Ambient particulate pollution and the world-wide prevalence of asthma, rhinoconjunctivitis and eczema in children: Phase One of the International Study of Asthma and Allergies in Childhood (ISAAC)

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Stephan K Weiland died on 19 March 2007.
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ABSTRACT

Objectives To investigate the effect of ambient particulate matter on variation in childhood prevalence of asthma, rhinoconjunctivitis and eczema.

Methods Prevalences of asthma, rhinoconjunctivitis and eczema obtained in Phase One of the International Study of Asthma and Allergies in Childhood (ISAAC) were matched with city-level estimates of residential PM_{10} obtained from a World Bank model. Associations were investigated using binomial regression adjusting for GNP per capita and for clustering within country. For countries with more than one centre, a two stage meta-analysis was carried out. The results were compared with a meta-analysis of published multi-centre studies.

Results Annual concentrations of PM_{10} at city level were obtained for 105 ISAAC centres in 51 countries. After controlling for GNP per capita, there was a weak negative association between PM_{10} and various outcomes. For severe wheeze in 13—14-year-olds, the OR for a 10 $\mu g/m^3$ increase in PM_{10} was 0.92 (95% CI 0.84 to 1.00). In 24 countries with more than one centre, most summary estimates for within-country associations were weakly positive. For severe wheeze in 13—14-year-olds, the summary OR for a 10 $\mu g/m^3$ increase in PM_{10} was 1.01 (0.92 to 1.10). This result was close to a summary OR of 0.99 (0.91 to 1.06) obtained from published multi-centre studies.

Conclusions Modelled estimates of particulate matter at city level are imprecise and incomplete estimates of personal exposure to ambient air pollutants. Nevertheless, our results together with those of previous multi-centre studies, suggest that urban background PM_{10} has little or no association with the prevalence of childhood asthma, rhinoconjunctivitis or eczema either within or between countries.

What this paper adds

- The reasons for the wide international variations in the prevalence of childhood asthma, rhinoconjunctivitis and eczema are not understood.
- One factor might be exposure to ambient particulate matter since this has been associated with exacerbations of asthma and may also play a role in the increased prevalence of asthma symptoms and allergy observed in some traffic-proximity studies.
- In a study of over half a million children from 105 cities in 51 countries, we found little or no evidence of associations with modelled city-level residential PM_{10}.
- The results suggest that community levels of ambient particulate matter are unlikely to explain international variations in prevalence.
- Future investigations of this topic should employ improved exposure assessment and control for confounding factors at the individual level.

INTRODUCTION

Childhood asthma is a major cause of illness and disability in childhood.[1] It shows large variations in occurrence world-wide and over time,[2 3] but the reasons for these variations and trends are largely unknown. Asthma is a condition characterised by inflammation and hyper-responsiveness of the airways, and those with asthma frequently report that air pollution aggravates or precipitates their asthma. It is therefore not surprising that ambient air pollution is widely believed to be one possible cause of variations in prevalence through effects on incidence, severity or prognosis. The particulate component of air pollution is widely measured as particulate matter with aerodynamic diameter less than 10 μm (PM_{10}), this being small enough to penetrate the intrathoracic respiratory tract. PM_{10} is a complex mixture arising from different sources with a range of physicochemical characteristics. While some components of PM_{10} are likely to be more toxic than others, these differences have been difficult to quantify.[4 5] Experimental evidence based on acute exposures suggests that particulate matter has the potential to increase airway reactivity, increase inflammatory responses in the lung and enhance allergic immune responses,[6 7] but studies at environmental concentrations have been equivocal.[8] Various reviews have concluded that while there is evidence that short-term increases in PM_{10} may aggravate symptoms of asthma, the evidence for effects of chronic exposure to PM_{10} on asthma incidence and prevalence is weak.[9–11] There is some evidence from birth cohort studies linking traffic exposure to atopic sensitisation.[12–14]

The evidence for effects on asthma of chronic exposure to particulate matter may be divided into those studies which have investigated the effects of

proximity to sources of traffic pollution and those which have investigated the effects of community-level concentrations of specific pollutants measured by urban background monitoring stations representing the residential environment. The contribution of traffic pollution to urban background concentrations varies. Traffic-proximity studies are usually conducted within a single urban area and tend to find that children living in close proximity to traffic have an increased risk of respiratory symptoms, including those of asthma, relative to those living further away.[15 16] The effects of community-level exposure on prevalence are usually investigated by comparing urban areas using urban background concentrations of pollutants; these studies tend to find associations with bronchitic type symptoms rather than with asthma or allergic symptoms, but interpretation is frequently hampered by the small number of areas compared, often as low as two, and by the ecological nature of such studies. We identified nine studies of children comparing five or more centres and none found evidence of a statistically significant positive association between ambient particulate matter and asthma symptoms.[17–25] This is unlikely to be entirely explained by exposure measurement error because the same studies often report other adverse effects, including bronchitic symptoms in those with and without asthma, reductions in lung function and increased mortality rates in adults.

