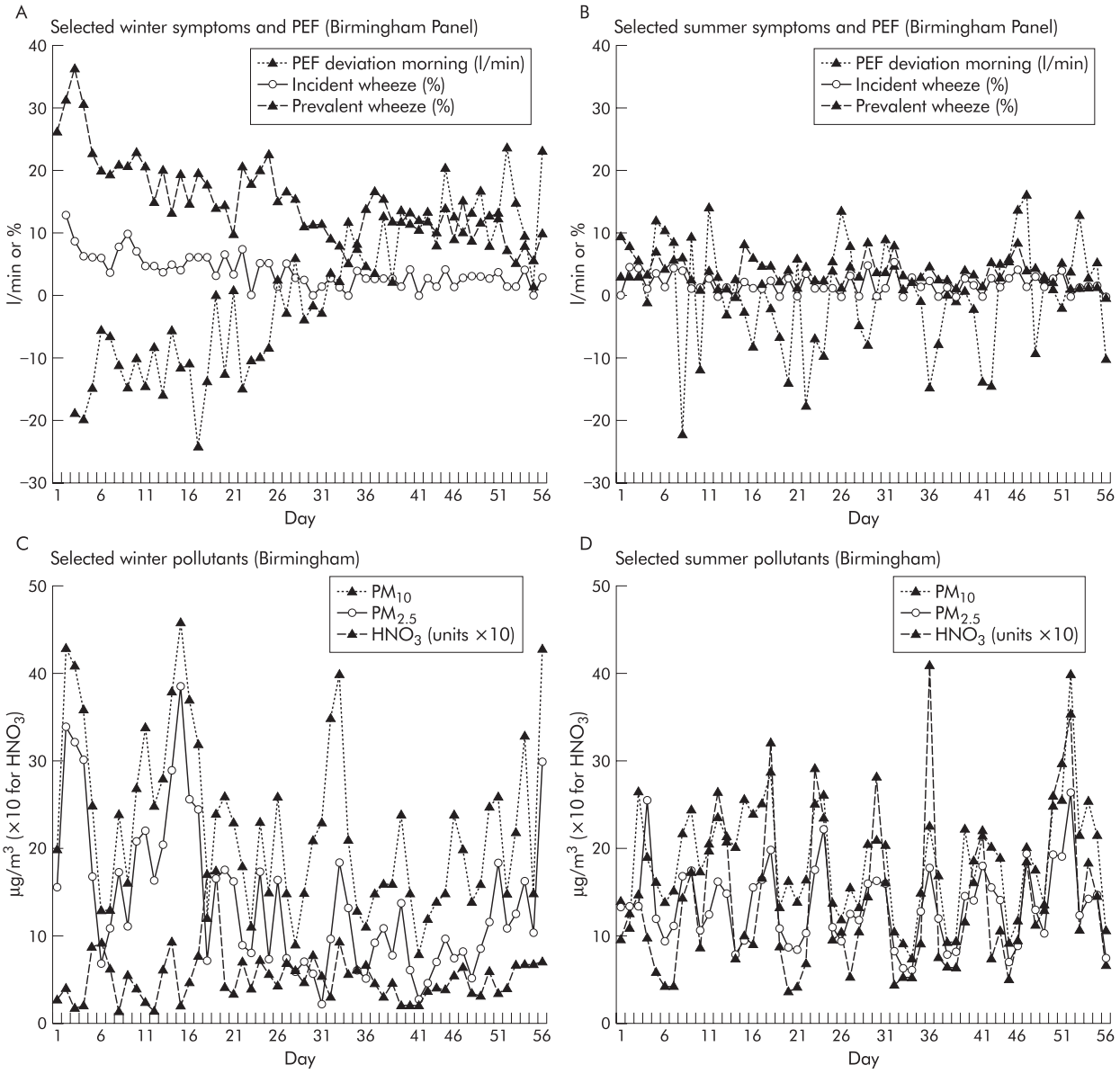

Figure 1 Selected time plots of ΔPEF, symptoms and pollutants for the winter (A, C) and summer (B, D) monitoring periods (data for Birmingham only shown).

addition to examining effect sizes in these groups, comparisons were also made with results from the remaining panel members.

RESULTS

Panel recruitment

Consent was obtained in 162 of 264 eligible children (table 1). Four children were lost to the panel before the summer period. The subgroup with a history of recent wheezing comprised 39 subjects; sleep disturbance was reported in 13 of these (33%) and wheezing severe enough to limit speech in five (13%). No significant differences in the proportion of children with a history of recent wheezing were found between schools or sexes.

No differences in baseline spirometric subgroups based on a history of recent wheezing were recorded. Children with a such a history were significantly more likely to be labelled atopic than those without recent wheezing and were more likely to show specific reactions to house dust mite allergen, tree pollen, and cat dander ($p<0.05$).

Data collection from subjects

Morning PEF records were available for a median of 140/162 subjects in winter (87% response, range 106–159) and 126/158 in summer (79% response, range 93–142). In general, symptoms were more frequently recorded in the winter than the summer (fig 1), the most frequently reported symptom being cough. Inadequate data collection resulted in the exclusion of 14 and 20 children, respectively, from the winter and summer periods. Direct questioning determined whether a child possessed anti-asthma medication, but individual dosages were poorly recorded so these data were discarded.

Environmental results

Wintertime pollutant levels were unexceptional and PM_{10} exceeded 40 $\mu g/m^3$ on only four occasions (table 2 and fig 1). Such peaks were associated with increased oxides of nitrogen and SO_2. A modest increase in ozone was seen in March. Poor weather meant that summer pollutant levels were generally low. PM_{10} exceeded 40 $\mu g/m^3$ only in the final week (fig 1), associated with increased oxides of nitrogen. Acid and anion concentrations were especially low as conditions for their

Table 2 Median (range) of environmental variables for the winter (13 January–10 March 1997) and summer (19 May–14 July 1997) monitoring periods

Environmental variable	Winter	Summer
NO_2 (ppb)	18.0 (4–35)	13.3 (3–29)
Ozone (ppb)	13.0 (2–33)	22.0 (10–41)
PM_{10} (μg/m^3)	21.5 (8–46)	18.7 (7–38)
$PM_{2.5}$ (μg/m^3)	12.7 (4–37)	12.3 (5–28)
SO_2 (ppb)	5.4 (2–18)	4.7 (2–10)
H^+ (ng/m^3)	8.6 (≤12.7)*	6.3 (≤7.6)*
Cl^- (μg/m^3)	3.0 (0.9–7.3)	0.8 (0.3–5.1)
HCl (μg/m^3)	0.3 (0.0–1.7)	0.3 (0.0–1.0)
HNO_3 (μg/m^3)	0.5 (0.2–2.2)	1.1 (0.4–3.8)
NH_3 (μg/m^3)	5.6 (0.9–23.8)	4.2 (0.6–8.8)
NH_4^+ (μg/m^3)	2.0 (0.2–15.5)	2.5 (0.5–7.1)
NO_3^- (μg/m^3)	3.6 (0.1–29.9)	3.5 (0.7–13.2)
SO_4^{2-} (μg/m^3)	2.4 (0.8–14.9)	3.8 (1.1–7.8)
Minimum temperature (°C)	2.5 (–3.5–8.1)	9.4 (2.1–14.1)
Mean temperature (°C)	5.5 (–1.0–9.9)	13.4 (8.1–19.1)
Maximum temperature (°C)	8.6 (1.5–13.3)	17.9 (10.6–25.5)
Relative humidity (%)	84 (67–96)	74 (47–92)
Barometric pressure (hPa/mb)	956 (923–977)	952 (926–966)
Wind speed (mph)	8 (2–18)	6 (3–15)

Levels indicate the 24 hour mean unless indicated otherwise and pollutant data averaged across up to five sites.
*Median of days where levels exceeded the detectable limit, but most days (39/56 winter and 47/56 summer) were below this limit of approximately 5 ng/m^3.

formation were unfavourable. Aerosol strong acidity (H^+) levels were detectable on only 17 winter and 9 summer days and were therefore not analysed.

