



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)

H. Ross Anderson, Ruth Ruggles, Kiran D Pandey, et al.

Occup Environ Med published online October 9, 2009
doi: 10.1136/oem.2009.048785

Updated information and services can be found at:
<http://oem.bmj.com/content/early/2009/11/05/oem.2009.048785>

These include:

**Supplemental
Material**

<http://oem.bmj.com/content/suppl/2010/05/25/oem.2009.048785.DC1.html>

References

Article cited in:
<http://oem.bmj.com/content/early/2009/11/05/oem.2009.048785#related-urls>

P<P

Published online October 9, 2009 in advance of the print journal.

**Email alerting
service**

Receive free email alerts when new articles cite this article. Sign up in the box at the top right corner of the online article.

Notes

Advance online articles have been peer reviewed and accepted for publication but have not yet appeared in the paper journal (edited, typeset versions may be posted when available prior to final publication). Advance online articles are citable and establish publication priority; they are indexed by PubMed from initial publication. Citations to Advance online articles must include the digital object identifier (DOIs) and date of initial publication.

To order reprints of this article go to:
<http://oem.bmj.com/cgi/reprintform>

To subscribe to *Occupational and Environmental Medicine* go to:
<http://oem.bmj.com/subscriptions>

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)

H Ross Anderson¹, Ruth Ruggles¹, Kiran D Pandey², Venediktos Kapetanakis¹, Bert Brunekreef³, Christopher K W Lai⁴, David P Strachan¹, Stephan K Weiland⁵, and the ISAAC Phase One Study Group⁶

¹ Division of Community Health Sciences, MRC-HPA Centre for Environment and Health, St George's, University of London, UK

² Environment Department, World Bank, Washington DC, USA

³ Institute for Risk Assessment Sciences, Utrecht University, Utrecht, The Netherlands; also affiliated with Julius Center for Health Sciences and Primary Care, University Medical Center, Utrecht.

⁴ Department of Medicine and Therapeutics, The Chinese University of Hong Kong, Hong Kong

⁵ Department of Epidemiology, University of Ulm, Germany. Died 19 March 2007

⁶ Members listed in Appendix 1

Address for correspondence:

Professor H R Anderson

Division of Community Health Sciences

MRC-HPA Centre for Environment and Health

St George's, University of London

Cranmer Terrace

London SW17 0RE

E-mail: r.anderson@sgul.ac.uk ,

Tel: +44 20 8725 5419

Fax: +44 20 8725 3584

Key Words: asthma, allergy, air pollution, prevalence

OVERVIEW

- 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 (PM) 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 PM₁₀.
- The results suggest that community levels of ambient PM 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.

ABSTRACT

Objectives. To investigate the role of ambient particulate matter in explaining international variations in the prevalence of asthma, rhinoconjunctivitis and eczema in children.

Methods. The prevalence of symptoms and diagnoses 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 particulate matter with aerodynamic diameter $< 10\mu\text{m}$ (PM_{10}) obtained from a World Bank model. Associations were investigated using a binomial regression model which adjusted for Gross National Product per capita and for clustering within country. For countries with more than one centre a two stage meta-analysis was done. 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 the various outcomes. For severe wheeze in the 13-14 year age group, the odds ratio for a $10\text{ }\mu\text{g}/\text{m}^3$ increase in PM_{10} was 0.92 (95% CI 0.84, 1.00). In 24 countries with more than one centre, most of the summary estimates for within-country associations were weakly positive. For severe wheeze in the 13-14 year age group, the summary odds ratio for a $10\text{ }\mu\text{g}/\text{m}^3$ increase in PM_{10} was 1.01 (0.92, 1.10). This result was close to a summary odds ratio of 0.99 (0.91, 1.06) obtained from published multi-centre studies.

Conclusions. Modelled estimates of PM at city level will necessarily be imprecise and incomplete estimates of personal exposure to ambient air pollutants. Nevertheless, the results of this world-wide ecological analysis, 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.

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. Since asthma is a condition characterized by inflammation and hyperresponsiveness of the airways, and asthmatics frequently report that air pollution aggravates or precipitates their asthma, it is not surprising that ambient air pollution is widely believed to be one possible cause of variations in prevalence. It could do so through effects on incidence, severity or prognosis. The particulate component of air pollution (PM) is widely measured as particulate matter with aerodynamic diameter less than 10 μ m (PM₁₀), this being small enough to penetrate the intrathoracic respiratory tract. PM₁₀ is a complex mixture arising from a range of sources and comprising a range of physicochemical characteristics. While some components of PM₁₀ 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 PM has the potential to increase airways 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 PM₁₀ may aggravate symptoms of asthma, the evidence for effects of chronic exposure to PM₁₀ on asthma incidence and prevalence is weak.[9-11] There is some evidence from birth cohort studies linking traffic exposure to atopic sensitization.[12-14]

The evidence for effects on asthma of chronic exposure to PM 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 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 9 studies of children comparing five or more centres and none found evidence of a statistically significant positive association between ambient PM 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 asthmatics and non asthmatics, 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, PM 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 5 largely European countries.[26] There are no published international studies of city-level average concentrations of background PM and asthma prevalence. The role of PM 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 PM 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 by 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) 4 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 amongst 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 one or both of rhinoconjunctivitis or eczema.

Various sources of data on community exposure to PM were explored, including the World Health Organization, 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 PM 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 PM 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 geographic 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 PM data in the 55 countries during the 1985-1999 period. The model used in our analysis was GMAPS 46, which estimated residential PM₁₀ levels for 1999.

Previous work with ISAAC Phase One has shown a weak positive association between gross national product per capita (GNP) 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 PM₁₀ for their city. Where there was more than one centre per city (5 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 PM₁₀ 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]

RESULTS

The prevalence, PM₁₀ and GNP data for each centre in a city with an estimate for PM₁₀ are summarized as quartiles in Table 1. The individual data for each centre are in Online Data Supplement 2.

Table 1. Quartile distribution of outcomes, PM₁₀ 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)	1 104	2 418	3 007	3 414	6 533
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 (µg/m ³)	15	23	37	52	136
GNP per capita* (USD)	340	2 750	8 030	19 380	39 640
* GNP per capita estimates were based on available data for 31 countries					
13 - 14 years (105 centres, 51 countries)	min	Q1	med	Q3	max
Participants per centre (n)	1 056	2 904	3 086	3 373	5 521
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 (µg/m ³)	15	22	34	49	158
GNP per capita** (USD)	100	1 480	3 480	18 720	39 640

* Data were available for 104 centres

** GNP per capita estimates are based on available data for 50 countries

For the 6-7 year age group, PM₁₀ estimates were obtained for 65 centres in 32 countries. The median annual PM₁₀ concentration was 37 µg/m³ (range 15 to 136). The median number of participants per centre was 3007 (range 1104 to 6533) and the total number of participants was 190 624. For the 13-14 year age group, annual PM₁₀ estimates were obtained from 105 centres in 51 countries. The median annual PM₁₀ concentration was 34 µg/m³ (range 15 to 158). The median number of participants per centre was 3086 (range 1056 to 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 8030 USD (range 340 to 39 640) and 3480 USD (range 100 to 39 640). The low GNP countries showed a wide range of PM₁₀ and contained all of the high PM₁₀ concentrations while high GNP countries tended to have levels only in the lower range (below 50 µg/m³) (Figure 1). A rank correlation test found a strong inverse relationship between GNP and PM₁₀ (Spearman rho = -0.62).

Figure 2 shows the relationship between severe wheeze and PM₁₀ for the 6-7 and 13-14 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 and clustering within country are shown in Table 2.

Table 2. Odds ratios for the association between PM₁₀ 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	PM₁₀ OR	95% Confidence Interval	
	(per 10 µg/m³)		
Current symptoms (% prevalence)			
Current wheeze	0.89	0.80	1.00
Severe wheeze	0.88	0.77	1.00*
Severe as % of current wheeze	0.97	0.94	1.00
Rhinoconjunctivitis	0.93	0.87	1.00
Eczema	0.92	0.83	1.02
Atopy	0.93	0.86	1.00**
Diagnoses ever (% prevalence)			
Asthma	0.88	0.76	1.02
Hay fever	0.97	0.86	1.10
Eczema	0.95	0.85	1.06

13-14 year age group (103 centres, 50 countries)			
Outcome	PM₁₀ OR	95% Confidence Interval	
	(per 10 µg/m³)		
Current symptoms (% prevalence)			
Current wheeze	0.91	0.84	0.99
Severe wheeze	0.92	0.84	1.00
Severe as % of current wheeze	1.00	0.97	1.03
Rhinoconjunctivitis	0.98	0.92	1.04
Eczema*	0.93	0.87	1.01
Atopy*	0.96	0.90	1.02
Diagnoses ever (% prevalence)			
Asthma	0.94	0.87	1.01
Hay fever	0.92	0.83	1.01
Eczema*	0.99	0.92	1.06

*0.9988 ; ** 0.9999

* Estimates are based on 102 centres, 50 countries

In both age groups, for all outcomes studied, the odds ratios for a 10 µg/m³ increase in PM₁₀ concentrations remained below unity, with the exception of severe wheeze amongst current wheezers in the 13-14 year age group. The upper confidence limit for the odds ratio 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.

Table 3. Meta-analysis of PM₁₀ and prevalence in countries with more than one centre*.
All the results are from random effects analysis.

6-7 year age-group (46 centres, 14 countries)			
Outcome	PM₁₀ OR	95% Confidence Interval	
	(per 10 µg/m³)		
Current symptoms (% prevalence)			
Current wheeze	1.03	0.95	1.13
Severe wheeze	1.00	0.90	1.11
Severe as % of current wheeze	0.97	0.92	1.01
Rhinoconjunctivitis	1.06	0.96	1.17
Eczema	0.98	0.91	1.05
Atopy	1.03	0.96	1.10
Diagnoses ever (% prevalence)			
Asthma	0.96	0.85	1.08
Hay fever	1.10	1.01	1.19
Eczema	0.97	0.87	1.08

13-14 year age-group (77 centres, 24 countries)			
Outcome	PM₁₀ OR	95% Confidence Interval	
	(per 10 µg/m³)		
Current symptoms (% prevalence)			
Current wheeze	1.05	0.97	1.13
Severe wheeze	1.01	0.92	1.10
Severe as % of current wheeze	0.97	0.92	1.02
Rhinoconjunctivitis	1.15	1.06	1.26
Eczema**	1.09	0.99	1.19
Atopy**	1.14	1.05	1.24
Diagnoses ever (% prevalence)			
Asthma	0.88	0.80	0.96
Hay fever	0.98	0.90	1.07
Eczema**	0.98	0.90	1.06

* Estimate for Portugal excludes Funchal (Madeira island)

** Estimates are based on 75 centres, 23 countries

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 odds ratios for the individual countries. The individual country estimates varied in size and direction but the overall random effects summary estimate was very close to zero. Results were similar when stratified by European vs non-European and by

higher vs lower GNP per capita. Each subgroup is shown ranked by annual average concentration of pollution and it is clear that neither the size nor 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 PM₁₀ at city level and the centre prevalence of wheeze which persisted after controlling for GNP 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 PM₁₀.