Current evidence therefore suggests that despite associations between asthma prevalence and proximity to traffic, and between asthma exacerbations and short-term variations in air pollution measured at community monitors, particulate matter does not play a role in determining asthma *prevalence* in a population. Current evidence is, however, based on comparisons of a limited number of cities or communities within individual developed countries. The exception is a study of nitrogen dioxide and asthma prevalence in 62 centres in five largely European countries.[26] There are no published international studies of city-level average concentrations of background particulate matter and asthma prevalence. The role of particulate matter in determining variations in asthma prevalence world-wide has not been investigated.

Phase One of the International Study of Asthma and Allergies in Childhood (ISAAC) study published prevalence estimates for symptoms and diagnoses of asthma, rhinoconjunctivitis and eczema from 6–7-year-old children in 91 centres in 38 countries and from 13–14-year-old children in 156 centres in 56 countries.[27] Measures of ambient air pollution in ISAAC centres are sparse. However, model estimates of annual concentrations of ambient particle concentrations (PM_{10}) in residential areas of all cities with a population of more than 100 000 are available from a model developed at the World Bank.[28] These had been used by WHO to estimate the global impact of particulate matter on mortality. This provided an opportunity to investigate the association between city-level estimates of residential exposure to urban background PM_{10} and the prevalence of asthma, rhinoconjunctivitis and eczema in children in a large number of cities world-wide.

METHODS

The ISAAC protocol and results for the prevalence of symptoms of asthma, rhinoconjunctivitis and eczema have been published.[27 29] Briefly, each centre obtained data on 13–14-year-old children from a self-completed questionnaire at school. Optionally, data on 6–7-year-old children were obtained using parent-completed questionnaires. The schools were selected to represent a defined geographical area with a target sample of 3000 children per centre per age group.

The International Data Centre in Auckland supplied the raw survey data. The definitions of current (past 12 months) symptoms of wheeze, rhinoconjunctivitis and eczema and of diagnoses (ever) of asthma, hay fever and eczema were the same as reported previously.[30] Additionally, the 12-month prevalence of moderate to severe wheezing ('severe wheeze') was based on one or more of: (1) four or more attacks of wheeze, (2) woken by wheeze on one or two nights per week or (3) wheezing severe enough to limit speech to only one or two words at a time, between breaths. The prevalence of severe wheeze among those with current wheeze was estimated by the proportion of the corresponding numbers of children in each of these symptom groups. 'Atopy' was defined as rhinoconjunctivitis and/or eczema.

Various sources of data on community exposure to particulate matter were explored, including the WHO, national electronic databases and information from the ISAAC centre investigators, but these were insufficient for our purpose because they were available for only a minority of centres and when available were not presented consistently. We therefore used the World Bank Global Model of Ambient Particulates (GMAPS) which had estimated for 1999 the annual exposure to particulate matter in residential areas of cities with populations greater than 100 000, details of which are published elsewhere[28] and may also be found in online data supplement 1. This is a reduced form of a fixed effect model developed using available particulate matter measurements from population based monitoring stations world-wide for 1985–1999. There were 572 locations in 304 cities in 55 countries, but these were heavily biased towards developed countries. The determinants in the model included factors such as fuel use and mix, scale and composition of economic activity, strength of local pollution regulation, and geographical and atmospheric conditions that affect pollutant transport. The model included a country-specific fixed effect to control for economic, social and natural factors not captured by the other explanatory variables. Model estimates for countries with no monitoring stations are based on an estimate of country-specific fixed effect from a secondary model. The model explained 88% of the observed variation in monitored particulate matter data in the 55 countries during the 1985–1999 period. The model used in our analysis was GMAPS 46, which estimated residential PM_{10} levels for 1999.