Multiple cross correlations were seen between pollutants for both the winter and summer periods. Very strong positive correlations between winter time PM_{10} and $PM_{2.5}$ (r=0.93) were accompanied by similar relationships to NO_2 and, in the negative direction, to ozone. These associations were especially strong for $PM_{2.5}$ (r=0.88 and r=–0.83, respectively). Weaker associations were noted with SO_2. Most individual acid and anion species also showed a strong degree of positive correlation with each other and the particulate mass measures ($PM_{2.5}$ more than PM_{10}). However, Cl^-, HCl, HNO_3 and, to a lesser extent, H^+ were poorly associated with each other (except Cl^-

Table 3 Results of the final models for the entire panel during the winter period: estimated effect size (change in ΔPEF (l/min) or symptom odds per pollutant rise across interquartile range) and 95% confidence intervals (CI) for mass concentration of particulates and gaseous pollutants

	Lag				
Pollutant	0	1 day	2 days	3 days	7 day mean
PM_{10} (μg/m^3): size of interquartile range 11.8					
ΔPEF					
Morning					
Effect size	0.38	–0.24	0.32	–0.12	0.79
Upper 95% CI	2.24	1.60	2.55	1.83	6.09
Lower 95% CI	–1.41	–2.23	–1.88	–2.12	–4.47
Afternoon					
Effect size	0.63	–0.12	–0.35	–1.65	–2.23
Upper 95% CI	2.64	1.94	1.73	0.25	3.69
Lower 95% CI	–1.29	–2.12	–2.47	–3.64	–8.11
Prevalent symptoms					
Cough					
Effect size	0.90	0.93	0.96	0.92	1.06
Upper 95% CI	1.02	1.07	1.13	1.07	1.57
Lower 95% CI	0.79	0.80	0.83	0.79	0.72
Ill					
Effect size	1.08*	1.01	1.07	1.06	1.28*
Upper 95% CI	1.17	1.09	1.17	1.15	1.60
Lower 95% CI	1.00	0.93	0.98	0.98	1.01
SOB					
Effect size	1.00	0.99	1.00	0.99	0.93
Upper 95% CI	1.12	1.08	1.12	1.08	1.22
Lower 95% CI	0.91	0.90	0.90	0.89	0.71
Wake					
Effect size	0.99	1.02	1.00	0.96	1.02
Upper 95% CI	1.09	1.13	1.12	1.07	1.33
Lower 95% CI	0.90	0.93	0.90	0.88	0.78
Wheeze					
Effect size	0.93	0.87*	0.87*	0.98	0.91
Upper 95% CI	1.05	0.96	0.99	1.12	1.28
Lower 95% CI	0.83	0.78	0.77	0.87	0.65

Table 3 continued

Pollutant	Lag 0	1 day	2 days	3 days	7 day mean
$PM_{2.5}$ (µg/m³): size of interquartile range 12.3					
ΔPEF					
Morning					
Effect size	0.80	0.62	−0.86	−2.47	−4.07
Upper 95% CI	3.67	3.54	2.47	0.36	2.42
Lower 95% CI	−1.97	−2.22	−4.32	−5.30	−10.60
Afternoon					
Effect size	0.95	−0.99	−1.60	−3.45*	1.00
Upper 95% CI	4.23	2.72	2.01	−0.25	13.56
Lower 95% CI	−2.22	−4.69	−5.18	−6.53	−11.47
Prevalent symptoms					
Cough					
Effect size	0.98	0.95	1.02	1.01	1.31
Upper 95% CI	1.18	1.17	1.24	1.23	2.09
Lower 95% CI	0.80	0.77	0.83	0.83	0.82
Ill					
Effect size	1.17*	1.07	1.16*	1.01	1.57*
Upper 95% CI	1.32	1.23	1.35	1.16	2.13
Lower 95% CI	1.05	0.95	1.01	0.90	1.15
SOB					
Effect size	1.07	0.98	0.96	0.91	0.82
Upper 95% CI	1.24	1.13	1.13	1.07	1.18
Lower 95% CI	0.94	0.84	0.82	0.79	0.58
Wake					
Effect size	1.10	1.05	0.98	0.94	0.93
Upper 95% CI	1.26	1.22	1.13	1.09	1.32
Lower 95% CI	0.96	0.90	0.83	0.81	0.66
Wheeze					
Effect size	0.98	0.90	1.00	1.13	1.02
Upper 95% CI	1.16	1.05	1.20	1.35	1.57
Lower 95% CI	0.83	0.75	0.83	0.95	0.68
NO_2 (ppb): size of interquartile range 13.6					
ΔPEF					
Morning					
Effect size	−0.81	0.08	−0.54	−1.49	−6.10
Upper 95% CI	2.01	2.95	2.60	1.63	2.53
Lower 95% CI	−3.66	−2.71	−3.93	−4.47	−14.91
Afternoon					
Effect size	0.26	−1.76	−0.27	−1.63	1.80
Upper 95% CI	3.31	0.96	2.82	1.41	13.20
Lower 95% CI	−2.71	−4.61	−3.39	−4.61	−9.49
Prevalent symptoms					
Cough					
Effect size	0.85	1.00	1.12	1.09	1.41
Upper 95% CI	1.05	1.27	1.40	1.35	2.67
Lower 95% CI	0.68	0.79	0.90	0.89	0.76
Ill					
Effect size	1.12	0.96	1.04	1.00	1.17
Upper 95% CI	1.26	1.08	1.20	1.15	1.80
Lower 95% CI	0.99	0.85	0.92	0.89	0.78
SOB					
Effect size	1.05	0.95	0.95	0.92	0.56*
Upper 95% CI	1.21	1.09	1.09	1.08	0.91
Lower 95% CI	0.91	0.83	0.80	0.78	0.35
Wake					
Effect size	1.08	1.00	0.96	0.92	0.66
Upper 95% CI	1.24	1.15	1.09	1.07	1.05
Lower 95% CI	0.95	0.87	0.83	0.80	0.42
Wheeze					
Effect size	0.85	0.91	0.85	1.08	0.83
Upper 95% CI	1.01	1.07	1.01	1.31	1.50
Lower 95% CI	0.73	0.77	0.72	0.91	0.46
Ozone (ppb): size of interquartile range 21.5					
ΔPEF					
Morning					
Effect size	3.10	1.23	2.28	4.00	17.53*
Upper 95% CI	8.26	6.11	7.42	8.91	28.52
Lower 95% CI	−1.94	−3.66	−2.80	−0.86	6.56
Afternoon					
Effect size	−0.43	1.25	1.85	3.23	0.28
Upper 95% CI	4.41	5.55	6.28	7.74	9.79
Lower 95% CI	−5.38	−3.01	−2.37	−1.29	−9.03