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 those between areas of one 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 PM₁₀ concentrations and the various outcomes studied.

Our outcome was based on a standardized 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.

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 PM₁₀ concentrations observed in the mainly developed cities for which monitor data were available but we do not know how well it predicted PM₁₀ in regions that were not well represented in the development of the model (Middle East, Africa, Asia). GMAPS model estimates of annual average PM₁₀ have recently been available for 1990-2005. PM₁₀ 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 the paper. Based on a few actual measurements in cities with ISAAC centres, we found that there had tended to be a decline in PM₁₀ 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 PM₁₀ 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, though 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 PM. 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 PM 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 PM₁₀ model. We investigated the association between PM₁₀ and the same climate variables as used in the study by Weiland and colleagues and found that there was no correlation within country between PM₁₀ 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 PM results would be unlikely to be explained by climate factors.

GNP, which was available at country level, was negatively associated with PM₁₀ (Figure 1) and positively associated with symptom prevalence in ISAAC.[31] Because the estimation of PM₁₀ 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 PM₁₀ was negative, though not generally significant after controlling for GNP.

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 (e.g. active and passive smoking, other sources of indoor pollution, dampness etc) were unavailable. ISAAC Phase 3, which was conducted during 2001-2 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 PM₁₀ and the various outcomes has been obscured by unknown confounding factors.

Our results were very similar to those found in published studies of PM₁₀ 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 odds ratios (because the results could not be converted to standardized odds ratios) also reported essentially null results for PM₁₀[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 PM₁₀ or Black Smoke, and in some cases employed study-directed monitors. Furthermore, most of these studies controlled for a range of individual-level confounding factors. The majority observed associations between PM₁₀ and bronchitic symptoms such as cough, suggesting that they might have been capable of detecting associations with wheeze symptom should this 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 motorized 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 3 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 standardized outcome instrument but we recognize 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 PM₁₀ and the prevalences of asthma, rhinoconjunctivitis or eczema.

ACKNOWLEDGMENTS AND FUNDING

We are grateful to the children and parents who willingly cooperated and participated in ISAAC Phase One and the coordination and assistance by the school staff is sincerely appreciated. We thank the Phase One National Coordinators, Principal Investigators and their colleagues, who helped make ISAAC Phase Three such a success. We would like to acknowledge and thank the many funding bodies throughout the world that supported the individual ISAAC centres and collaborators and their meetings. In particular, we wish to thank the New Zealand funding bodies, the Health Research Council of New Zealand, the Asthma and Respiratory Foundation of New Zealand, the Child Health Research Foundation, the Hawke's Bay Medical Research Foundation, the Waikato Medical Research Foundation, Glaxo Wellcome New Zealand, the NZ Lottery Board and Astra Zeneca New Zealand. Glaxo Wellcome International Medical Affairs supported the Regional Coordination and the ISAAC International Data Centre. Without help from all of the above, ISAAC would not have given us all these results from so many countries.

APPENDIX 1: ISAAC Phase One study group

ISAAC Steering Committee: N Ait-Khaled (Union Internationale Contre la Tuberculose et les Maladies Respiratoires, Paris, France); G Anabwani (Princess Marina Hospital, Gaborone, Botswana); HR Anderson (Department of Public Health Sciences, St Georges Hospital Medical School, London, UK); MI Asher (Department of Paediatrics, Faculty of Medical and Health Sciences, The University of Auckland, New Zealand); R Beasley (Medical Research Institute of New Zealand, Wellington, New Zealand); B Björkstén (Institute of Environmental Medicine, Karolinska Institutet, Stockholm, Sweden); ML Burr (Department of Epidemiology, Statistics & Public Health, University of Wales College of Medicine, Cardiff, UK); J Crane (Wellington Asthma Research Group, Wellington School of Medicine, New Zealand); U Keil (Institut für Epidemiologie und Sozialmedizin, Universität Münster, Germany); CKW Lai (Department of Medicine and Therapeutics, The Chinese University of Hong Kong, SAR China); J Mallol (Department of Respiratory Medicine, University of Santiago de Chile, Chile); FC Martinez (Arizona Respiratory Center, University of Arizona, Tucson, Arizona, USA); EA Mitchell (Department of Paediatrics, Faculty of Medical and Health Sciences, The University of Auckland, New Zealand); S Montefort (Department of Medicine, University of Malta, Malta); N Pearce (Centre for Public Health Research, Massey University, Wellington, New Zealand); CF Robertson (Department of Respiratory Medicine, Royal Children's Hospital, Parkville, Australia); JR Shah (Jaslok Hospital & Research Centre, Mumbai, India); AW Stewart (Population Health, Faculty of Medical and Health Sciences, The University of Auckland, New Zealand); DP Strachan (Department of Public Health Sciences, St Georges Hospital Medical School, London, UK); E von Mutius (Dr von Haunerschen Kinderklinik de Universität München, Germany); SK Weiland (Department of Epidemiology, University of Ulm, Germany); HC Williams (Centre for Evidence Based Dermatology, Queen's Medical Centre, University Hospital, Nottingham, UK).

ISAAC International Data Centre: MI Asher, TO Clayton, P Ellwood, EA Mitchell, Department of Paediatrics, and AW Stewart, School of Population Health, Faculty of Medical and Health Sciences, The University of Auckland, New Zealand.

ISAAC Phase One principal investigators: Algeria: Dr A Bezzaoucha (Algiers); Ethiopia: Assoc Prof K Melaku (Addis Ababa); Ethiopia: Prof B Seyoum (Jima); Kenya: Dr FO Esamai (Eldoret), Dr JA Odhiambo (Nairobi); Nigeria: Prof BO Onadeko (Ibadan); South Africa: Prof R Ehrlich (Cape Town); China: Prof Y-Z Chen (Beijing), Prof K-H Chen (Chongqing),

Prof N-S Zhong (Guangzhou), Dr M Bao-Shan (Shanghai); Hong Kong: Dr C Lai (Hong Kong 13-14 yr), Prof Y Lung Lau (Hong Kong 6-7 yr); Indonesia: Prof Dr K Baratawidjaja (Bandung); Japan: Prof S Nishima (Fukuoka); Malaysia: Dr LW Yeong (Ipoh), Assoc Prof BS Quah (Kota Bharu); Philippines: Prof F Cua-Lim (Metro Manila); Republic of Korea: Dr S-I Lee (Seoul); Singapore: Prof B-W Lee (Singapore); Taiwan: Prof K-H Hsieh (deceased) (Taipei); Thailand: Dr P Vichyanond (Bangkok), Assoc Prof M Trakultivakorn (Chiang Mai); Iran: Dr M-R Masjedi (Rasht and Tehran); Kuwait: Dr JA al-Momen (Kuwait); Lebanon: Dr FM Ramadan (Beirut); Morocco: Prof Z Bouayad (Casablanca and Marrakech), Prof A Bennis (Rabat); Pakistan: Dr ZA Bhutta (Karachi); Argentina: Dr N Salmun (Buenos Aires and Rosario); Brazil: Prof N Rosário (Curitiba), Prof R Stein (Porto Alegre), Dr PGM Bezerra (Recife), Assoc Prof L de Freitas Souza (Salvador), Prof D Solé (Sao Paulo); Chile: Dr I Sanchez (Central Santiago), Dr L Amarales (Punta Arenas), Dr MA Calvo (Valdivia); Mexico: Prof I Romieu (Cuernavaca); Panama: Dr G Cukier (David-Panama); Paraguay: Dr JA Guggiari-Chase (Asuncion); Peru: Dr P Chiarella (Lima); Uruguay: Dra D Holgado (Montevideo); Canada: Prof M Sears (Hamilton), Dr B Taylor (Saskatoon); USA: Dr V Persky (Chicago (3)), Prof GJ Redding (Seattle); Albania: Prof A Priftanji (Tirane); Estonia: Dr M-A Riikjärv (Tallinn); Finland: Dr M Kajosaari (Helsinki), Dr TA Koivikko (Turku and Pori County); Georgia: Dr N Khetsuriani (Kutaisi), Prof A Gamkrelidze (Tbilisi); Latvia: Dr M Leja (Riga); Poland: Assoc Prof G Lis (Krakow), Dr A Brêborowicz (Poznan); Romania: Prof D Dumitrascu (Cluj); Russian Federation: Prof RM Khaitov (Moscow); Sweden: Dr L Nilsson (Linköping), Dr T Foucard (Stockholm/Uppsala); Uzbekistan: Prof T Aripova (Samarkand and Tashkent); Australia: Dr D Kennedy (Adelaide), Prof C Robertson (Melbourne), Prof L Landau (Perth), Dr J Peat (Sydney 6-7 yr), Prof A Bauman (Sydney 13-14 yr); New Zealand: Prof MI Asher (Auckland), Assoc Prof P Pattemore (Christchurch), Prof J Crane (Wellington); India: Dr RM Maheshwari (Akola), Dr MK Joshi (Bombay (16)), Prof L Kumar (Chandigarh), Dr KC Jain (Jodhpur), Dr TU Sukumaran (Kottayam), Dr N Somu (Madras (3)), Prof GR Sethi (New Delhi (7)), Dr G Jayaraj (Neyveli), Dr NM Hanumante (Pune); Austria: Dr J Riedler (Salzburg); Belgium: Prof P Vermeire (Antwerp); France: Prof D Charpin (Marseilles), Prof P Godard (Montpellier), Dr C Kopferschmitt-Kubler (Strasbourg); Germany: Prof Dr U Keil (Munster); Greece: Assoc Prof C Gratziou (Athens); Italy: Dr F Forastiere (Cosenza and Roma), Dr E Chellini (Firenze), Dr L Bisanti (Milano), Dr G Ciccone (Torino), Dr S Piffer (Trento), Prof A Boner (Verona); Portugal: Dr FD Borges (Funchal), Prof JE Rosado Pinto (Lisbon), Dr JM Lopes dos Santos (Porto); Spain: Dr RM Busquets (Barcelona), Dr AD Rubio (Bilbao), Dr AR Asensio (Cadiz), Prof L García-Marcos (Cartagena), Dr A Arnedo-Pena (Castellon), Prof F Guillén-Grima (Pamplona), Prof MMM Suárez-Varela (Valencia), Prof A Blanco Quirós (Valladolid); United Kingdom: Prof HR Anderson (South Thames).

COMPETING INTERESTS

None of the authors has any competing interests.

The Corresponding Author has the right to grant on behalf of all authors and does grant on behalf of all authors, an exclusive licence (or non-exclusive for government employees) on a worldwide basis to the BMJ Publishing Group Ltd and its Licensees to permit this article (if accepted) to be published in OEM and any other BMJ PGL products to exploit all subsidiary rights, as set out in our licence.

CAPTIONS TO FIGURES

Figure 1. Correlation between PM₁₀ (average for all centres within a country) and Gross National Product per capita.

Figure 2. Association between PM₁₀ and the prevalence of severe wheeze in 6-7 and 13-14 year old children

Figure 3. Meta-analysis of the association between PM₁₀ 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 PM₁₀. Odds ratios for 10µg/m³ PM₁₀.