Previous work with ISAAC Phase One has shown a weak positive association between gross national product (GNP) per capita and asthma symptoms.[31] For this reason, we decided to control our analyses at a country level for GNP per capita in 1993.[32]

Centres were selected if there was a GMAPS estimate for annual average PM_{10} for their city. Where there was more than one centre per city (five cities), we selected one centre at random, to avoid overweighting that city estimate. The number of centres and some of the sample sizes differ in detail from the original Phase One reports[2 27] because we included some centres that were too late for inclusion in the first report. The associations between PM_{10} and the various outcomes were estimated using a binomial logistic regression model which adjusted for GNP per capita and allowed for clustering by country according to the Huber–White estimates of variance.

For 24 countries with ISAAC centres in two or more cities, the within-country association with PM_{10} was estimated by fitting a separate binomial logistic regression for each country (without adjustment for GNP per capita). The country-level results for PM_{10} were subsequently combined using random effects meta-analysis to obtain a combined estimate.

The proportion of variability between studies attributed to heterogeneity rather than chance was estimated from I^2 values. Statistical analyses were performed using STATA.[33]

Table 1 Quartile distribution of outcomes, PM_{10} and GNP per capita in the 6–7- and 13–14-year age groups

6–7 Years (65 centres, 32 countries)	Min	Q1	Median	Q3	Max
Participants per centre (n)	1104	2418	3007	3414	6533
Current symptoms (% prevalence)					
Current wheeze	0.8	6.4	9.3	17.3	27.2
Severe wheeze	0.5	2.1	3.3	7.0	15.3
Severe as % of current wheeze	21.8	32.4	37.9	43.2	62.5
Rhinoconjunctivitis	0.8	3.9	6.4	9.8	14.9
Eczema	0.0	3.3	6.7	10.2	18.4
Atopy	1.1	7.0	12.3	17.4	23.3
Diagnoses ever (% prevalence)					
Asthma	1.0	4.1	7.7	14.4	30.8
Hay fever	0.0	4.8	6.7	12.7	29.0
Eczema	0.3	4.7	13.0	18.9	57.2
Air pollution and GNP per capita					
PM_{10} ($\mu g/m^3$)	15	23	37	52	136
GNP per capita* (US$)	340	2750	8030	19380	39640
13–14 Years (105 centres, 51 countries)	**Min**	**Q1**	**Median**	**Q3**	**Max**
Participants per centre (n)	1056	2904	3086	3373	5521
Current symptoms (% prevalence)					
Current wheeze	1.6	6.8	10.7	16.1	33.5
Severe wheeze	0.7	2.7	4.4	7.2	16.6
Severe as % of current wheeze	21.8	36.7	42.3	48.1	76.6
Rhinoconjunctivitis	1.4	8.4	12.7	16.6	39.7
Eczema†	0.3	4.0	6.0	9.3	20.5
Atopy†	1.5	12.1	18.4	22.5	46.5
Diagnoses ever (% prevalence)					
Asthma	1.4	5.5	9.6	14.1	30.4
Hay fever	0.0	6.1	14.2	24.2	54.4
Eczema†	0.2	5.5	10.1	15.7	49.3
Air pollution and GNP per capita					
PM_{10} ($\mu g/m^3$)	15	22	34	49	158
GNP per capita‡ (US$)	100	1480	3480	18720	39640

*GNP per capita estimates were based on available data for 31 countries.
†Data were available for 104 centres.
‡GNP per capita estimates are based on available data for 50 countries.
GNP, gross national product; max, maximum; min, minimum.

RESULTS

The prevalence, PM_{10} and GNP data for each centre in a city with an estimate for PM_{10} are summarised as quartiles in table 1. The individual data for each centre are given in online data supplement 2.

For the 6–7-year age group, PM_{10} estimates were obtained for 65 centres in 32 countries. The median annual PM_{10} concentration was 37 $\mu g/m^3$ (range 15–136). The median number of participants per centre was 3007 (range 1104–6533) and the total number of participants was 190 624. For the 13–14-year age group, annual PM_{10} estimates were obtained from 105 centres in 51 countries. The median annual PM_{10} concentration was 34 $\mu g/m^3$ (range 15–158). The median number of participants per centre was 3086 (range 1056–5521) and the total number of participants was 322 529.

For the 6–7- and 13–14-year age groups, the respective median per capita GNP was US$8030 (range 340–39 640) and US$3480 (range 100–39 640). The low GNP countries showed a wide range of PM_{10} levels and contained all of the high PM_{10} concentrations, while high GNP countries tended to have levels only in the lower range (below 50 $\mu g/m^3$) (figure 1). A rank correlation test found a strong inverse relationship between GNP and PM_{10} (Spearman rho=−0.62).