Table 3 continued

Pollutant	Lag 0	1 day	2 days	3 days	7 day mean
Prevalent symptoms					
Cough					
Effect size	1.44*	1.12	1.16	1.02	0.88
Upper 95% CI	2.05	1.59	1.62	1.40	1.81
Lower 95% CI	1.00	0.77	0.84	0.74	0.42
Ill					
Effect size	0.91	1.32*	1.04	1.02	1.53
Upper 95% CI	1.12	1.62	1.29	1.27	2.53
Lower 95% CI	0.74	1.09	0.84	0.84	0.94
SOB					
Effect size	1.00	1.21	1.27	1.24	2.79*
Upper 95% CI	1.27	1.53	1.62	1.59	4.95
Lower 95% CI	0.77	0.94	0.98	0.96	1.56
Wake					
Effect size	1.00	1.09	1.24	1.24	1.97*
Upper 95% CI	1.27	1.37	1.56	1.56	3.50
Lower 95% CI	0.79	0.86	0.96	0.98	1.12
Wheeze					
Effect size	1.40*	1.35	1.37*	0.83	1.59
Upper 95% CI	1.84	1.77	1.84	1.09	3.31
Lower 95% CI	1.06	1.00	1.02	0.61	0.77
SO_2 (ppb): size of interquartile range 4.0					
ΔPEF					
Morning					
Effect size	–0.60	0.08	–0.16	0.27	–1.15
Upper 95% CI	1.32	1.86	1.64	2.09	3.74
Lower 95% CI	–2.51	–1.67	–1.99	–1.51	–6.09
Afternoon					
Effect size	–0.32	–0.88	–0.76	–0.20	–1.19
Upper 95% CI	2.04	1.10	1.25	1.63	6.46
Lower 95% CI	–2.71	–2.87	–2.79	–2.07	–8.88
Prevalent symptoms					
Cough					
Effect size	0.92	1.00	1.05	1.03	0.81
Upper 95% CI	1.05	1.15	1.19	1.17	1.15
Lower 95% CI	0.81	0.87	0.92	0.90	0.58
Ill					
Effect size	1.09*	1.03	1.07	0.98	1.32*
Upper 95% CI	1.18	1.11	1.17	1.06	1.64
Lower 95% CI	1.01	0.95	0.99	0.90	1.06
SOB					
Effect size	1.02	1.00	0.98	0.97	0.81
Upper 95% CI	1.13	1.09	1.08	1.07	1.03
Lower 95% CI	0.93	0.90	0.89	0.89	0.63
Wake					
Effect size	1.00	1.05	1.06	0.94	0.87
Upper 95% CI	1.10	1.15	1.16	1.04	1.10
Lower 95% CI	0.91	0.96	0.96	0.87	0.68
Wheeze					
Effect size	0.96	0.96	0.95	1.01	0.91
Upper 95% CI	1.07	1.07	1.06	1.13	1.23
Lower 95% CI	0.85	0.86	0.85	0.90	0.69

*p<0.05 for t test to determine probability that effect size different from zero (PEF) or 1 (symptom odds).

and HCl) and other pollutants. A similar pattern of association was noted in the summer, although the values of r were generally lower. However, in the summer, levels of HNO_3 were correlated with those for the particulate mass measures (PM_{10}, r=0.77; $PM_{2.5}$, r=0.81) and NO_2 (r=0.65).

Particulate levels were similar between the two locations, particularly in the case of $PM_{2.5}$, consistent with its long atmospheric lifetime (winter $PM_{2.5}$, r=0.80). Measured components of the particulate matter (SO_4^{2-}, NO_3^-, NH_4^+, Cl^-) were reasonably correlated between the two sites (r=0.63–0.93), while the gaseous acid and anions (HCl, HNO_3, NH_3) showed a lower degree of correlation (r=0.12–0.73).

Identification of regression models

For ΔPEF, square root trend terms were included as this improved model fit for the Birmingham panel. Similarly, quadratic trend terms were included in symptom models as model fit was generally improved for both panels. Minimum temperature was included in all models, although variations were seen in the lag chosen. The closest association between wintertime ΔPEF, prevalent symptoms, and minimum temperature was seen for the 7 day prior mean. In contrast, incident symptoms were most clearly associated with the same day's minimum temperature (except Birmingham illness and wheeze models which included the 7 day prior mean). The majority of summer outcomes were most closely associated with the same or previous day's minimum temperature, except incident and prevalent illness for which models also included the 7 day mean. Additionally, inclusion of relative humidity improved model fit for winter ΔPEF and prevalent symptoms, but not other meteorological variables or summer pollen count.

Table 4 Results of the final models for the entire panel during the winter period: estimated effect size (change in ΔPEF (l/min) or symptom odds per pollutant rise across interquartile range) and 95% confidence intervals (CI) for mass concentration of particulates and gaseous pollutants

	Lag				
Pollutant	0	1 day	2 days	3 days	7 day mean
HNO_3 (μg/m³): size of interquartile range 0.4					
ΔPEF					
Morning					
Effect size	−1.16	−1.07	−0.21	−1.03	−1.78
Upper 95% CI	0.36	0.37	1.35	0.44	1.89
Lower 95% CI	−2.67	−2.50	−1.77	−2.51	−5.45
Afternoon					
Effect size	−0.35	0.87	0.41	−0.87	−0.27
Upper 95% CI	1.24	2.31	1.96	0.62	6.34
Lower 95% CI	−1.94	−0.57	−1.13	−2.36	−6.87
Prevalent symptoms					
Cough					
Effect size	1.04	1.05	1.05	0.90*	1.14
Upper 95% CI	1.16	1.16	1.16	1.00	1.54
Lower 95% CI	0.93	0.95	0.94	0.81	0.84
Ill					
Effect size	0.97	0.96	1.01	1.02	1.09
Upper 95% CI	1.04	1.03	1.07	1.09	1.32
Lower 95% CI	0.91	0.90	0.94	0.95	0.90
SOB					
Effect size	0.97	0.9*	0.91*	1.00	0.79*
Upper 95% CI	1.05	0.97	0.98	1.08	0.99
Lower 95% CI	0.90	0.83	0.84	0.92	0.63
Wake					
Effect size	0.96	0.90*	0.90*	1.02	0.78*
Upper 95% CI	1.04	0.97	0.98	1.10	0.96
Lower 95% CI	0.89	0.83	0.84	0.94	0.63
Wheeze					
Effect size	1.00	0.98	0.89*	0.97	0.76*
Upper 95% CI	1.10	1.07	0.98	1.07	0.99
Lower 95% CI	0.91	0.89	0.82	0.88	0.58
SO_4^{2-} (μg/m³): size of interquartile range 4.8					
ΔPEF					
Morning					
Effect size	−1.75	−0.91	−0.62	−1.82	−3.22
Upper 95% CI	0.50	1.62	1.91	0.64	1.58
Lower 95% CI	−4.00	−3.44	−3.16	−4.27	−8.03
Afternoon					
Effect size	0.99	0.79	−1.89	−1.73	−1.96
Upper 95% CI	3.55	4.00	1.21	1.23	9.42
Lower 95% CI	−1.58	−2.42	−4.99	−4.69	−13.35
Prevalent symptoms					
Cough					
Effect size	1.01	1.02	0.99	0.86	0.78
Upper 95% CI	1.20	1.24	1.20	1.05	1.14
Lower 95% CI	0.84	0.85	0.82	0.71	0.53
Ill					
Effect size	1.06	1.15*	1.14*	1.04	1.30*
Upper 95% CI	1.17	1.28	1.28	1.18	1.66
Lower 95% CI	0.96	1.03	1.00	0.92	1.00
SOB					
Effect size	0.96	0.98	0.94	0.93	0.80
Upper 95% CI	1.07	1.12	1.07	1.08	1.07
Lower 95% CI	0.85	0.86	0.82	0.81	0.59
Wake					
Effect size	0.97	1.01	1.00	0.93	0.79
Upper 95% CI	1.08	1.15	1.14	1.07	1.05
Lower 95% CI	0.87	0.89	0.88	0.82	0.59
Wheeze					
Effect size	1.00	0.96	0.88	1.12	0.83
Upper 95% CI	1.15	1.13	1.04	1.32	1.20
Lower 95% CI	0.87	0.82	0.75	0.95	0.58
NO_3^- (μg/m³): size of interquartile range 6.7					
ΔPEF					
Morning					
Effect size	−2.08*	−0.64	0.71	−1.38	−0.92
Upper 95% CI	−0.15	1.59	3.11	0.84	3.47
Lower 95% CI	−4.02	−2.87	−1.69	−3.61	−5.32
Afternoon					
Effect size	0.24	−0.72	−1.37	−2.54	0.21
Upper 95% CI	2.38	2.43	2.38	0.66	8.11
Lower 95% CI	−1.89	−3.87	−5.11	−5.74	−7.67