Figure 4. Meta-analysis of published multi-centre studies of PM₁₀ and the prevalence of moderate to severe wheezing. Odds ratios for 10µg/m³ PM₁₀.

REFERENCES

- (1) *Global Strategy for Asthma Management and Prevention*, Global Initiative for Asthma (GINA) 2007. Available at: <http://www.ginasthma.org> (accessed March 2008).
- (2) ISAAC Steering Committee. Worldwide variations in the prevalence of asthma symptoms: the International Study of Asthma and Allergies in Childhood (ISAAC). *Eur Respir J* 1998;12:315-35.
- (3) Pearce N, Ait-Khaled N, Beasley R et al. Worldwide trends in the prevalence of asthma symptoms: phase III of the International Study of Asthma and Allergies in Childhood (ISAAC). *Thorax* 2007;62:758-66.
- (4) Pope CA III, Dockery DW. Health effects of fine particulate air pollution: lines that connect, *J Air Waste Manag. Assoc.* 2006;56:709-742.
- (5) World Health Organization Regional Office for Europe 2007, Health relevance of particulate matter from various sources: report on a WHO workshop, Bonn, Germany, March 2007 WHO, Copenhagen.
- (6) Brunekreef B, Holgate ST. Air pollution and health. *Lancet* 2002;360:1233-42.
- (7) Riedl M, Diaz-Sanchez D. Biology of diesel exhaust effects on respiratory function. *J Allergy Clin Immunol* 2005;115:221-8.
- (8) Holgate ST, Sandstrom T, Frew AJ et al. Health effects of acute exposure to air pollution. Part I: Healthy and asthmatic subjects exposed to diesel exhaust. *Res Rep Health Eff Inst* 2003;112:1-30.
- (9) Department of Health Committee on the Medical Effects of Air Pollutants. *Asthma and outdoor air pollution*. London: HMSO; 1995.
- (10) World Health Organisation. Air quality guidelines: global update 2005, particulate matter, ozone, nitrogen dioxide and sulphur dioxide. Copenhagen: WHO Regional Office for Europe; 2006.
- (11) WHO European Centre for Environment and Health. *Effects of air pollution on children's health and development - a review of the evidence*. Bonn: WHO Regional Office for Europe; 2005.
- (12) Brauer M, Hoek G, Smit HA. et al. Air pollution and development of asthma, allergy and infections in a birth cohort. *Eur Respir J* 2007;29:879-888.
- (13) Morgenstern V, Zutavern A, Cyrus Jet al. Atopic diseases, allergic sensitization, and exposure to traffic-related air pollution in children. *Am.J.Respir.Crit Care Med* 2008;177:1331-1337.
- (14) Nordling E, Berglind N, Melen E... Traffic-related air pollution and childhood respiratory symptoms, function and allergies. *Epidemiology* 2008;19:401-408.
- (15) Salam MT, Islam T, Gilliland FD. Recent evidence for adverse effects of residential proximity to traffic sources on asthma. *Curr Opin Pulm Med* 2008;14:3-8.

- (16) Heinrich J, Wichmann HE. Traffic related pollutants in Europe and their effect on allergic disease. *Curr Opin Allergy Clin Immunol* 2004;4:341-8.
- (17) World Health Organisation. Study on chronic respiratory diseases in children in relation to air pollution. Geneva: WHO; 1980.
- (18) Florey CD, Swan AV, Van der Lende R et al. Report on the EC epidemiological survey on the relationship between air pollution and respiratory health in primary schoolchildren. Brussels: Commission of the European Communities; 1983.
- (19) Braun-Fahrlander C, Vuille JC, Sennhauser FH et al. Respiratory health and long-term exposure to air pollutants in Swiss schoolchildren. SCARPOL Team. Swiss Study on Childhood Allergy and Respiratory Symptoms with Respect to Air Pollution, Climate and Pollen. *Am J Respir Crit Care Med* 1997;155:1042-9.
- (20) Dockery DW, Speizer FE, Stram DO et al. Effects of inhalable particles on respiratory health of children. *Am J Respir Crit Care Med* 1989;139:587-94.
- (21) Baldi I, Tessier JF, Kauffmann F, et al. Prevalence of asthma and mean levels of air pollution: results from the French PAARC survey. Pollution Atmospherique et Affections Respiratoires Chroniques. *Eur Respir J* 1999;14:132-8.
- (22) Dockery DW, Cunningham J, Damokosh AI et al. Health effects of acid aerosols on North American children: Respiratory symptoms. *Environ Health Perspect* 1996;104:500-5.
- (23) Guo YL, Lin YC, Sung FC et al. Climate, traffic-related air pollutants and asthma prevalence in middle-school children in Taiwan. *Environ Health Perspect* 1999;107:1001-6.
- (24) Peters JM, Avol E, Navidi W et al. A study of twelve Southern California communities with differing levels and types of air pollution. I. Prevalence of respiratory morbidity. *Am J Respir Crit Care Med* 1999;159:760-7.
- (25) Shima M, Nitta Y, Ando M et al. Effects of air pollution on the prevalence and incidence of asthma in children. *Arch Environ Health* 2002;57:529-35.
- (26) Pattenden S, Hoek G, Braun-Fahrlander C et al. NO₂ and children's respiratory symptoms in the PATY study. *Occupational and Environmental Medicine* 2006;63:828-835.
- (27) ISAAC Steering Committee. Worldwide variation in prevalence of symptoms of asthma, allergic rhinoconjunctivitis, and atopic eczema: ISAAC. The International Study of Asthma and Allergies in Childhood (ISAAC) Steering Committee. *Lancet* 1998;351:1225-32.
- (28) Pandey KD, Wheeler D, Ostro B et al. Ambient particulate matter concentrations in residential areas of world cities: new estimates based on global model of ambient pollutants (GMAPS). Washington DC: World Bank; 2003.
- (29) Asher MI, Keil U, Anderson HR et al. International Study of Asthma and Allergies in Childhood (ISAAC): rationale and methods. *Eur Respir J* 1995;8:483-91.
- (30) Asher MI, Montefort S, Bjorksten B, et al. Worldwide time trends in the prevalence of symptoms of asthma, allergic rhinoconjunctivitis, and eczema in childhood: ISAAC Phases One and Three repeat multi-country cross-sectional surveys. *Lancet* 2006;368:733-43.

- (31) Stewart AW, Mitchell EA, Pearce N, et al. The relationship of per capita gross national product to the prevalence of symptoms of asthma and other atopic diseases in children (ISAAC). *Int J Epidemiol* 2001;30:173-9.
- (32) World Bank. World Development Report. Oxford: Oxford University Press; 1995.
- (33) STATA/SE 9.2 Statistics/Data Analysis. Stata Corporation, College Station, Texas: 2007.
- (34) Anderson HR, Gupta R, Kapetanakis V et al. International correlations between indicators of prevalence, hospital admissions and mortality for asthma in children. *Int J Epidemiol* 2008;37:573–582
- (35) Zeger SL, Thomas D, Dominici F et al. Exposure measurement error in time-series studies of air pollution: concepts and consequences. *Environ. Health Perspect* 2000;108:419-426.
- (36) Weiland SK, Husing A, Strachan DP et al. Climate and the prevalence of asthma, allergic rhinitis and atopic eczema in children. *Occup Environ Med* 2004;61:609-615.
- (37) McCreanor J, Cullinan P, Nieuwenhuijsen MJ et al. Respiratory effects of exposure to diesel traffic in persons with asthma. *N Engl J Med* 2007;357:2348-58.

Online data Supplement 1.

Details of World Bank Global Model of Air Pollution (GMAPS) used for estimating annual average PM₁₀ concentrations in cities with more than 100,000 inhabitants.

Air pollution measurements used in Estimating Annual Average Concentrations

The availability of measurements of ambient concentrations of PM varies widely across the globe, making estimation of annual average concentrations a considerable challenge (Krzyzanowski and Schwela 1999). To estimate ambient PM concentrations for all 14 WHO regions, a model (GMAPS) was developed by the World Bank to estimate city level PM₁₀ based on available PM measurements at population-oriented monitors (Pandey et al., 2003). The model incorporates information on factors such as fuel mix, level of economic development, demographics and weather to predict ambient concentrations of PM₁₀ in urban residential areas.

The GMAPS model developed by the World Bank can be used to generate estimates of PM₁₀ concentrations in all world cities with populations greater than 100,000 and national capitals regardless of size. The estimation model is based on available PM₁₀ and TSP measurements from population-oriented monitoring stations in cities worldwide for the period 1985 to 1999 available through October 2001. In all cases, data from a monitoring site were included if and only if it was clearly identified as a residential or mixed residential site. For instance, city averages reported for many Chinese cities (National EPA China, 2000) were not included in the model estimation because the location of these sites could not be ascertained.

In principle, the monitoring data used for calculation of annual averages should be collected throughout the year, since seasonal patterns in the data are fairly common. More than 85% of European and US cities have measurements of PM collected throughout the year. The representativeness of the data for cities in other parts of the world could not be confirmed. In addition, in many countries where PM was measured throughout the year, it was only measured on every sixth-day. The methods for measuring concentrations of PM varied and included both gravimetric and automatic methods (TEOMS or beta gauge).

Most of the annual average ambient concentration data used in the model was obtained from AMIS (WHO Air Quality and Health 2001). This information is submitted to WHO by national environmental agencies and air quality control authorities who perform these measurements using nationally approved methods and standards of data quality. The data set contains annual mean concentration of selected air pollutants including PM by monitoring site. Additional data, such as 95th percentiles of daily means, are also available for some sites. Though WHO requests all member states to provide data for compilation in the AMIS database, the reported data is still limited because many countries do not have air quality monitoring networks. Additionally, some countries with monitoring networks may not report the data because of poor data quality or limited ability to process and report the data.

The AMIS data was supplemented with monitored TSP and PM₁₀ data from other sources. These included: data for European cities collected by WHO/ECEH for the HIAAP project in 1999 from both national and local environmental agencies (WHO 2001), data for Canadian cities provided by Environment Canada (Environment Canada), and data for US cities from the US EPA's AIRS database (USEPA Airs data base). Electronically available data were also obtained for Chinese cities from the Environmental Quality Reports from China (National EPA China, 2000), and Mexican cities from the Instituto Nacional de Ecologia (INE), SEMARNAP, Mexico (SEMARNAP). To limit undue influence of the data from US cities, data from the US AIRS database were limited to the years 1996-1999.¹

Monitored annual average PM₁₀ and TSP data were available for 512 unique locations in 304 cities in 55 countries over the period of 1985 to 1999 and provided 1,997 time-location data points. For some sites and years, both TSP and PM₁₀ data were available yielding a total of 2,344 individual observations.² 304 cities reported either the annual average PM₁₀ or TSP concentrations for at least one year between 1985 and 1999. Of these, 51 cities reported both PM₁₀ and TSP while 165 cities, mostly in North America and Western Europe (NAWE) reported PM₁₀ only and the remaining 88 reported TSP data only.