Figure 2 shows the relationship between severe wheeze and PM_{10} for the 6–7- and 13–14-year age groups. There was a moderate to weak negative association (Spearman rho=−0.4) in both groups. The results of the logistic regression analysis adjusting for GNP per capita and clustering within country are shown in table 2.

In both age groups, for all outcomes studied, the ORs for a 10 $\mu g/m^3$ increase in PM_{10} concentrations remained below unity, with the exception of severe wheeze among those with current wheeze in the 13–14-year age group. The upper confidence limit for the OR was also below unity for severe wheeze and atopy in the 6–7-year age group and for current wheeze in the 13–14-year age group.

Table 3 shows the results of the meta-analysis of within-country relationships where there was more than one centre per country.

Most of the outcomes, including those measuring wheeze and severe wheeze, showed positive summary estimates, but most had lower 95% confidence limits below unity. Three of the four estimates for which the confidence limit did not include unity were positive (hay fever in the 6–7-year age group, and rhinoconjunctivitis and atopy in the 13–14-year age group) and one was negative (asthma diagnosis in the 13–14-year age group). A more detailed description of one of these meta-analyses, that for severe wheeze in the 13–14-year age group, is shown in figure 3 which shows the ORs for the individual countries. The individual country estimates varied in size and direction, but the

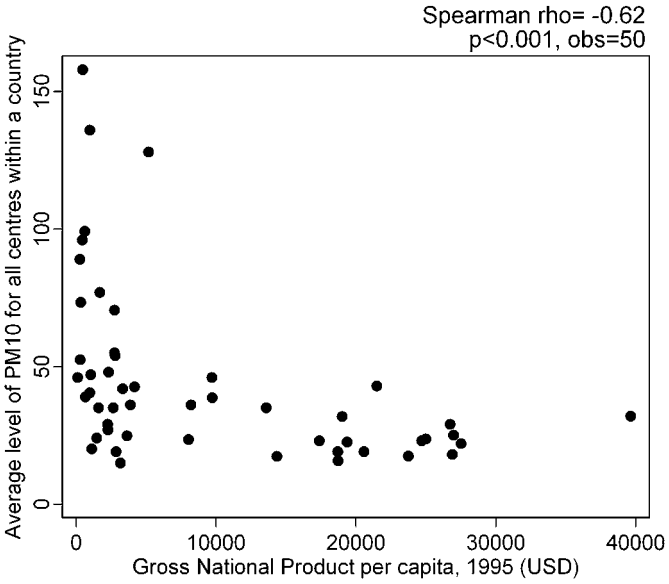

Figure 1 Correlation between PM_{10} (average for all centres within a country) and gross national product per capita.

overall random effects summary estimate was very close to zero. Results were similar when stratified by European versus non-European and by higher versus lower GNP per capita. Each subgroup is shown ranked by annual average concentration of pollution and it is clear that neither the size nor the direction of the estimates was related to the mean level of PM_{10}.

For both age groups, the results for severe wheeze in ISAAC countries with more than one centre were compared to the results from a meta-analysis of published multi-city studies (mostly within one country or region). This is shown in figure 4. None of the individual published studies found a significant association between wheeze symptom and PM_{10}. There was little heterogeneity and the overall estimate without the present study was, for a 10 unit increase in PM_{10}, 0.99 (95% CI 0.91 to 1.06).

DISCUSSION

We generally found a weak negative relationship between concentrations of modelled residential PM_{10} at city level and the centre prevalence of wheeze which persisted after controlling for GNP per capita and allowing for clustering within country. A meta-analysis of within-country associations in those countries with more than one centre found mainly null associations with respect to the various symptoms with the exception of positive associations with hay fever in the 6–7-year age group and rhinoconjunctivitis and atopy in the 13–14-year age group. The results for severe wheeze were similar for European and non-European centres and not related to the mean level of PM_{10}.