Table 4 continued

Pollutant	Lag 0	1 day	2 days	3 days	7 day mean
Prevalent symptoms					
Cough					
Effect size	0.92	0.91	0.99	0.87	0.71*
Upper 95% CI	1.07	1.07	1.17	1.03	0.97
Lower 95% CI	0.80	0.77	0.83	0.73	0.52
Ill					
Effect size	1.05	1.11*	1.13*	1.13*	1.13
Upper 95% CI	1.14	1.22	1.26	1.26	1.38
Lower 95% CI	0.97	1.01	1.01	1.01	0.92
SOB					
Effect size	0.99	1.01	0.93	0.98	0.85
Upper 95% CI	1.10	1.13	1.05	1.13	1.08
Lower 95% CI	0.90	0.90	0.82	0.86	0.67
Wake					
Effect size	0.98	1.05	0.99	0.99	0.84
Upper 95% CI	1.08	1.16	1.12	1.12	1.05
Lower 95% CI	0.89	0.94	0.88	0.87	0.67
Wheeze					
Effect size	0.98	1.00	0.89	1.11	0.80
Upper 95% CI	1.10	1.14	1.03	1.30	1.07
Lower 95% CI	0.87	0.87	0.77	0.95	0.61

*p<0.05 (*t* test) to determine probability that effect size different from zero (PEF) or 1 (symptom odds).

Table 5 Results of the final models for the entire panel during the summer period: estimated effect size (change in ΔPEF (l/min) or symptom odds per pollutant rise across interquartile range) and 95% confidence intervals (CI) for mass concentration of particulates and gaseous pollutants

Pollutant	Lag 0	1 day	2 days	3 days	7 day mean
PM_{10} (μg/m³): size of interquartile range 9.0					
ΔPEF					
Morning					
Effect size	−1.56	−0.10	0.90	3.36*	1.24
Upper 95% CI	0.68	2.33	3.36	5.61	6.29
Lower 95% CI	−3.81	−2.53	−1.56	1.12	−3.82
Afternoon					
Effect size	−1.28	−1.56	−0.15	−0.05	−0.85
Upper 95% CI	0.67	0.41	1.85	2.03	3.40
Lower 95% CI	−3.23	−3.54	−2.15	−2.13	−5.09
Prevalent symptoms					
Cough					
Effect size	1.13*	1.04	0.96	0.89*	0.86
Upper 95% CI	1.23	1.14	1.05	0.96	1.07
Lower 95% CI	1.05	0.95	0.88	0.82	0.71
Ill					
Effect size	1.01	0.97	0.96	0.97	0.96
Upper 95% CI	1.13	1.11	1.08	1.10	1.41
Lower 95% CI	0.89	0.85	0.84	0.86	0.65
SOB					
Effect size	0.98	1.06	1.00	0.96	1.27
Upper 95% CI	1.14	1.25	1.16	1.11	1.78
Lower 95% CI	0.85	0.91	0.86	0.82	0.91
Wake					
Effect size	0.92	0.75*	0.91	0.92	1.24
Upper 95% CI	1.10	0.91	1.10	1.08	2.05
Lower 95% CI	0.77	0.62	0.74	0.78	0.75
Wheeze					
Effect size	0.96	0.90	0.88	0.82*	0.95
Upper 95% CI	1.14	1.06	1.05	0.96	1.53
Lower 95% CI	0.83	0.76	0.74	0.69	0.59
$PM_{2.5}$ (μg/m³): size of interquartile range 6.3					
ΔPEF					
Morning					
Effect size	−1.49	0.21	2.5*	3.41*	3.90
Upper 95% CI	0.67	2.55	4.72	5.44	10.33
Lower 95% CI	−3.65	−2.12	0.28	1.40	−2.53
Afternoon					
Effect size	−0.49	−0.78	0.57	0.16	−0.08
Upper 95% CI	1.45	1.16	2.49	2.17	5.27
Lower 95% CI	−2.43	−2.72	−1.35	−1.85	−5.43

Table 5 continued

Pollutant	Lag 0	1 day	2 days	3 days	7 day mean
Prevalent symptoms					
Cough					
Effect size	1.13*	1.04	0.94	0.89*	0.81
Upper 95% CI	1.22	1.13	1.02	0.96	1.06
Lower 95% CI	1.04	0.94	0.87	0.82	0.62
Ill					
Effect size	1.02	1.00	0.96	0.97	0.68
Upper 95% CI	1.13	1.13	1.07	1.09	1.13
Lower 95% CI	0.91	0.89	0.85	0.86	0.41
SOB					
Effect size	1.04	1.08	0.97	0.93	1.16
Upper 95% CI	1.20	1.25	1.13	1.08	1.77
Lower 95% CI	0.90	0.93	0.84	0.81	0.76
Wake					
Effect size	0.93	0.81*	0.91	0.97	1.04
Upper 95% CI	1.10	0.98	1.09	1.13	1.90
Lower 95% CI	0.78	0.67	0.77	0.83	0.57
Wheeze					
Effect size	1.02	0.98	0.87	0.85*	0.96
Upper 95% CI	1.19	1.16	1.02	0.99	1.81
Lower 95% CI	0.88	0.84	0.74	0.72	0.51
NO_2 (ppb): size of interquartile range 7.0					
ΔPEF					
Morning					
Effect size	0.46	1.20	1.87*	1.54	0.91
Upper 95% CI	2.33	3.09	3.68	3.33	4.73
Lower 95% CI	−1.42	−0.70	0.06	−0.26	−2.90
Afternoon					
Effect size	−0.77	−0.67	−0.02	0.08	1.21
Upper 95% CI	0.76	0.87	1.55	1.73	4.33
Lower 95% CI	−2.31	−2.20	−1.58	−1.55	−1.91
Prevalent symptoms					
Cough					
Effect size	1.09*	0.98	0.93*	0.94	0.87
Upper 95% CI	1.17	1.06	1.00	1.01	1.04
Lower 95% CI	1.01	0.91	0.87	0.87	0.74
Ill					
Effect size	1.01	0.99	0.95	0.96	0.78
Upper 95% CI	1.12	1.10	1.07	1.08	1.09
Lower 95% CI	0.91	0.89	0.84	0.85	0.56
SOB					
Effect size	1.11	1.04	1.02	0.99	1.14
Upper 95% CI	1.24	1.18	1.15	1.11	1.46
Lower 95% CI	0.99	0.93	0.91	0.89	0.89
Wake					
Effect size	0.99	0.87	0.98	0.96	0.99
Upper 95% CI	1.17	1.01	1.13	1.11	1.42
Lower 95% CI	0.83	0.74	0.85	0.84	0.70
Wheeze					
Effect size	0.97	0.91	0.89	0.89	0.93
Upper 95% CI	1.10	1.03	1.04	1.04	1.39
Lower 95% CI	0.85	0.80	0.77	0.76	0.62
Ozone (ppb): size of interquartile range 10.2					
ΔPEF					
Morning					
Effect size	−1.61	−2.39	−3.42*	−2.51	−5.66*
Upper 95% CI	1.01	0.34	−0.72	0.20	−0.09
Lower 95% CI	−4.24	−5.11	−6.12	−5.23	−11.21
Afternoon					
Effect size	−0.13	−2.32	−0.12	2.02	−0.14
Upper 95% CI	2.40	0.04	2.40	4.38	5.04
Lower 95% CI	−2.66	−4.68	−2.64	−0.34	−5.34
Prevalent symptoms					
Cough					
Effect size	0.99	1.07	1.05	1.02	0.95
Upper 95% CI	1.08	1.18	1.16	1.13	1.19
Lower 95% CI	0.89	0.97	0.96	0.93	0.76
Ill					
Effect size	0.91	1.08	1.11	1.11	1.16
Upper 95% CI	1.05	1.29	1.29	1.27	1.60
Lower 95% CI	0.79	0.91	0.95	0.96	0.85
SOB					
Effect size	1.02	1.04	1.07	1.16	1.35
Upper 95% CI	1.22	1.24	1.27	1.38	1.94
Lower 95% CI	0.85	0.87	0.91	0.98	0.95