Coverage of cities and populations with monitored data varies significantly across different WHO regions. For instance, monitoring data were available for one or two or fewer cities for five of the regions AfrD, AfrE, AmrD, EmrB, EmrD, SearD. In contrast, 218 cities in NAWE have monitored data of which 174 report PM₁₀ data. The 304 world cities with monitored data account for 9% of the total cities larger than 100,000 worldwide and have a combined 2000 population of around 559 million or about 28% of the urban population in these cities.

World Bank Global Model of Ambient Particulates (GMAPS) Model

The World Bank GMAPS model econometrically estimates a fixed effect model of urban ambient PM concentrations using the latest available data from the WHO and other sources as outlined above. The estimating equation (1) focuses on the anthropogenic sources of pollution and the dissipative/dispersive capacity of the natural environment.³ Its determinants include the scale and composition of economic activity, the energy mix,

¹ US cities account for about 40% of the observations in the estimation model even after this exclusion.

² Monitored data is available for 1 additional city/country, Skopje in Macedonia but is not used in the estimation model because of missing explanatory variables. In addition, 150 observations primarily from Germany (94), Lithuania (30) and other East European states (26) during the early 90s were excluded because of uncertainties in defining appropriate explanatory variables.

³ The model presented here is one of several versions of the GMAPS developed by the World Bank. Another alternative model jointly estimates PM₁₀ and TSP concentrations in residential and non-residential sites.

the strength of local pollution regulation, and geographic and atmospheric conditions that affect pollutant transport.

$$\begin{aligned}
 C_{ijkt} = & \sum_{k=1}^K \beta_k Z_k + \sum_{f=1}^F \beta_{Ef} E_{fkt} + \sum_{g=1}^{G2} \beta_{Mg} M_{gjk} + \beta_R R_{kt} + \beta_N N_{jkt} + \beta_D D_{jk} + \\
 (1) \quad & \beta_{Scale} Scale_{jkt} + \beta_Y Y_{kt} + \beta_T Trend_{ijkt} + \beta_{YT} Y_{kt} Trend_{ijkt} + \\
 & \theta_S S_{ijkt} + \theta_{Scale} S_{ijkt} Scale_{jkt} + \theta_Y S_{ijkt} Y_{kt} + \theta_T S_{ijkt} Trend_{ijkt} + \theta_{YT} S_{ijkt} Y_{kt} Trend_{ijkt} + \\
 & \sum_{g=1}^{G1} \theta_{Mg} S_{ijkt} M_{gjk} + \varepsilon_{ijkt}
 \end{aligned}$$

where,

- C_{ijkt} = log of PM concentration in monitoring station i, city j, country k, at time t
- Z_k = Binary variable for country k
- E_{fkt} = log of Per capita Energy Consumption of energy source type f for country k at time t (f=1..F)
- M_{gjk} = log of meteorological/geographic factor g for city j, country k (Factors g=1..G1 affect PM₁₀ concentration differently than TSP concentration. Factors g=G1+1...G2 do not make a distinction between PM₁₀ and TSP)
- R_{kt} = log of Population density of country k at time t
- N_{jkt} = log of Population of city j, country k, at time t
- D_{jk} = log of Local population density in the vicinity of city j in country k
- $Scale_{jkt}$ = log of Scale of economy (intensity of economic activity) for city j, country k at time t
- Y_{kt} = log of Income per capita (one-year lagged three year moving average) of country k at time t
- $Trend_{ijkt}$ = time trend (1985=1, 1986=2, ... 1999=15)
- S_{ijkt} = binary variable for PM type measured at monitoring station i, city j, country k, at time t, (1=TSP, 0=PM₁₀), and

the β s and θ s are the parameters that are estimated by the model.

The estimating equation (1) jointly determines the concentrations of total suspended particulate matter (TSP) and inhalable particulates (PM₁₀) in residential areas. Most cities in developing countries only monitor TSP and not PM₁₀. Adoption of the pooled specification permits use of all available data and provides better information about the PM concentrations especially for cities in developing country. Limiting the estimation sample to PM₁₀ observations is sensible only if knowledge of a city's TSP concentration makes no contribution to predicting PM₁₀. Since PM₁₀ comprises the smaller size particles within TSP, this assumption is clearly unreasonable. The pooled specification allows for separate estimation of PM₁₀ and TSP concentration levels for each city by setting the binary variable S_{ijkt} , equal to zero or one, as shown in equations (2) and (3).

$$(2) \quad \log[PM10_{ijkt}] = \sum_{k=1}^K \beta_k Z_k + \sum_{f=1}^F \beta_{Ef} E_{fkt} + \sum_{g=1}^{G2} \beta_{Mg} M_{gjk} + \beta_R R_{kt} + \beta_N N_{jkt} + \beta_D D_{jk} + \beta_{Scale} Scale_{jkt} + \beta_Y Y_{kt} + \beta_T Trend_{ijkt} + \beta_{YT} Y_{kt} Trend_{ijkt}$$

$$(3) \quad \log[TSP_{ijkt}] = \sum_{k=1}^K \beta_k Z_k + \sum_{f=1}^F \beta_{Ef} E_{fkt} + \sum_{g=1}^{G2} \beta_{Mg} M_{gjk} + \beta_R R_{kt} + \beta_N N_{jkt} + \beta_D D_{jk} + \beta_{Scale} Scale_{jkt} + \beta_Y Y_{kt} + \beta_T Trend_{ijkt} + \beta_{YT} Y_{kt} Trend_{ijkt} + \theta_S + \theta_{Scale} Scale_{jkt} + \theta_Y Y_{kt} + \theta_T Trend_{ijkt} + \theta_{YT} Y_{kt} Trend_{ijkt} + \sum_{g=1}^{G1} \theta_{Mg} M_{gjk}$$

To reduce undue influence from extreme values, all of the continuous variables in the model are specified in log form and each exogenous variable in the estimation sample is truncated to the middle 98% range observed in the estimation sample.

The estimation equation (1) includes country-specific binary variables, Z_k , to control for economic, social and natural factors that are not captured by the other explanatory variables. These include differences in ambient concentration data quality and collection methods across countries, the degree of regulatory heterogeneity within a country, the relative importance of inter-city transport, proximity of and pollution levels in neighboring cities and the composition of economic activity. The country-specific binary variables measure the average PM concentration in each country during the 15-year period 1986-1999, controlling for within country variations due to factors accounted for in the remainder of the estimating equation (1). In contrast, the rest of the estimation model (1) explains the marginal contribution of the included factors to deviations in the ambient city concentration from this average level.

The primary determinants of the observed within country variations in the ambient PM concentrations in the estimation model are:

Energy Consumption The model separately includes six per capita energy consumption categories -- coal, oil, natural gas, nuclear, hydro, combustible renewables and wastes -- that accounts for all energy consumed in each country available from the International Energy Agency's (IEA) Annual Energy Balance database (International Energy Agency 2001a, b). The separate inclusion of each energy source type accounts for differences in emission factors, variations in economic activity and intensity of fuel use across countries. In addition, the model also includes per capita gasoline and diesel used in the transportation sector also available from IEA's database to capture additional detail about one of the most significant contributors to ambient PM concentrations.

Meteorological and Geographic factors The model includes 22 atmospheric and geographic factors for each city to account for both the dissipative/dispersive capacity of the natural environment and natural sources of particulates such as desert dust storms, forest fires, and sea spray. These include a suite of 18 climatic variables representing the

long term average climatic conditions related to local atmospheric conditions and transport of PM consisting of the annual average (average of the monthly data) and seasonal changes (measured as the standard deviation of the monthly data) for the following nine factors: mean temperature, diurnal temperature, mean precipitation, barometric pressure, wind speed, percent cloud cover and, frequency of wet days, sunny days and frosty days (New, Hulme & Jones 1999).⁴ In addition, two meteorological variables related to energy demand (heating and cooling degree days) are estimated for each city from the mean monthly temperature. Two topographical variables related to atmospheric transport – distance from the city center to the nearest point on the coastline calculated using geographic information system (GIS) and elevation of the city derived from a global digital elevation model (USGS 1996) – are also included in the model.

City and national population and national population density These variables provide measures of scale and intensity of the pollution problem in each city. The population data comes from the Demographic Yearbook published by the United Nations (UN 2001).

Local population density The local population density in the vicinity of each city provides a measure of the intensity of pollution. It is estimated from the Gridded Population of the World (version 2), available from the Consortium for International Earth Science Information Network (CIESIN: <http://www.ciesin.org/datasets/gpw/globldem.doc.html>.) This dataset provides the best available population data for about 120,000 administrative units, converted to a regular grid of population counts at a resolution of about five kilometers. The local population density in the vicinity of each city is the average population density for all grid cells within a twenty-kilometer radius from the city center.

Local intensity of economic activity Most cities do not collect data on the level or composition of economic activity. Instead, the local GDP per square kilometer computed as the product of the national per capita Gross Domestic Product and the local population density in the vicinity of each city is used as a proxy for the intensity of economic activity within each city (World Bank 2002).

National income per capita This variable is used to capture the following country level indicators: valuation of environmental quality, strength of environmental policy and regulation, the institutional capacity to enforce environmental policies, and the potential use of cleaner fuels along the fuel-use chain as countries develop. It is measured as a one-year lag of the average of the previous three years (World Bank 2002).

Time trends The model includes 2 time trend variables (with 1985=1 ...1999=15) to allow for differential time trends for PM₁₀ and TSP particulate pollution. Both of these variables are in turn interacted with lagged national per capita income to allow trends to

⁴ The climatic variables have been constructed from a global mean monthly climatology map with a 0.5° lat × 0.5° resolution developed by researchers at the Climate Research Unit of the University of East Anglia. This data is available at http://ipcc-ddc.cru.uea.ac.uk/cru_data/examine/have_index.html). For each city all of the climate variables are based on the conditions for the city center.

vary across countries based on differential valuation and improvements in environmental quality across countries as measured by the level of economic development. These trends measure changes in pm levels due to factors not already captured in the model such as technological changes, improvements in knowledge and structural shifts in the composition of economic activity. They do not represent the unconditional aggregate trends in PM levels.