The study design was ecological, with the centre as the unit of analysis. This is appropriate for a study of ambient air pollution because the exposure measurement is at an ecological level. Measurement of chronic exposure at a personal level for a multi-centre prevalence study is impractical. Although many previous studies used an ecological design, most had insufficient power due to the small number of communities compared. Our study is by far the largest in terms of breadth of exposure and outcome variables, numbers of units of analysis and precision of centre prevalence estimates. In ecological analyses, it is possible to have relationships at a between-country level that are different from

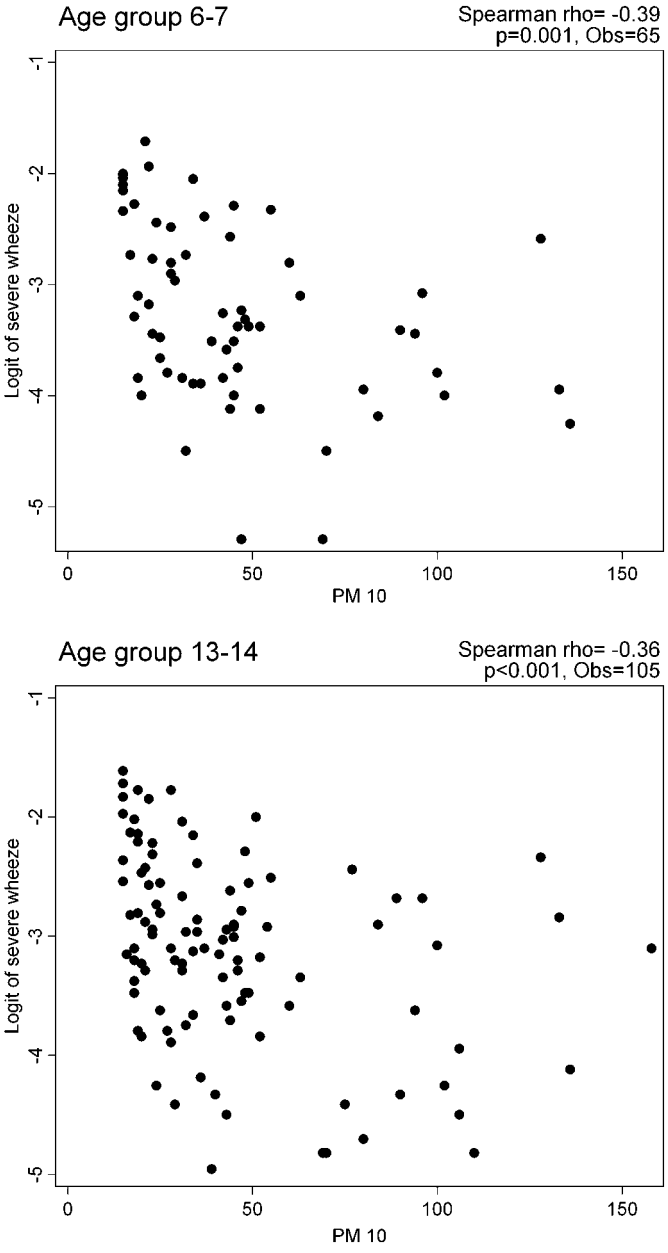

Figure 2 Association between PM_{10} and the prevalence of severe wheeze in 6–7- and 13–14-year-old children.

those between areas of the same country. We found that for severe wheeze, the between-country analysis (allowing for clustering of centres within country) showed a generally convincing negative association, whereas for the within-country analysis the summary estimates were more generally null. We do not know what explains this difference, but neither result supports a positive association between city-level PM_{10} concentrations and the various outcomes studied.

Our outcome was based on a standardised validated questionnaire and the asthma symptoms have been shown to correlate with national hospital admissions and mortality rates for childhood asthma.[34] Further, prevalence estimates were obtained independently from the parents of 6–7-year-olds and from the 13–14-year-olds themselves. The sample size of each centre was large enough to ensure sufficient precision of the prevalence estimates.

Table 2 ORs for the association between PM_{10} and prevalence at centre level, adjusted for GNP per capita and allowing for clustering within country

6–7-Year age group (63 centres, 31 countries)		
Outcome	**PM_{10} OR (per 10 μg/m^3)**	**95% CI**
Current symptoms (% prevalence)		
Current wheeze	0.89	0.80 to 1.00
Severe wheeze	0.88	0.77 to 1.00*
Severe as % of current wheeze	0.97	0.94 to 1.00
Rhinoconjunctivitis	0.93	0.87 to 1.00
Eczema	0.92	0.83 to 1.02
Atopy	0.93	0.86 to 1.00†
Diagnoses ever (% prevalence)		
Asthma	0.88	0.76 to 1.02
Hay fever	0.97	0.86 to 1.10
Eczema	0.95	0.85 to 1.06
13–14-Year age group (103 centres, 50 countries)		
Outcome	**PM_{10} OR (per 10 μg/m^3)**	**95% CI**
Current symptoms (% prevalence)		
Current wheeze	0.91	0.84 to 0.99
Severe wheeze	0.92	0.84 to 1.00
Severe as % of current wheeze	1.00	0.97 to 1.03
Rhinoconjunctivitis	0.98	0.92 to 1.04
Eczema‡	0.93	0.87 to 1.01
Atopy‡	0.96	0.90 to 1.02
Diagnoses ever (% prevalence)		
Asthma	0.94	0.87 to 1.01
Hay fever	0.92	0.83 to 1.01
Eczema‡	0.99	0.92 to 1.06