Table 5 continued

Pollutant	Lag 0	1 day	2 days	3 days	7 day mean
Wake					
Effect size	0.98	0.98	0.90	0.96	1.18
Upper 95% CI	1.19	1.18	1.08	1.18	1.87
Lower 95% CI	0.81	0.81	0.75	0.79	0.75
Wheeze					
Effect size	0.83*	0.8*	0.83*	0.88	0.88
Upper 95% CI	0.98	0.93	1.00	1.06	1.38
Lower 95% CI	0.71	0.69	0.70	0.74	0.57
SO_2 (ppb): size of interquartile range 2.2					
ΔPEF					
Morning					
Effect size	0.91	0.29	0.95	2.7*	6.83*
Upper 95% CI	2.78	2.14	2.82	4.38	12.69
Lower 95% CI	−0.95	−1.56	−0.92	1.03	0.98
Afternoon					
Effect size	−0.89	−0.02	−0.41	0.02	−2.48
Upper 95% CI	0.83	1.65	1.24	1.61	2.59
Lower 95% CI	−2.61	−1.68	−2.05	−1.58	−7.56
Prevalent symptoms					
Cough					
Effect size	1.08*	1.04	1.02	0.98	0.96
Upper 95% CI	1.15	1.11	1.09	1.05	1.22
Lower 95% CI	1.02	0.97	0.95	0.91	0.75
Ill					
Effect size	1.05	1.02	1.00	0.94	1.07
Upper 95% CI	1.14	1.12	1.10	1.02	1.47
Lower 95% CI	0.96	0.94	0.92	0.86	0.78
SOB					
Effect size	0.98	1.00	1.02	0.92	0.92
Upper 95% CI	1.10	1.13	1.16	1.05	1.36
Lower 95% CI	0.87	0.89	0.90	0.81	0.62
Wake					
Effect size	1.00	1.02	0.95	0.94	1.13
Upper 95% CI	1.14	1.16	1.08	1.06	1.88
Lower 95% CI	0.87	0.89	0.84	0.83	0.67
Wheeze					
Effect size	1.05	1.00	1.06	0.94	0.90
Upper 95% CI	1.19	1.13	1.20	1.07	1.33
Lower 95% CI	0.92	0.88	0.94	0.83	0.60

*p<0.05 (*t* test) to determine probability that effect size different from zero (PEF) or 1 (symptom odds).

Table 6 Results of the final models for the entire panel during the summer period: estimated effect size (change in ΔPEF (l/min) or symptom odds per pollutant rise across interquartile range) and 95% confidence intervals (CI) for mass concentration of particulates and gaseous pollutants

Pollutant	Lag 0	1 day	2 days	3 days	7 day mean
HNO_3 (μg/m³): size of interquartile range 1.3					
ΔPEF					
Morning					
Effect size	−1.09	0.53	0.72	2.26*	−0.59
Upper 95% CI	1.07	2.81	3.06	4.43	6.14
Lower 95% CI	−3.26	−1.74	−1.62	0.08	−7.31
Afternoon					
Effect size	−0.08	−0.72	0.36	−1.92	−4.67
Upper 95% CI	1.97	1.40	2.49	0.17	0.96
Lower 95% CI	−2.14	−2.84	−1.77	−4.01	−10.29
Prevalent symptoms					
Cough					
Effect size	1.09*	1.01	0.94	0.89*	0.66*
Upper 95% CI	1.19	1.11	1.03	0.97	0.88
Lower 95% CI	1.00	0.92	0.86	0.82	0.49
Ill					
Effect size	0.92	0.98	0.95	1.04	0.79
Upper 95% CI	1.04	1.12	1.08	1.18	1.34
Lower 95% CI	0.83	0.86	0.83	0.92	0.46