Binary variable to differentiate PM₁₀ and TSP The model includes a binary variable indicating whether PM is measured as TSP or PM₁₀. This binary variable is also allowed to interact in the model with other variables to allow for size class differences in the composition of particulates across cities and countries. It provides a better representation of inter city differences across the world than assuming a uniform relationship across all cities. The log of the ratio of PM₁₀ to total suspended particulate matter in each city can be estimated by subtracting equation (3) from (2), as shown in equation (4). The key determinants of this ratio are the scale of economic activity, differential trends across countries, level of economic development and strength of environmental policy, and the subset of meteorological variables that are directly related to particle size class (annual mean and seasonal variations in wind speed, precipitation, and frequency of wet days).

$$(4) \quad \log[PM_{10}^{ijkt}] - \log[TSP^{ijkt}] = -\theta_S - \theta_{Scale} Scale_{jkt} - \theta_Y Y_{kt} - \theta_T Trend_{ijkt} - \theta_{YT} Y_{kt} Trend_{ijkt} - \sum_{g=1}^{G1} \theta_{Mg} M_{gjk}$$

In order to facilitate predictions for countries not included in the estimation, a secondary model shown in equation (5) is estimated to explain the average level of ambient PM concentration in each country.

$$(5) \quad \hat{\beta}_k = \sum_{f=1}^F \gamma_{Ef} \bar{E}_{fk} + \gamma_R \bar{R}_k + \gamma_Y \bar{Y}_k + u_k$$

where,

$\hat{\beta}_k$ = country-specific binary variable coefficient estimated in equation (1)

$\bar{E}_{fk}$ = log of average per capita energy consumption of energy type f for country k during 1985-1999 (f=1..F)

$\bar{R}_k$ = log of average population density of country k during 1985-1999

$\bar{Y}_k$ = log of average national per capita income of country k during 1985-1999 (one-year lagged average of previous three years)

This secondary model (5) explains the average level of pollution under reference conditions for a country based on the scale of the economy, the composition of economic

activity as measured by the energy mix, and the strength of local pollution regulations and the institutional capacity for implementing these regulations.

Empirical Results

The GMAPS model is designed to obtain the best city-level PM prediction for a wide range of cities based on the limited amount of monitored data available; so it focuses on increasing the fit of the model. It is not designed to provide a causal model for ambient air pollution concentrations. The estimation model (1) explains 88% of the variation in the observed monitored data, indicating a good fit (Pandey et al 2003). The overall correlation between the actual and the predicted data is around 0.9 for both PM₁₀ and TSP observations (see Table 3). It is higher than 0.80 for all years and for both PM₁₀ and TSP observations with the exception of PM₁₀ in 1985. The correlation by region is smaller than that over time but is still high for regions with a large number of data points. The correlations for regions with few data points are smaller and less precisely estimated. The negative correlation for EurB is driven by a single erroneous observation for Bucharest where the observed PM₁₀ level is higher than the TSP observations. (The results originated from two different monitoring locations.) Had the model been re-estimated without this particular PM₁₀ observation the correlation for the region would have been 0.32.

Region- and PM type-specific scatter plots of model predictions against actual data also shows a clustering of points around the solid line drawn at a 45° angle indicating that the actual values are close to the predicted values. As would be expected, the predicted values are less extreme than the actual values at both tails due to the truncation of all explanatory variables to the mid 98% range of the estimation sample. F-tests revealed that all of the eight aggregate factors in the model added significant explanatory power to the regression.

The secondary estimation model (5) explains 85% of the variation in the estimated average level of pollution in a country indicating a good fit of this model. The explanatory power of the secondary model is not as robust to changes in the estimation sample due to significant uncertainties in the estimated of the dependent variable.

Out of sample predictions were used to validate the model using both statistical and heuristics criteria. The model was re-estimated using subsamples of the data based on different cutoff points for per capita income to examine the appropriateness of extrapolating from a model primarily based on industrialized cities in NAWA to developing country cities. The resulting model estimates were used to predict PM₁₀ levels in residential areas in the out of sample cities located in poorer countries. A second set of estimates were also done using income based subsamples using only the available monitored PM₁₀ data in residential sites. These validation estimates consistently showed that out of sample correlations were higher when tsp data was included in the estimations. Further, the out of sample correlations on aggregate ranged between 0.40 and 0.59 based on the income cutoff used, validating the modeling approach.

Since cities with monitored data in developing countries are not a representative sample of cities and account for a small fraction of urban residents in these countries, the following heuristics criteria were also used to evaluate the model.

- Comparison of the relative variation of the predictions within countries and between countries relative to the actual data. (The model predictions exhibit significant variations both across countries and across cities within a country. The predicted within country variations are about 60% of the between country variations and are comparable to the corresponding variations in the actual data).
- Number of cities for which predictions were outside the estimation sample range. (The PM₁₀ predictions are within the range observed in the actual data. They continue to be within bounds when the same fractions of values are removed from the tails of the estimated and actual data).
- Magnitude of predictions outside the range observed in the estimation sample. (Out of the 304 cities with monitored data, PM₁₀ levels exceed 200 µg/m³ in 3 cities and TSP levels exceed 400 µg/m³ in 10 cities. In contrast, the predicted PM₁₀ level exceeds 200 µg/m³ in only 4 out of 3226 cities).
- Range of the PM₁₀/TSP ratio. (The PM₁₀/TSP ratio predicted by the model is between 0.24 and 0.98 and spans the middle 95% of the range observed in the actual data. The mean ratio predicted by the model is 0.49; the ratio for half of the cities lies between 0.39 and 0.56).
- Comparison of the uncertainty in city estimates relative to the amount of available information for neighboring cities. (Bootstrap error estimates of the city prediction error shows that the confidence intervals are wider for cities with no monitored data and are largest in the countries with no monitored data).

The robustness of the model was tested using alternative specifications of the model based on the goodness of fit of the model and the heuristic criteria outlined above. The alternative models that were considered were:

- *Linear model* The linear model provides undue weight to the extreme values in the explanatory variables resulting in predictions that are orders of magnitude larger than those for monitored cities.
- *Explanatory variable truncation* The model was re-estimated with four different levels of truncation for the explanatory variables: no truncation, truncation to the actual range for the monitored cities, truncation to the mid 98% range of all explanatory variables for the monitored cities, and truncation to the mid 90% range for the monitored cities. Estimates based on the first two were sensitive to some of the extreme data points in the estimation sample resulting in large variations in the predictions. Estimates from the last truncation were rejected because over a quarter of the observations were truncated leading to a poorer model fit.
- *Energy consumption variables* The model was re-estimated with 3 alternative measures for the energy consumption variables: energy consumption per area, total per capita energy consumption and share of each energy type in the total energy mix, and the product of national per capita energy consumption by energy type and city population density. The per area specification resulted in

predictions that were unstable and orders of magnitude larger than those observed in any city because of truncation of extreme values in countries with missing fuels data. The second and third specifications resulted in poorer fits with over predictions for over 100 cities outside of the observed PM_{10} range.

- *Income* The model was estimated with income squared and income cubed terms to measure the impact of national per capita income. Higher order terms were unstable and resulted in predictions that were orders of magnitude larger than those observed in any city.
- *PM_{10}/TSP ratio* A number of different models were estimated from full interactivity of the binary variable S_{ijkt} with all of the continuous variables to no interactivity with the continuous variables. The full interactivity model was rejected because it predicted physically implausible PM_{10}/TSP ratios of 2 for a significant number of cities. The limited model with no interactivity was rejected because it over-predicted the results for many cities in the Middle East and North Africa that contain a larger fraction of wind-blown coarser particles. Other models were estimated that incrementally added groups of variables such as energy type and the other climate variables. These were all rejected using the heuristics criteria outlined above.
- *Location of monitoring sites* The sensitivity of the model predictions to the inclusion of mixed residential sites was examined by re-estimating the model with only pure residential sites included. While estimates for some individual cities change in significant ways, predictions at the regional level and for most countries are not statistically different than those when mixed sited are included.
- *Inclusion of non-residential sites* A more inclusive model which jointly estimates residential and non-residential PM levels indicated that most model parameters were relatively stable and that the model predictions for regional residential PM_{10} concentrations were not significantly different.
- *Additional monitoring data* The sensitivity of the model was tested to the inclusion of additional monitoring data that became available between October 2001 and July 2002. The aggregate PM predictions are not statistically different for all regions except for EmrD where PM levels increase by nearly 100%. This is primarily due to the inclusion of data for Kuwait City, which is the only city for which monitored data is available in this region.
- *Influential data point* The sensitivity of the model predictions to influential data points was examined using bootstrap error techniques. Variations in the predictions based on different sub-samples of the data were used to estimate the degree of uncertainty in the model estimates.

Estimating city PM Ambient Concentrations

The average regional ambient concentrations were estimated from the city-level model predictions for 1999, the latest year for which all of the explanatory variables are available. The estimates of PM_{10} levels in each city for 1999 were generated using a three-step approach. First, for all cities located in countries with at least one population-oriented monitoring site, PM_{10} concentration was estimated using the GMAPS model as specified in equation (1). PM_{10} levels cannot be estimated using equation (1) alone for cities in every country, because the average pollution level in the country as measured by

the country binary variable is not available for countries without monitors. Therefore, in the second step, the secondary equation (5) is used to predict the country coefficient for countries without monitors. These predictions are combined with estimates from equation (1) that explains variations around the average level to generate 1999 PM₁₀ levels for these cities in these countries.

Finally, for cities with actual monitored data, a best 1999 city PM₁₀ estimate is generated by incorporating information on concentrations from previous years. Specifically, an average residual for each city is determined by comparing each year-specific predicted value generated from the estimation model (1) with the actual monitored value for that year and city. This serves to adjust the model predictions for local factors that are known but unmeasured in the model such as the composition of the local economic activity. Given the large year to year variations in the available measured data even at the same monitoring station, correcting for the average residual provides a better representation of long term average factors affecting PM levels in a city than using the actual monitored value for the last year of monitored data alone.

References

CIESIN. Consortium for International Earth Science Information Network:

<http://sedac.ciesin.columbia.edu/gpw>

International Energy Agency (2001a) *Energy balance of non-OECD countries 1995–1999*. International Energy Agency, Vienna.

International Energy Agency (2001b) *Energy Balance of OECD Countries 1995–1999*. International Energy Agency, Vienna.

Krzyzanowski M, Schwela D. Patterns of air pollution in developing countries. In: Holgate ST, Samet JM, Koren HS, Maynard R, eds. *Air Pollution and Health*. Academic Press, London, England; 1999:105-114.

National EPA of China (2000). *Environmental Statistical Yearbook*. Environmental Publishing House, Beijing; 2000.

New M, Hulme M, Jones P. Representing twentieth-century space–time climate variability. Part I: Development of a 1961–90 mean monthly terrestrial climatology. *J Clim* 1999;12(3):829–856, http://www.cru.uea.ac.uk/~markn/cru05/cru05_intro.html.

Pandey KD, Bolt K, Deichmann U, et al *The Human Cost of Air Pollution: New Estimates for Developing Countries*. Development Research Group and the Environment Department, The World Bank, Washington DC. (2003 in press)

INE. Instituto Nacional de Ecología (2000) *Almanaque de datos y tendencias de la calidad del aire en ciudades Mexicanas [Temperature data and trends in Mexican cities]*. Dirección General de Gestión e Información Ambiental del Instituto Nacional de Ecología, Secretaría de Medio Ambiente y Recursos Naturales (SEMARNAP) [The Secretariat of Environment and Natural Resources], Mexico. Unpublished document, available at: <http://www.ine.gob.mx>.

UN 2001. *Demographic Yearbook 1998*. (United Nations publication, Sales No. E/F.97.XIII.1). Data also available at: <http://unstats.un.org/unsd/citydata/>

USGS 1996, GTOPO30 – *Global Digital Elevation Model*, US Geological Survey, Eros Data Center, Sioux Falls, SD. Available at: <http://edcdaac.usgs.gov/gtopo30>.