*0.9988;
†0.9999.
‡Estimates are based on 102 centres, 50 countries.

Table 3 Meta-analysis of PM_{10} and prevalence in countries with more than one centre*

6–7-Year age group (46 centres, 14 countries)		
Outcome	**PM_{10} OR (per 10 μg/m^3)**	**95% CI**
Current symptoms (% prevalence)		
Current wheeze	1.03	0.95 to 1.13
Severe wheeze	1.00	0.90 to 1.11
Severe as % of current wheeze	0.97	0.92 to 1.01
Rhinoconjunctivitis	1.06	0.96 to 1.17
Eczema	0.98	0.91 to 1.05
Atopy	1.03	0.96 to 1.10
Diagnoses ever (% prevalence)		
Asthma	0.96	0.85 to 1.08
Hay fever	1.10	1.01 to 1.19
Eczema	0.97	0.87 to 1.08
13–14-Year age group (77 centres, 24 countries)		
Outcome	**PM_{10} OR (per 10 μg/m^3)**	**95% CI**
Current symptoms (% prevalence)		
Current wheeze	1.05	0.97 to 1.13
Severe wheeze	1.01	0.92 to 1.10
Severe as % of current wheeze	0.97	0.92 to 1.02
Rhinoconjunctivitis	1.15	1.06 to 1.26
Eczema†	1.09	0.99 to 1.19
Atopy†	1.14	1.05 to 1.24
Diagnoses ever (% prevalence)		
Asthma	0.88	0.80 to 0.96
Hay fever	0.98	0.90 to 1.07
Eczema†	0.98	0.90 to 1.06

All results are from random effects analysis.
*Estimate for Portugal excludes Funchal (Madeira island).
†Estimates are based on 75 centres, 23 countries.

In using estimates from the GMAPS model, we were able to include a far wider range of cities than would have been otherwise possible. In development, the model explained 88% of the PM_{10} concentrations observed in the mainly developed cities for which monitor data were available, but we do not know how well it predicted PM_{10} in regions that were not well represented in the development of the model (Middle East, Africa, Asia). GMAPS model estimates of annual average PM_{10} have recently been available for 1990–2005. PM_{10} estimates for 1995 and 1999 are highly correlated (r=0.98) and use of the estimates for 1999 is not expected to alter any of the findings reported in this paper. Based on a few actual measurements in cities with ISAAC centres, we found that there had tended to be a decline in PM_{10} from the mid-1990s to 1999, the year of the modelled concentrations and that this was steeper in the more polluted cities. This means that the concentrations in more polluted cities in 1995 will probably have been underestimated by the 1999 GMAPS model.

It is inevitable that annual average PM_{10} concentrations for a city will be a poor indicator of individual exposure and dose to the lung. This raises the possibility that measurement error may be obscuring a real underlying effect. However, exposure estimated at the community level is likely to have Berkson-type error rather than classical measurement error, so that effect estimates, although less precise, will not be biased towards the null.[35] There are also two strands of empirical evidence which support our use of community-average concentrations of particulate matter. The first is that similar ecological study designs have found positive associations with cough symptom and reduced lung function in children.[11] The second is that city-level concentrations of particulate matter have been associated with mortality in multi-city cohort studies and with a wide range of health outcomes in daily time-series studies. Therefore, in spite of many issues concerning the measurement of particulate matter, we think that if an important association with symptom prevalence had been present, we would have observed some positive relationships. We did not have the opportunity to investigate associations with pollutant gases, but the current evidence from multi-city studies cited earlier does not suggest that city-average concentrations of ozone, sulphur dioxide or nitrogen dioxide are related to community asthma prevalence.