Table 6 continued

Pollutant	Lag 0	1 day	2 days	3 days	7 day mean
SOB					
Effect size	1.04	1.01	0.99	0.95	1.02
Upper 95% CI	1.21	1.18	1.15	1.10	1.61
Lower 95% CI	0.90	0.86	0.85	0.82	0.65
Wake					
Effect size	0.83*	0.76*	0.94	0.89	0.93
Upper 95% CI	0.99	0.92	1.12	1.05	1.73
Lower 95% CI	0.69	0.62	0.78	0.75	0.50
Wheeze					
Effect size	0.93	0.87	0.87	0.7*	0.71
Upper 95% CI	1.09	1.02	1.04	0.82	1.20
Lower 95% CI	0.80	0.74	0.73	0.60	0.43
SO_4^{2-} (μg/m³): size of interquartile range 3.1					
ΔPEF					
Morning					
Effect size	–0.72	–1.69	1.35	3.38*	2.98
Upper 95% CI	1.82	0.90	3.97	5.72	10.13
Lower 95% CI	–3.27	–4.28	–1.27	1.03	–4.17
Afternoon					
Effect size	–0.32	0.84	–0.08	–0.25	–2.20
Upper 95% CI	2.17	3.30	2.44	2.19	5.12
Lower 95% CI	–2.81	–1.63	–2.61	–2.69	–9.51
Prevalent symptoms					
Cough					
Effect size	1.08	1.03	0.97	0.9*	0.73*
Upper 95% CI	1.20	1.15	1.07	0.99	0.97
Lower 95% CI	0.98	0.93	0.88	0.82	0.54
Ill					
Effect size	0.98	0.97	1.01	0.95	0.72
Upper 95% CI	1.11	1.12	1.16	1.09	1.12
Lower 95% CI	0.86	0.84	0.88	0.84	0.46
SOB					
Effect size	0.95	1.07	1.04	0.94	0.58
Upper 95% CI	1.14	1.28	1.24	1.12	1.04
Lower 95% CI	0.80	0.89	0.87	0.80	0.33
Wake					
Effect size	0.95	0.81*	0.93	0.87	0.77
Upper 95% CI	1.16	0.99	1.13	1.05	1.48
Lower 95% CI	0.78	0.67	0.76	0.72	0.41
Wheeze					
Effect size	0.97	1.09	1.00	0.81*	1.30
Upper 95% CI	1.17	1.32	1.22	0.97	2.50
Lower 95% CI	0.80	0.89	0.82	0.69	0.68
NO_3^- (μg/m³): size of interquartile range 3.7					
ΔPEF					
Morning					
Effect size	–0.80	0.68	1.42	2.54*	1.74
Upper 95% CI	1.15	2.67	3.58	4.59	6.13
Lower 95% CI	–2.74	–1.31	–0.73	0.48	–2.66
Afternoon					
Effect size	–0.72	–0.59	–0.33	0.66	0.47
Upper 95% CI	1.03	1.18	1.45	2.58	4.29
Lower 95% CI	–2.47	–2.36	–2.11	–1.26	–3.36
Prevalent symptoms					
Cough					
Effect size	1.05	1.01	0.95	0.89*	0.81*
Upper 95% CI	1.13	1.10	1.03	0.96	0.97
Lower 95% CI	0.97	0.93	0.88	0.83	0.68
Ill					
Effect size	0.97	0.98	0.95	0.94	0.74
Upper 95% CI	1.09	1.10	1.06	1.05	1.03
Lower 95% CI	0.87	0.87	0.85	0.85	0.54
SOB					
Effect size	1.04	1.12	1.04	0.90	1.06
Upper 95% CI	1.18	1.28	1.20	1.03	1.43
Lower 95% CI	0.90	0.98	0.90	0.79	0.78
Wake					
Effect size	0.94	0.86	0.94	0.92	0.95
Upper 95% CI	1.09	1.01	1.11	1.07	1.47
Lower 95% CI	0.80	0.72	0.79	0.79	0.62
Wheeze					
Effect size	1.01	0.96	0.95	0.87	1.04
Upper 95% CI	1.17	1.11	1.10	1.01	1.60
Lower 95% CI	0.87	0.83	0.82	0.75	0.67

*p<0.05 (*t* test) to determine probability that effect size different from zero (PEF) or 1 (symptom odds).

Table 7 Analysis of subgroups based on atopic status (Birmingham n=27, Sandwell n=23) and parental history of recent wheezing (Birmingham n=23, Sandwell n=16) subgroups. Results are only shown for selected pollutants and morning ΔPEF (l/min)

		Subgroup with atopy or history of recent wheezing		Subgroup without atopy or history of wheezing		Difference between subgroups
Pollutant	Lag (days)	Effect size†	95% CI	Effect size†	95% CI	
Subgroups based on atopic status:						
PM_{10}	0	–0.088	–0.403 to 0.226	0.086	–0.285 to 0.456	
	1	–0.105	–0.407 to 0.198	0.008	–0.363 to 0.379	
	2	0.118	–0.220 to 0.456	–0.014	–0.439 to 0.412	
	3	–0.034	–0.363 to 0.295	–0.005	–0.399 to 0.388	
$PM_{2.5}$	0	–0.072	–0.527 to 0.383	0.126	–0.413 to 0.666	
	1	–0.271	–0.701 to 0.159	0.193	–0.340 to 0.728	
	2	0.127	–0.354 to 0.608	–0.170	–0.788 to 0.447	
	3	0.055	–0.391 to 0.501	–0.314	–0.846 to 0.216	
HNO_3	0	3.506	–4.273 to 11.285	–5.964	–15.195 to 3.266	p<0.05
	1	–0.445	–8.083 to 7.192	–3.866	–12.741 to 5.010	
	2	–7.616*	–14.989 to –0.242	2.588	–6.644 to 11.819	p<0.05
	3	3.240	–4.568 to 11.048	–5.384	–14.498 to 3.730	
SO_4^{2-}	0	0.200	–0.755 to 1.156	–0.613	–1.714 to 0.488	
	1	–0.219	–1.318 to 0.881	–0.174	–1.423 to 1.075	
	2	–0.431	–1.526 to 0.664	0.006	–1.243 to 1.253	
	3	1.200*	0.095 to2.305	–1.080	–2.308 to 0.148	p<0.05
NO_3^-	0	–0.036	–0.627 to 0.555	–0.434	–1.116 to 0.248	
	1	0.142	–0.573 to 0.857	–0.201	–1.002 to 0.600	
	2	0.000	–0.760 to 0.759	0.154	–0.703 to 1.010	
	3	0.689	–0.061 to 1.439	–0.605	–1.422 to 0.210	p<0.05
Subgroups based on parental history of recent wheezing:						
PM_{10}	0	0.072	–0.069 to 0.212	0.019	–0.235 to 0.273	
	1	0.094	–0.045 to 0.233	–0.065	–0.324 to 0.193	
	2	0.013	–0.139 to 0.166	0.031	–0.267 to 0.330	
	3	–0.044	–0.189 to 0.102	–0.005	–0.276 to 0.265	
$PM_{2.5}$	0	0.187	–0.008 to 0.382	0.026	–0.341 to 0.395	
	1	–0.006	–0.207 to 0.195	0.068	–0.307 to 0.444	
	2	–0.011	–0.226 to 0.204	–0.099	–0.535 to 0.335	
	3	–0.037	–0.228 to 0.154	–0.252	–0.615 to 0.110	
HNO_3	0	1.005	–2.115 to 4.124	–4.324	–10.556 to 1.907	
	1	–2.266	–5.135 to 0.603	–2.982	–8.869 to 2.904	
	2	–1.835	–4.775 to 1.105	–0.157	–6.499 to 6.183	
	3	–0.442	–3.366 to 2.481	–3.445	–9.496 to 2.607	
SO_4^{2-}	0	0.457*	0.003 to 0.910	–0.622	–1.379 to 0.136	p<0.05
	1	0.078	–0.503 to 0.660	–0.272	–1.147 to 0.602	
	2	–0.102	–0.656 to 0.452	–0.138	–1.005 to 0.728	
	3	0.002	–0.609 to 0.613	–0.496	–1.359 to 0.367	
NO_3^-	0	0.228	–0.054 to 0.511	–0.482*	–0.952 to –0.012	p<0.05
	1	0.476*	0.060 to 0.892	–0.276	–0.846 to 0.294	p<0.05
	2	0.196	–0.202 to 0.594	0.078	–0.520 to 0.675	
	3	0.083	–0.321 to 0.487	–0.298	–0.864 to 0.268	

*Effect estimate significantly different from zero (p<0.05).
†Effect size=ΔPEF per μg/m^3 increase in pollutant.

In general, first order autocorrelation terms were adequate to remove autoregressive effects from the model residuals, but winter SOB and summer morning ΔPEF required additional higher order terms.

Pollutant effects on health outcomes

Statistically significant associations between pollutants and ΔPEF or respiratory symptoms were seen in both winter (tables 3 and 4) and summer (tables 5 and 6). However, there were no consistent changes, either adverse or otherwise, in any symptom or lung function index when the total panel was considered. Results for incident symptoms and the acid and anion species HCl, Cl^-, NH_4^+ and NH_3 are not shown for brevity. No pattern in the nature of the pollutants or the lag of greatest measured effect were noted and, in particular, there were no consistent responses to ozone or particles as PM_{10} or $PM_{2.5}$.