WHO 2001. *Health impact assessment of air pollution in the WHO European Region* (Technical Report from WHO/ECEH Project). WHO European Centre for Environment and Health, Bonn; Nov 2001.

WHO Air Quality and Health 2001. Air Management Information System, AMIS 3.0 CD-ROM, World Health Organisation, Geneva; 2001.

World Bank. *World Development Indicators 2002*. World Bank, Washington DC; 2002

Online Data Supplement 2

13 - 14 years

Country	Centre	PM ₁₀	GNP per capita	Number	Current wheeze	Severe wheeze	Severe/Current wheeze	Rhino- conjunctivitis	Eczema symptoms	Atopy	Asthma	Hay fever	Eczema diagnoses
Albania	Tirane	39	670	2957	2.6	0.7	27.3	4.0	0.8	4.7	1.6	2.3	1.3
Algeria	Algiers	35	1600	1173	7.8	4.9	62.6	18.2	5.2	20.9	6.4	24.3	6.7
Argentina	Buenos Aires	23	8030	2996	9.9	4.8	48.5	21.0	7.3	25.2	6.6	12.5	10.5
	Rosario	24	8030	3008	11.8	6.1	51.5	24.6	7.3	27.5	7.9	14.2	11.9
Australia	Sydney	18	18720	2839	24.7	11.7	47.4	15.4	8.5	20.7	24.8	24.2	9.6
	Melbourne	15	18720	2758	27.3	13.8	50.6	16.6	10.3	23.0	26.6	40.5	15.9
	Perth	15	18720	3650	31.4	13.8	44.0	22.6	10.1	28.3	30.2	49.2	17.4
	Adelaide	15	18720	3030	33.5	16.6	49.6	22.6	9.8	28.0	30.4	54.4	19.8
Austria	Salzburg	18	26890	3371	11.5	3.9	33.8	11.5	5.1	15.2	6.3	20.0	4.4
Belgium	Antwerp	23	24710	1515	12.0	5.0	41.8	14.5	6.7	19.1	8.1	17.0	21.5
Brazil	Sao Paulo	44	3640	3007	23.3	6.8	29.1	12.6	3.7	15.3	10.0	31.7	14.0
	Porto Alegre	15	3640	3195	24.7	8.6	34.9	17.6	4.8	20.5	21.9	24.4	12.6
	Recife	21	3640	3086	19.7	8.1	41.1	11.3	4.6	14.6	20.9	18.3	11.4
	Salvador	19	3640	3162	27.0	9.9	36.7	25.0	9.2	29.6	12.5	24.7	3.7
	Curitiba	25	3640	3004	18.4	7.2	39.1	14.1	3.9	16.5	8.6	7.9	10.0
Canada	Hamilton	28	19380	3051	30.6	14.5	47.3	25.0	9.5	30.5	19.2	27.7	14.5
	Saskatoon	17	19380	1901	24.0	10.6	44.3	12.0	9.1	18.4	12.2	12.1	17.3
Chile	Central Santiago	63	4160	2944	11.7	3.4	29.1	15.7	7.5	20.4	12.4	10.8	7.0
	Valdivia	37	4160	3231	11.5	4.3	37.4	9.8	11.4	18.5	11.9	10.2	9.0
	Punta Arenas	28	4160	3482	6.8	2.0	29.5	8.4	5.6	12.0	7.3	10.5	7.9
China*	Beijing	106	620	4167	5.1	1.9	37.1	7.9	1.6	9.1	6.9	6.0	10.3
	Guangzhou	75	620	3855	3.4	1.2	35.1	8.4	0.8	9.0	3.9	2.9	18.3
	Shanghai	110	620	3483	3.3	0.8	24.3	5.0	0.8	5.7	7.1	3.2	6.9
	Chongqing	106	620	4296	4.7	1.1	23.3	4.9	1.3	5.9	7.1	2.9	10.1
Estonia	Tallinn	19	2860	3560	8.5	2.2	25.7	4.7	6.5	10.0	3.3	14.7	14.9
Ethiopia	Addis Ababa	49	100	2951	10.7	7.2	67.1	10.6	19.9	26.2	2.8	7.5	11.2
	Jima	43	100	3027	1.9	1.1	56.9	1.8	3.2	4.7	2.2	4.0	5.6
Finland	Helsinki	20	20580	2855	19.8	7.8	39.5	22.9	17.3	33.2	7.4	30.9	25.9
	Turku and Pori County	18	20580	3085	15.0	4.3	28.7	13.8	14.8	24.7	7.8	27.0	23.6
France	Marseilles	17	24990	3494	14.9	5.6	37.6	14.4	8.9	20.3	14.4	11.0	22.8
	Montpellier	23	24990	3384	18.2	9.0	49.5	25.5	12.3	31.8	14.2	27.1	25.1

Online Data Supplement 2

13 - 14 years

Country	Centre	PM ₁₀	GNP per capita	Number	Current wheeze	Severe wheeze	Severe/Current wheeze	Rhino- conjunctivitis	Eczema symptoms	Atopy	Asthma	Hay fever	Eczema diagnoses
Georgia	Strasbourg	31	24990	5403	10.2	3.8	37.2	13.6	10.2	20.6	10.1	14.8	21.0
	Tbilisi	102	440	3449	3.7	1.4	37.5	4.3	2.3	6.1	2.4	6.1	4.1
	Kutaisi	90	440	3297	3.6	1.3	36.1	4.5	2.8	6.6	3.8	4.7	1.8
Germany	Munster	22	27510	4003	14.1	7.1	50.4	14.4	7.1	19.1	7.0	21.1	10.0
Greece	Athens	36	8210	2561	3.7	1.5	40.0	6.3	3.1	8.5	4.5	12.7	3.9
Hong Kong	Hong Kong	43	21500	4666	12.4	5.0	40.2	24.0	2.7	25.6	11.2	4.7	15.4
India	Neyveli	47	340	3281	6.0	2.8	46.7	8.2	6.4	12.8	2.4	9.0	5.5
	Madras (centre no 3)	49	340	3086	6.0	3.0	50.3	3.2	1.6	4.3	1.8	7.3	4.8
	Kottayam	34	340	2047	17.8	10.4	58.5	21.4	20.5	33.6	12.4	15.8	22.1
	New Delhi (centre no 7)	133	340	3026	13.0	5.5	42.2	10.4	5.5	14.4	5.3	13.8	5.1
	Chandigarh	94	340	3139	4.2	2.6	62.1	5.4	3.5	7.8	3.3	7.0	3.0
	Jodhpur	84	340	1094	10.7	5.2	48.7	9.0	6.1	13.4	6.4	11.9	4.8
	Akola	69	340	2138	1.6	0.8	50.0	1.4	0.3	1.5	2.6	2.0	0.2
	Pune	70	340	2702	1.8	0.8	44.9	1.6	0.6	2.1	4.9	4.4	3.5
	Bombay (centre no 16)	80	340	4225	1.9	0.9	47.5	2.3	1.1	3.2	3.6	4.0	2.5
	Bandung	136	980	2249	2.1	1.6	76.6	5.3	1.2	6.3	1.6	0.0	0.4
Iran	Tehran	42	.	5521	10.1	4.6	45.5	9.9	3.2	12.2	3.2	5.8	8.9
	Rasht	100	.	3182	9.7	4.4	45.3	5.9	3.1	8.0	2.7	4.6	10.5
Italy	Torino	46	19020	1242	8.6	3.9	44.9	15.1	9.4	21.7	9.4	18.6	12.7
	Milano	31	19020	3373	10.6	3.8	35.8	16.4	7.0	20.4	10.7	21.0	11.8
	Firenze	52	19020	1171	10.5	4.0	38.2	18.4	5.9	22.5	9.6	18.6	4.4
	Roma	31	19020	3323	9.8	3.6	36.8	14.7	4.9	18.0	11.3	16.4	5.1
	Cosenza	18	19020	1068	7.1	3.3	46.1	12.7	4.4	15.0	8.1	19.4	4.1
	Trento	20	19020	4426	5.9	2.1	35.6	9.0	5.6	13.1	7.5	12.6	9.9
	Verona	25	19020	2208	7.5	2.6	34.3	9.9	3.9	12.4	11.8	4.4	8.0
Japan	Fukuoka	32	39640	2831	13.4	4.9	36.7	14.8	10.5	22.4	18.9	22.6	36.0
Kenya	Eldoret	54	280	3021	10.4	5.1	49.0	12.1	11.5	19.5	6.8	15.9	13.2
	Nairobi	51	280	3243	17.1	11.9	69.5	16.1	9.4	22.1	15.4	25.3	18.4
Kuwait	Kuwait	23	17390	1056	17.0	9.8	57.2	12.5	8.3	18.3	17.5	17.5	13.0
Latvia	Riga	27	2270	2994	8.4	2.2	26.3	5.3	5.2	9.8	3.9	3.5	5.4
Lebanon	Beirut	35	2660	2993	14.4	8.4	58.2	15.4	4.7	18.4	11.6	19.6	12.0

Online Data Supplement 2

13 - 14 years

Country	Centre	PM ₁₀	GNP per capita	Number	Current wheeze	Severe wheeze	Severe/Current wheeze	Rhino- conjunctivitis	Eczema symptoms	Atopy	Asthma	Hay fever	Eczema diagnoses
Malaysia	Kota Bharu	52	3890	3113	6.8	2.1	30.7	9.6	7.1	14.4	8.6	20.0	4.1
	Ipoh	20	3890	3313	10.0	3.8	38.1	18.0	6.5	21.4	11.4	13.5	1.1
Mexico	Cuernavaca	42	3320	3102	6.6	3.4	51.2	9.4	4.4	12.3	5.5	5.4	3.9
Morocco	Rabat	21	1110	3276	6.8	3.6	52.9	10.2	5.0	13.6	6.6	18.3	8.5
	Casablanca	21	1110	3184	9.9	5.3	53.7	15.5	12.0	23.1	12.1	27.4	13.9
	Marrakech	18	1110	2900	5.6	3.0	53.7	10.4	9.2	17.3	17.1	20.9	13.1
New Zealand	Auckland	15	14340	3206	26.5	12.2	46.0	18.9	12.4	26.9	22.9	33.7	23.5
	Wellington	15	14340	4424	31.6	15.2	48.1	19.8	13.2	28.4	26.3	37.3	27.8
	Christchurch	22	14340	3191	29.6	13.6	45.9	19.4	12.3	27.0	25.9	40.4	24.8
Nigeria	Ibadan	89	260	3057	10.7	6.4	59.9	39.7	17.7	46.5	18.4	16.1	38.4
Pakistan	Karachi	158	460	1829	8.5	4.3	51.0	18.1	9.6	23.9	7.3	21.0	16.2
Panama	David-Panama	55	2750	2885	17.6	7.5	42.5	9.4	7.8	15.4	16.9	3.2	7.2
Paraguay	Asuncion	77	1690	2966	19.4	8.0	41.2	34.5	10.8	38.8	12.2	38.3	16.3
Peru	Lima	48	2310	3158	26.0	9.2	35.4	19.3	8.2	24.7	28.0	32.5	16.1
Philippines	Metro Manilla	47	1050	3207	12.3	5.8	47.2	15.3	5.2	18.4	17.6	32.5	7.1
Poland	Poznan	48	2790	3631	7.9	3.0	38.0	6.4	5.3	10.4	2.0	12.0	13.2
	Krakow (centre no 3)	60	2790	2786	7.5	2.7	35.9	11.8	4.6	14.8	2.3	19.8	14.7
Portugal	Lisbon	28	9740	3030	11.1	4.3	38.7	6.5	4.0	9.5	12.3	5.1	10.3
	Funchal (Madeira)	45	9740	3532	10.6	4.7	44.4	7.7	5.4	11.6	13.1	8.9	15.0
	Porto	43	9740	3131	7.4	2.7	36.6	6.2	4.4	9.6	11.3	4.2	9.2
Republic of Korea	Seoul	46	9700	2993	8.3	3.6	43.5	10.7	4.6	14.1	2.8	8.4	7.7
Romania	Cluj	24	1480	3396	3.0	1.4	47.1	5.2	6.3	10.2	3.7	2.2	3.7
Russian Federation	Moscow	29	2240	3411	4.4	1.2	27.3	6.2	3.0	8.6	2.4	3.8	4.7
Singapore	Singapore	29	26730	4206	9.7	3.9	40.2	15.1	7.4	20.4	20.9	3.7	4.0
South Africa	Cape Town	15	3160	5173	16.1	7.3	45.4	15.1	8.3	20.4	13.1	29.1	9.6
Spain	Cartagena	45	13580	3017	10.5	5.1	48.6	16.8	5.8	20.3	10.5	7.2	7.7
	Barcelona	35	13580	3031	14.3	5.4	37.9	11.7	3.9	14.6	11.1	8.5	12.6
	Bilbao	25	13580	3212	11.9	5.7	47.9	17.2	4.5	20.3	16.3	11.0	8.3