Climate factors such as temperature, humidity and rainfall have been found to have some effect on the prevalence of asthma, eczema and hay fever in previous analyses of these ISAAC data.[36] The mechanisms are not understood and it was unclear to us whether temperature should be included as a potential confounder. We also noted that climate variables were included in the GMAPS PM_{10} model. We investigated the association between PM_{10} and the same climate variables as used in the study by Weiland and colleagues and found that there was no correlation within country between PM_{10} and any climate variable. When we investigated the between-countries correlations, there were few significant correlations and these were weak. We therefore concluded that the particulate matter results would be unlikely to be explained by climate factors.

GNP, which was available at country level, was negatively associated with PM_{10} (figure 1) and positively associated with symptom prevalence in ISAAC.[31] Because the estimation of PM_{10} used GNP per capita as an explanatory variable, we performed the between-country analysis both with and without adjustment for GNP. In both cases, the relationship between the different outcomes and PM_{10} was negative, although not generally significant after controlling for GNP.

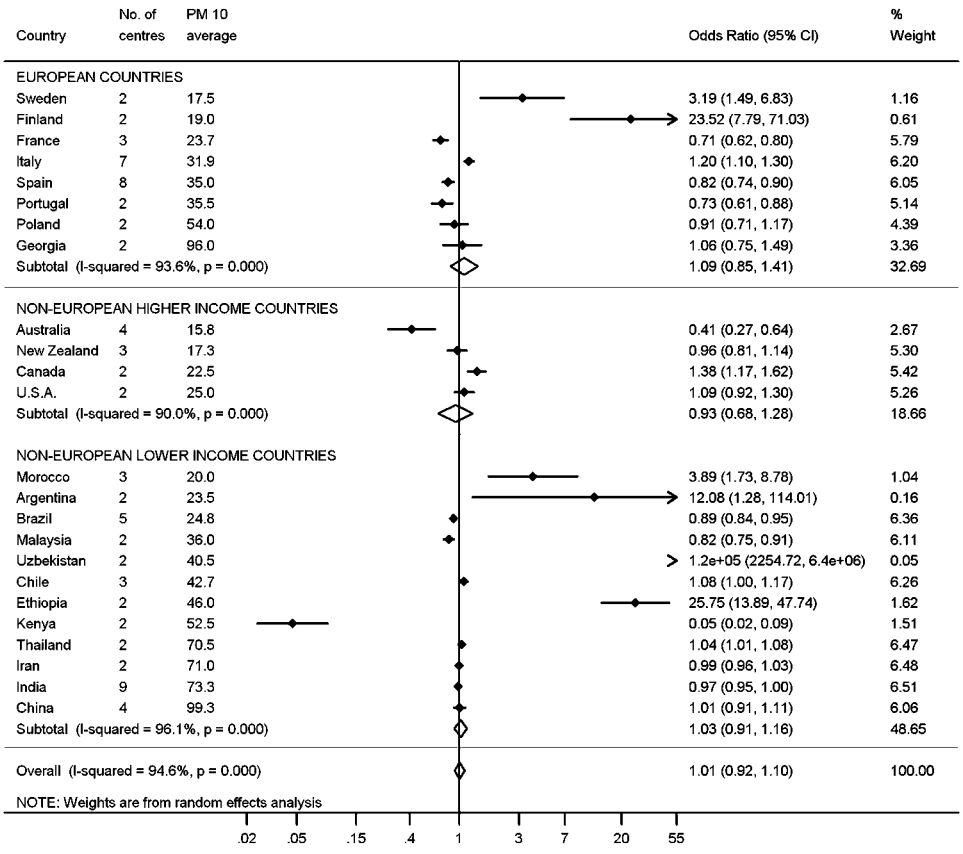

Figure 3 Meta-analysis of the association between PM_{10} and the prevalence of severe wheeze in the 13–14-year-age group for countries with more than one centre. Stratified by region and ranked by mean concentration of PM_{10}. ORs for 10 μg/m^3 PM_{10}.

We had little scope for controlling for confounders at the individual level. Age and sex were controlled for by design but the range of individual level confounders customarily controlled for in prevalence studies (eg, active and passive smoking, other sources of indoor pollution, dampness, etc) were unavailable. ISAAC Phase Three, which was conducted during 2001–2002, included a risk factor questionnaire and future analyses using this later dataset will have the potential to adjust for some confounders at an individual level. Notwithstanding these limitations, we think that it is unlikely that any real and substantial underlying causal association between PM_{10} and the various outcomes has been obscured by unknown confounding factors.