Analysis of subgroups based on atopic status or history of recent wheezing

The results do not indicate that children with atopy or a history of recent wheezing are more susceptible to the short term respiratory health effects of air pollutants. Few statistically significant results were noted and the results are presented for winter morning ΔPEF only (table 7). However, no pattern between pollutants, their lags, or apparent direction of measured effect are evident for any of the health outcomes studied, nor is there any apparent consistency between the two locations.

DISCUSSION

This study provides little evidence for a relationship between the measured pollutants and daily changes in health outcomes after correction for the confounding effects of weather, trends in the data, and autocorrelation. In particular, there is no suggestion that $PM_{2.5}$ provides a better index of short term health effects than PM_{10}, and that individual acid or anion species were more closely associated with such effects than particulate mass measures. In epidemiological studies involving multiple comparisons it is important not to overemphasise individual "significant" results, but rather to attempt to identify clear consistent patterns. In this study no such consistency in pollutant, lag, or location was noted.

The identification of particulate health effects where aerosol strong acidity is very low[3] has focused attention away from acid species generally, and these compounds have not been regarded as important in the UK since the Clean Air Act. In this study, aerosol strong acidity was virtually undetectable and no relationships with acid or basic species, gas or aerosol, were found, although concentrations were low. Sulphate has been regarded by some authors as a surrogate for the mass concentration of fine particulates[19] and, in situations of high aerosol strong acidity, has been found to be more strongly related to respiratory admissions and some symptoms than PM measures.[9 20] In contrast, low levels of aerosol strong acidity were reported in a wintertime Dutch panel of children which identified small effects of PM_{10}, NO_2, SO_4^{2-}, NO_3^-, and HNO_3 (but not SO_2) on lung function,[10] although only short lags were considered. The effects of SO_2 and SO_4^{2-} on respiratory symptoms were also reported.

Our findings are consistent with those from the PEACE study in which urban and rural panels of 6–12 year old children with a history of recent night time cough or wheeze were monitored across 14 centres for at least two winter months.[7] Measures of fine particulate levels and acid species were omitted from this study and few statistically significant associations were found overall, despite a wide range of pollutant and climatic experiences. The authors identified a number of possibilities for these negative findings. Firstly, overall panel effect estimates could potentially be biased by a subgroup within the panel with a different pattern of response. In the PEACE study children with diagnosed asthma taking respiratory medication showed a positive relationship between PEF and pollutant levels, although bronchodilator use was not related to pollutants.[18] In our study, subgroup analyses revealed no consistent effects of pollutants on PEF or respiratory symptoms in children with a previous history of wheezing or atopy. Other authors report contrasting findings; a study of Dutch adults demonstrated that airway "lability", expressed as PEF variability or bronchial hyperresponsiveness (BHR), predicted susceptibility to pollutant effects[21] and, in Dutch children, "allergy", in addition to BHR, has been implicated in susceptibility to increased PM_{10}, NO_2, and SO_2.[22] It has been suggested that, in susceptible subjects, pollutants may act as "potentiators", increasing the effects of other factors such as allergens which could influence lung function.[23] However, such a relationship could potentially be reversed by the action of bronchodilating medication so that the inclusion of children with diagnosed asthma in an epidemiological study of air pollutants may obscure any real relationships or lead to the paradoxical result of high pollutant levels associated with better health outcomes. This could occur if those with asthma modify their behaviour on high pollutant days, either by the use of bronchodilating drugs[3] or by staying indoors and reducing activity.

Selecting individuals with a history of recent wheezing on the basis of a questionnaire may also result in a heterogeneous group. In contrast to our symptomatic subgroup, selected on the basis of recent wheezing only, most centres in the PEACE study included children with nocturnal cough alone. Such children were in the majority in many panels and had a lower prevalence of atopy, higher MMEF, and lower day to day PEF variability[24] and could have responded differently to air pollutants.[18]

Unmeasured confounders which vary across a suitable time course—for example, respiratory tract infections—could also be important, although fever has proved to be a relatively insensitive surrogate marker for this.[7] In our study the daily prevalence of school absence (or days' data missing if at weekends) said to be due to illness (excluding accidental injury) was used as an imperfect measure of such infections and was not found to be associated with daily pollutant levels. Data missing from an individual's record due to ill health could weaken the apparent effect of pollutants if the missed days included illness precipitated or exacerbated by air pollution. The validity of the health outcome measures where children record their own data is not known and misclassification arising in this area could weaken any apparent effects of pollutants. Invented, misread, or inadequate PEF values can occur and these have been shown to increase with time.[25] Less is known about the validity and accuracy of symptom responses, but these may reduce with waning interest. In addition, the low prevalence of symptom reporting, particularly in the summer, may also have reduced the sensitivity of our study.

The number of subjects enrolled in this study was greater than in some widely reported panel studies that have shown an association between PM_{10} and decrements in PEF in this age group.[2–4] However, these studies have exclusively examined populations selected on the basis of existing respiratory symptoms or asthma. In addition, in all these cases pollutant levels were greater than seen in this study where, in general, pollutant levels were modest in winter, though not unrepresentative of the UK, and very low in summer. It may therefore be that this study had insufficient power to detect effects in an unselected cohort of children.

In conclusion, this study does not provide evidence for day to day respiratory health effects of pollutants, including particulates and individual acid and anion species, in a panel of UK inner city primary schoolchildren or subgroups with atopy or pre-existing wheeze. However, only short term effects were considered so these results do not preclude an effect of very fine particulates or acid species on longer term changes in lung function, symptoms, or lung development. Previous authors have suggested that short term pollutant effects occur without threshold. We believe that, if such effects exist, they are likely to be marginal at these observed pollutant concentrations. It is likely that the complexity of adequately dealing with both intraindividual and interindividual variability, in addition to quantitatively small associations between population average responses and pollutants, may be beyond the modelling approach adopted by the PEACE study. Further work should concentrate on more homogeneous groups thought to be at high risk of adverse effects and attempt to improve the validity of health status monitoring.

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This study was funded by the Department of Health, UK. The authors acknowledge the assistance of Dr G McGregor, Department of Geography, University of Birmingham, Dr John Middleton, Sandwell Health Authority, Sandwell Environmental Services, and the Pollen Research Unit, WCHE, Worcester, and thank the teachers and pupils of the five participating junior schools from Birmingham (Bromford Road, Ward End and Firs) and Sandwell (Springfield and Perryfields).

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THORAX

Effects of daily variation in outdoor particulates and ambient acid species in normal and asthmatic children

D J Ward, K T Roberts, N Jones, R M Harrison, J G Ayres, S Hussain and S Walters

*Thorax*2002 57: 489-502
doi: 10.1136/thorax.57.6.489

PostScript

LETTERS TO THE EDITOR

IL-5 in asthma

We have recently published two manuscripts on the effects of interleukin (IL)-5 administration to patients with mild asthma in the *American Journal of Respiratory & Critical Care Medicine*[1] and in *Thorax*.[2] We are addressing this letter to the Editors of both journals.

The data described in both papers have been obtained from one experiment performed in the same group of patients with mild asthma. While the paper in the *American Journal of Respiratory & Critical Care Medicine* reports primarily on the phenotypic changes in circulating blood eosinophils and CD34+ cells, the *Thorax* paper describes the changes in the airways with measurements of bronchial responsiveness and of eosinophil counts in sputum, together with eotaxin levels in the serum. Both manuscripts, however, detail the changes in blood eosinophil counts and serum IL-5 changes derived from these nine patients, which constitutes a partial duplication of the data described in the two papers. At the time of submission of the manuscripts to the two journals we did not inform the respective journals of the existence and submission of the other manuscript.