Online Data Supplement 2

13 - 14 years

Country	Centre	PM ₁₀	GNP per capita	Number	Current wheeze	Severe wheeze	Severe/Current wheeze	Rhino- conjunctivitis	Eczema symptoms	Atopy	Asthma	Hay fever	Eczema diagnoses
	Castellon	44	13580	3094	7.1	2.4	33.6	13.4	2.9	15.3	7.8	6.7	6.8
	Pamplona	32	13580	3040	5.5	2.3	41.9	14.6	4.2	17.5	8.7	6.1	8.4
	Valladolid	34	13580	3178	6.1	2.5	40.7	12.7	4.6	16.0	6.3	7.7	10.1
	Valencia	34	13580	3179	11.0	4.2	38.3	12.0	3.3	14.3	12.1	14.4	15.0
	Cadiz	31	13580	3270	15.4	6.5	42.3	21.8	6.0	24.6	11.2	13.0	12.8
Sweden	Linkoping	16	23750	3376	11.2	4.1	36.5	11.3	15.6	23.0	10.0	23.4	46.9
	Stockholm/Uppsala	19	23750	3075	14.8	5.7	38.5	12.0	13.3	22.0	10.8	24.8	49.3
Thailand	Bangkok	96	2740	3713	13.5	6.4	47.5	15.4	6.8	19.6	14.1	30.7	25.4
	Chiang Mai	45	2740	3927	12.6	5.2	41.2	15.6	9.6	22.5	9.3	24.8	27.1
United Kingdom	South Thames	19	18700	2296	31.4	14.5	46.2	16.6	16.6	27.9	20.5	38.4	20.9
Uruguay	Montevideo	128	5170	3072	19.0	8.8	46.2	16.0	7.2	19.9	15.3	25.1	7.4
USA	Chicago (center no 3)	31	26980	1422	24.6	11.5	46.9	17.8	.	.	17.8	19.6	.
	Seattle	19	26980	2330	22.9	10.5	45.9	13.4	8.5	19.1	16.4	33.6	8.2
Uzbekistan	Tashkent	40	970	2904	6.0	1.3	21.8	3.8	2.2	5.6	1.4	5.3	3.0
	Samarkand	41	970	1758	14.4	4.1	28.5	10.4	4.3	13.5	2.3	4.6	4.4

* Selection of Urban and Rural areas

Online data Supplement 2

6 - 7 years													
Country	Centre	PM ₁₀	GNP per capita	Number	Current wheeze	Severe wheeze	Severe/Current wheeze	Rhino-conjunctivitis	Eczema symptoms	Atopy	Asthma	Hay fever	Eczema diagnoses
Albania	Tirane	39	670	2981	7.6	2.9	37.9	4.1	2.5	5.9	3.1	2.9	1.5
Algeria	Algiers	35	1600	.	.	.	.	.	.	.	.	.	.
Argentina	Buenos Aires	23	8030	3005	15.4	5.9	38.2	8.7	6.8	13.7	4.1	15.9	10.5
	Rosario	24	8030	3007	17.3	8.0	46.3	10.5	8.2	16.1	6.5	15.7	10.8
Australia	Sydney	18	18720	2804	22.3	9.3	41.8	9.4	10.1	17.4	24.4	12.2	18.8
	Melbourne	15	18720	2840	27.2	11.5	42.4	9.8	11.1	18.7	28.6	14.9	22.6
	Perth	15	18720	2192	22.0	10.9	49.6	14.9	11.4	22.4	28.4	20.6	25.1
	Adelaide	15	18720	3063	26.2	11.8	45.0	14.5	11.0	22.6	27.5	23.5	24.9
Austria	Salzburg	18	26890	3658	9.7	3.6	37.2	6.4	5.9	11.1	4.2	8.8	10.1
Belgium	Antwerp	23	24710	6533	7.3	3.1	42.6	4.9	7.7	11.5	4.2	5.0	16.8
Brazil	Sao Paulo	44	3640	3005	21.3	7.1	33.3	12.5	6.8	16.6	6.1	28.8	13.2
	Porto Alegre	15	3640	2846	23.5	8.8	37.4	10.6	6.6	15.5	16.8	26.0	17.7
	Recife	21	3640	1410	27.2	15.3	56.3	10.3	9.6	17.4	20.4	11.3	12.4
	Salvador	19	3640	.	.	.	.	.	.	.	.	.	.
	Curitiba	25	3640	.	.	.	.	.	.	.	.	.	.
Canada	Hamilton	28	19380	3336	20.1	7.7	38.3	14.3	8.4	19.8	17.2	10.7	20.6
	Saskatoon	17	19380	2418	14.1	6.1	43.1	8.2	8.7	14.6	11.2	7.2	22.1
Chile	Central Santiago	63	4160	1458	16.5	4.3	26.1	11.2	11.3	19.0	9.7	8.8	8.0
	Valdivia	37	4160	3138	20.5	8.4	41.1	8.0	12.6	18.2	16.5	10.9	10.8
	Punta Arenas	28	4160	3060	17.1	5.2	30.4	8.8	9.5	15.7	10.4	11.3	15.0
China*	Beijing	106	620	.	.	.	.	.	.	.	.	.	.
	Guangzhou	75	620	.	.	.	.	.	.	.	.	.	.
	Shanghai	110	620	.	.	.	.	.	.	.	.	.	.
	Chongqing	106	620	.	.	.	.	.	.	.	.	.	.
Estonia	Tallinn	19	2860	3070	9.3	2.1	22.4	3.5	9.8	12.3	1.4	2.7	12.4
Ethiopia	Addis Ababa	49	100	.	.	.	.	.	.	.	.	.	.
	Jima	43	100	.	.	.	.	.	.	.	.	.	.
Finland	Helsinki	20	20580	.	.	.	.	.	.	.	.	.	.
	Turku and Pori County	18	20580	.	.	.	.	.	.	.	.	.	.

Online data Supplement 2

6 - 7 years													
Country	Centre	PM ₁₀	GNP per capita	Number	Current wheeze	Severe wheeze	Severe/Current wheeze	Rhino-conjunctivitis	Eczema symptoms	Atopy	Asthma	Hay fever	Eczema diagnoses
France	Marseilles	17	24990	.	.	.	.	.	.	.	.	.	.
	Montpellier	23	24990	.	.	.	.	.	.	.	.	.	.
	Strasbourg	31	24990	.	.	.	.	.	.	.	.	.	.
Georgia	Tbilisi	102	440	3414	5.9	1.8	30.3	2.3	4.1	5.9	1.8	4.3	11.6
	Kutaisi	90	440	3356	9.3	3.2	34.3	3.9	5.1	8.3	4.5	5.7	4.7
Germany	Munster	22	27510	3739	9.6	4.0	41.8	5.4	6.7	11.0	4.1	6.0	13.7
Greece	Athens	36	8210	1654	7.6	2.0	26.2	3.5	4.1	6.8	5.4	9.3	5.0
Hong Kong	Hong Kong	43	21500	3618	9.1	2.7	29.8	13.7	3.9	16.1	7.7	1.1	27.2
India	Neyveli	47	340	1498	1.5	0.5	31.8	4.8	0.7	5.5	1.0	1.8	0.3
	Madras (centre no 3)	49	340	2491	8.5	3.3	38.7	3.5	3.3	6.0	2.2	7.3	4.7
	Kottayam	34	340	2156	24.6	11.4	46.4	9.6	11.5	17.6	14.4	6.0	18.7
	New Delhi (centre no 7)	133	340	2938	6.9	1.9	27.6	3.4	2.8	5.7	3.7	5.9	2.6
	Chandigarh	94	340	2891	5.4	3.1	57.7	4.6	3.3	7.0	2.8	7.2	2.4
	Jodhpur	84	340	1104	3.5	1.5	43.6	2.4	1.9	4.1	4.1	6.6	1.7
	Akola	69	340	2030	0.8	0.5	62.5	0.8	0.5	1.1	1.3	1.5	0.7
	Pune	70	340	3248	2.3	1.1	48.0	1.6	1.5	2.8	4.2	2.9	2.5
	Bombay (centre no 16)	80	340	3967	3.8	1.9	49.7	2.6	1.9	4.2	3.8	5.1	1.1
	Bandung	136	980	1390	4.1	1.4	33.3	3.8	0.0	3.8	6.6	0.0	1.9
Iran	Tehran	42	.	5149	5.3	2.1	39.6	2.2	1.8	3.8	2.2	2.2	3.8
	Rasht	100	.	3013	5.3	2.2	41.3	1.2	1.3	2.4	4.1	2.3	9.8
Italy	Torino	46	19020	1429	6.4	2.3	36.3	5.1	5.5	9.8	7.6	5.6	15.2
	Milano	31	19020	3616	7.0	2.1	30.0	5.8	6.8	11.4	9.1	6.6	16.7
	Firenze	52	19020	1138	9.9	3.3	33.6	6.3	5.5	11.2	8.8	6.7	12.7
	Roma	31	19020	4027	7.2	2.1	29.3	5.1	5.5	9.5	10.3	6.6	13.0
	Cosenza	18	19020	.	.	.	.	.	.	.	.	.	.
	Trento	20	19020	.	.	.	.	.	.	.	.	.	.
	Verona	25	19020	2076	7.4	2.5	33.8	4.3	6.6	9.7	11.7	0.9	13.3
Japan	Fukuoka	32	39640	2900	17.3	6.1	35.3	7.8	16.9	21.9	18.2	9.8	57.2
Kenya	Eldoret	54	280	.	.	.	.	.	.	.	.	.	.
	Nairobi	51	280	.	.	.	.	.	.	.	.	.	.
Kuwait	Kuwait	23	17390	.	.	.	.	.	.	.	.	.	.