Our results were very similar to those found in published studies of PM_{10} and the prevalence of current asthma symptoms with five or more study areas[19 20 22 24 25] (figure 4). Four multi-area studies that could not be adapted for the meta-analysis of ORs (because the results could not be converted to standardised ORs) also reported essentially null results for PM_{10}[23] or black smoke.[17 18 21] The present study, also shown on figure 4, was in line with these results and the summary estimate for all multi-centre studies is convincingly null. Unlike the present study which used modelled data, all of these studies used measured concentrations of PM_{10} or black smoke, and in some cases employed study-directed monitors. Furthermore, most of these

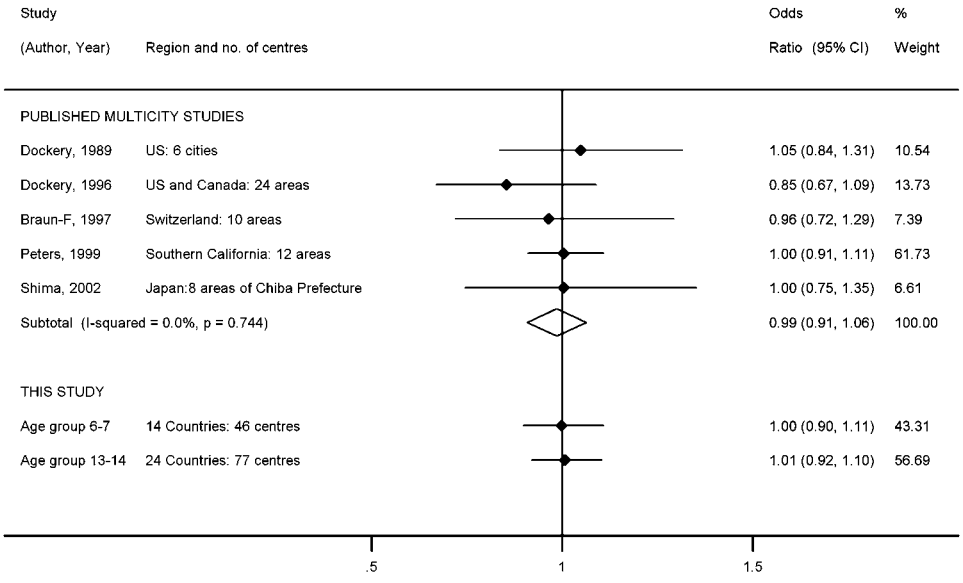

Figure 4 Meta-analysis of published multi-centre studies of PM_{10} and the prevalence of moderate to severe wheezing. ORs for 10 μg/m^3 PM_{10}.

studies controlled for a range of individual-level confounding factors. The majority observed associations between PM_{10} and bronchitic symptoms such as cough, suggesting that they might have been capable of detecting associations with wheeze symptom should these have existed. Unfortunately, the ISAAC asthma questionnaire did not include questions on cough.

There is some evidence from within-city studies that the prevalence of asthma symptoms and of allergy may be higher in populations who are exposed to traffic than in those less exposed.[9 10] This could be explained by fresh traffic exhaust being more toxic[37] or by exposure being much higher. There is therefore a need to reconcile this evidence with that of the present study. One explanation may be that traffic pollution becomes less toxic with time and distance from the road, another is that concentrations of traffic pollution become too low and diluted with other sources for a health signal to be detected using prevalence studies such as ours. Yet another is that the contribution of traffic to the high background levels found in low GNP countries is likely to be relatively small because there is far less motorised traffic and far more uncontrolled emissions from home heating, industry, energy production, etc. An alternative explanation is that the associations observed in traffic-proximity studies are not due to pollution but to some other factor. In more recent years, better city-level data on sources have become available and we plan further studies using the ISAAC Phase Three data to investigate whether some sources are more relevant than others.

The strengths of this study lie in its world-wide scope, large sample size and standardised outcome instrument, but we recognise its relative weaknesses in exposure assessment and inability to control for confounding factors at the city and individual level. It may be possible to address some of these defects in future studies using the ISAAC data. For the present, however, we conclude that our results do not support the existence of an association between city-level concentrations of residential ambient PM_{10} and the prevalences of asthma, rhinoconjunctivitis or eczema.

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Ambient particulate pollution and the world-wide prevalence of asthma, rhinoconjunctivitis and eczema in children: Phase One of the International Study of Asthma and Allergies in Childhood (ISAAC)

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