We would also like to take the opportunity of pointing out one mistake and two differences in the two manuscripts:

(1) Table 1 in *Thorax* contains mistakes regarding the FEV_1 values; table 1 in the *Am J Respir Crit Care Med* paper shows the correct values.

(2) The *Am J Respir Crit Care Med* paper quotes the median values in the text while mean values are plotted in fig 2, and the *Thorax* paper the geometric mean.

(3) The blood eosinophil counts were analysed in the *Am J Respir Crit Care Med* paper as paired *t* tests while in the *Thorax* paper we used repeated measures analysis of variance (as recommended by a reviewer) which does not provide significant differences in eosinophil counts.

We recognise that it has been an error of judgement on our part in having the experimental data from this study reported in two separate manuscripts, and also in not informing you (and the reviewers) of the existence of these two separate manuscripts at the time of submission. We have not intentionally set out to duplicate publication of our experimental data and regret that this has happened. We also would like to apologise for the concern that this may cause to the high reputation of both journals.

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Bronchoconstrictor effect of deep inspiration in asthma

I was interested in the article by Burns and Gibson in the February issue of *Thorax*,[1] but feel that the authors should exclude the following possible confounding factors which should be addressed before their hypothesis can be accepted.

(1) The time course of the bronchoconstrictor response to deep breaths in mild asthma is brief (usually 60–90 seconds), so the precise timing of the sGaw measurements after the manoeuvre is critical. Have the authors taken this into consideration?

(2) Although the pre-test and test breathing pattern was standardised as far as possible, have changes in P_{CO_2} been excluded since hypocapnia can have a larger effect on sGaw even in normal subjects than that described here.[2]

(3) Why do their normal subjects show a fall from baseline sGaw after deep breaths rather than the consistent small rise seen in previous studies as quoted in the discussion?

If these points can be answered, then further investigation of their inherently speculative hypothesis might indeed be worthwhile.

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Authors' reply

We agree with Dr Sterling that the bronchoconstrictor effect of a deep inspiration in asthma is brief and that the timing of the sGaw measurement is critical. The relevant comparison is between the sGaw performed after the timed non-forced inspiratory manoeuvres and that performed after the forced inspiratory manoeuvres. In each case, as stated in our paper,[1] subjects returned to functional residual capacity (FRC) immediately after the final full inspiration, ensuring both parity in the timing of the two manoeuvres and that in each case sGaw was measured as soon as practically possible after the inspiration.

P_{CO_2} was not measured but the inspiratory/expiratory manoeuvres preceding the measurement of sGaw were designed to be identical in their time-volume relationship. This was in order to minimise any difference in the behaviour of the smooth muscle (or any other element responsive to stretch), but it would, of course, also ensure that any difference in ventilation, and thus P_{CO_2}, was also minimised.

We compared sGaw after two different types of inspiratory manoeuvre which were designed to be identical in every respect other than the intrathoracic pressure generated. The constraints of this requirement meant that the inspiratory manoeuvres were different from the usual rapid deep inspiration preceding the measurement of sGaw in the referenced studies. The longer inspiratory manoeuvre in our study would be expected to produce a significantly diminished bronchodilating effect than that produced by the usual rapid deep inspiration.[2] This probably explains the absence of any significant difference between the baseline sGaw (before deep inspiration) and that performed after deep inspiration (without resistance) in healthy subjects.

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Inhaled sodium cromoglycate in children with asthma

We admire the perseverence of Dr Edwards and colleagues to dispute the conclusions of our systematic review on sodium cromoglycate in asthmatic children.[1 2] We note that they restrict their present comments to only a single point—interpretation of the tolerance interval. In fact, our conclusions were based not only on this finding but also on the apparent publication bias and the small overall treatment effect. Hence, we stick to our conclusion that there is insufficient evidence that maintenance treatment with sodium cromoglycate is beneficial in children with asthma.

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The editors will decide as before whether to also publish it in a future paper issue.

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Body mass index and asthma

We read with interest the report by von Mutius *et al* on the association between body mass index (BMI) and asthma in children.[1] The finding that the association between asthma and obesity may be mediated by mechanical factors or by an alternative inflammatory mechanism rather than eosinophilic inflammation is important and contributes to our understanding of the causal pathway.

With regard to breastfeeding, the authors state: "Breast feeding was no longer a significant predictor of asthma once BMI was introduced into the model. However, this may be because the intermediate variable (BMI) was introduced in the model." The authors then surmise that BMI is an independent variable, and the results of their multivariate analyses—including breastfeeding—do not support the notion that "BMI might be an intermediate step". However, if the former is correct, then lack of breastfeeding is the problem and a reduction of BMI may not reduce asthma, as claimed by the authors. The conclusions drawn appear to be contradictory and also do not reflect the limitations of cross sectional analyses.

The question is whether: (1) lack of breastfeeding results in increased BMI and increased BMI is an intermediate step in the aetiology of asthma; or (2) the association between BMI and asthma is a spurious correlation and both are caused by lack of breastfeeding; or (3) both increased BMI and shortened breastfeeding are independent risk factors.

Acknowledging the restriction of cross sectional analyses, the authors need to clarify their conclusions and provide the respective models and path (or partial) coefficients that support one or other of the models suggested above.

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Reference

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BOOK REVIEW

Pulmonary Physiology and Pathophysiology

J B West. Lippincott Williams & Wilkins, 2000. $31.95. ISBN 0 7817 2910 6

John West's classic texts *Respiratory Physiology: The Essentials* and *Pulmonary Pathophysiology: The Essentials* are read by almost all respiratory medicine specialists at some stage of their training. This new book is aimed at medical students. It condenses both into one volume and adopts a case based approach. Each chapter opens with a clinical vignette to introduce a physiological topic. While this might appear attractive in placing the physiology in a clinical context, abandoning the clear and logical route taken by the previous volumes does make the new book very hard work to read. In the first chapter we meet a competitive cyclist and, before the end of the first page, we are on to her exercise test results and discussing anaerobic thresholds. After the inevitable mountaineering trip in chapter 2, subsequent chapters start with the stories of patients with COPD, asthma, pulmonary fibrosis, pulmonary embolism, pulmonary oedema, pneumoconiosis, and ARDS. Some of the chapters work well; others feel as if several different sections of the previous books have been pasted together, between a case history to start and an extract from a textbook of clinical respiratory medicine to end. Nevertheless, this book contains a wealth of material and will repay careful study by those adopting a case based approach to medicine. For my money, I would start with *Respiratory Physiology: The Essentials*, even though it costs about the same as the new two-in-one integrated version.

W Kinnear

NOTICE

6th International Mesothelioma Conference

The 6th Conference of the International Mesothelioma Interest Group will be held at the Queen Elizabeth II Medical Centre, Perth, Western Australia on 1–3 December 2002. For further information contact Mrs Maree Branigan, University Department of Medicine, 4th Floor, G Block, QEII Medical Centre, Verdun Street, Nedlands, Perth, Western Australia 6009; telephone +61 (0)8 9346 2005, fax +61 (0) 8 9346 2816, e-mail: branigan@cyllene.uwa.edu.au

CORRECTION

In the paper entitled "Effects of daily variation in outdoor particulates and ambient acid species in normal and asthmatic children" by D J Ward *et al* which appeared in the June issue of *Thorax* (2002;**57**:489–502), the first sentence in the Conclusion of the abstract should have read: "These data do not suggest that adverse health outcomes are associated with daily variations in **pollutants**". We apologise for this error.