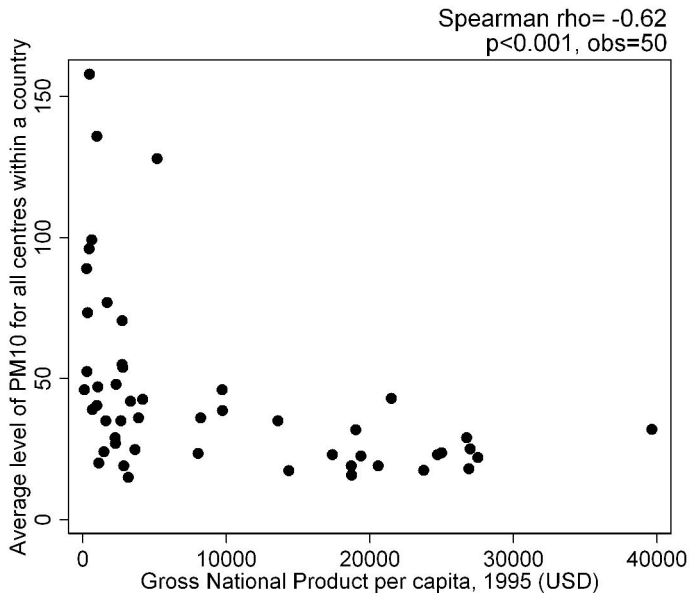
Online data Supplement 2

6 - 7 years													
Country	Centre	PM ₁₀	GNP per capita	Number	Current wheeze	Severe wheeze	Severe/Current wheeze	Rhino-conjunctivitis	Eczema symptoms	Atopy	Asthma	Hay fever	Eczema diagnoses
Latvia	Riga	27	2270	2965	7.4	2.2	29.7	3.1	8.1	10.2	1.6	0.9	5.6
Lebanon	Beirut	35	2660	.	.	.	.	.	.	.	.	.	.
Malaysia	Kota Bharu	52	3890	3819	5.6	1.6	28.5	3.8	10.2	12.4	10.4	15.9	1.4
	Ipoh	20	3890	2506	6.3	1.8	28.5	4.6	6.0	9.4	10.3	7.7	2.4
Mexico	Cuernavaca	42	3320	3097	8.6	3.7	43.2	8.6	4.9	12.4	5.1	3.7	3.5
Morocco	Rabat	21	1110	.	.	.	.	.	.	.	.	.	.
	Casablanca	21	1110	.	.	.	.	.	.	.	.	.	.
	Marrakech	18	1110	.	.	.	.	.	.	.	.	.	.
New Zealand	Auckland	15	14340	3526	22.5	10.4	46.3	9.8	14.4	20.7	23.8	12.4	22.3
	Wellington	15	14340	3838	25.1	11.9	47.5	10.4	16.6	23.3	30.8	12.7	30.6
	Christchurch	22	14340	3318	27.2	12.6	46.3	11.2	15.8	23.0	28.4	14.6	28.8
Nigeria	Ibadan	89	260	.	.	.	.	.	.	.	.	.	.
Pakistan	Karachi	158	460	.	.	.	.	.	.	.	.	.	.
Panama	David-Panama	55	2750	3042	23.5	8.9	37.9	7.1	7.9	12.8	19.3	3.8	6.3
Paraguay	Asuncion	77	1690	.	.	.	.	.	.	.	.	.	.
Peru	Lima	48	2310	.	.	.	.	.	.	.	.	.	.
Philippines	Metro Manilla	47	1050	3558	11.3	3.8	33.6	9.2	5.1	12.8	16.4	26.2	4.3
Poland	Poznan	48	2790	2710	8.1	3.5	43.2	4.6	5.4	8.6	1.3	4.9	19.5
	Krakow (centre no 3)	60	2790	2264	14.3	5.7	39.8	10.2	7.3	14.7	4.1	15.6	19.9
Portugal	Lisbon	28	9740	2143	13.1	5.7	43.4	8.6	11.1	16.5	8.3	2.9	11.2
	Funchal (Madeira)	45	9740	1797	14.7	9.2	62.5	11.2	12.4	19.7	17.5	15.9	13.3
	Porto	43	9740	.	.	.	.	.	.	.	.	.	.
Republic of Korea	Seoul	46	9700	2582	15.1	3.3	21.8	10.9	10.7	18.9	9.0	15.5	23.5
Romania	Cluj	24	1480	.	.	.	.	.	.	.	.	.	.
Russian Federation	Moscow	29	2240	.	.	.	.	.	.	.	.	.	.
Singapore	Singapore	29	26730	2353	15.7	4.9	31.2	8.5	2.8	10.6	18.5	6.5	1.3
South Africa	Cape Town	15	3160	.	.	.	.	.	.	.	.	.	.
Spain	Cartagena	45	13580	3335	8.4	2.9	34.6	6.7	2.7	8.7	6.2	6.5	15.0

Online data Supplement 2

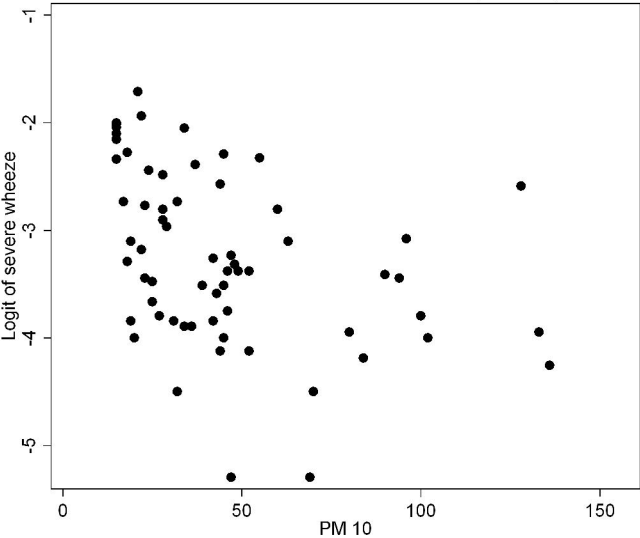
6 - 7 years													
Country	Centre	PM ₁₀	GNP per capita	Number	Current wheeze	Severe wheeze	Severe/Current wheeze	Rhino- conjunctivitis	Eczema symptoms	Atopy	Asthma	Hay fever	Eczema diagnoses
	Barcelona	35	13580	.	.	.	.	.	.	.	.	.	.
	Bilbao	25	13580	3019	8.0	3.0	37.6	6.5	4.4	9.8	10.1	6.6	16.1
	Castellon	44	13580	3594	4.7	1.6	34.3	3.8	3.1	6.2	4.3	3.6	15.1
	Pamplona	32	13580	2996	3.5	1.1	31.4	3.6	3.2	6.4	4.3	4.8	15.4
	Valladolid	34	13580	.	.	.	.	.	.	.	.	.	.
	Valencia	34	13580	3940	6.2	2.0	32.4	4.4	3.2	6.8	6.2	5.1	18.9
	Cadiz	31	13580	.	.	.	.	.	.	.	.	.	.
Sweden	Linkoping	16	23750	.	.	.	.	.	.	.	.	.	.
	Stockholm/Uppsala	19	23750	3028	10.4	4.3	41.3	5.9	18.4	21.8	8.0	7.5	35.7
Thailand	Bangkok	96	2740	3629	11.0	4.4	40.1	10.0	12.5	19.2	9.3	29.0	22.5
	Chiang Mai	45	2740	3828	5.5	1.8	32.7	4.8	11.4	14.5	4.2	17.9	20.5
United Kingdom	South Thames	19	18700	.	.	.	.	.	.	.	.	.	.
Uruguay	Montevideo	128	5170	3071	18.0	7.0	38.9	6.6	8.6	13.3	12.0	22.3	9.6
USA	Chicago (center no 3)	31	26980	.	.	.	.	.	.	.	.	.	.
	Seattle	19	26980	.	.	.	.	.	.	.	.	.	.
Uzbekistan	Tashkent	40	970	.	.	.	.	.	.	.	.	.	.
	Samarkand	41	970	.	.	.	.	.	.	.	.	.	.

* Selection of Urban and Rural areas



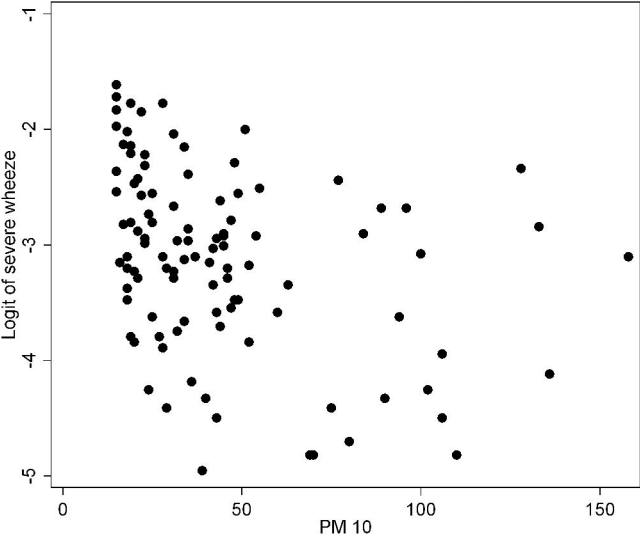
Age group 6-7

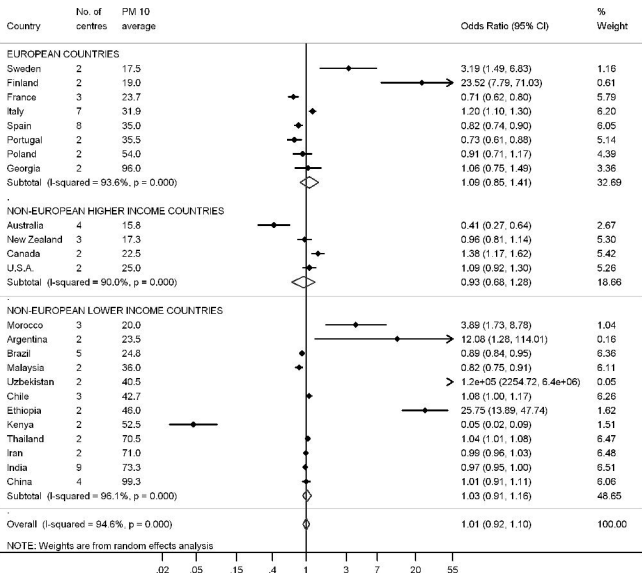
Spearman rho= -0.39
p=0.001, Obs=65

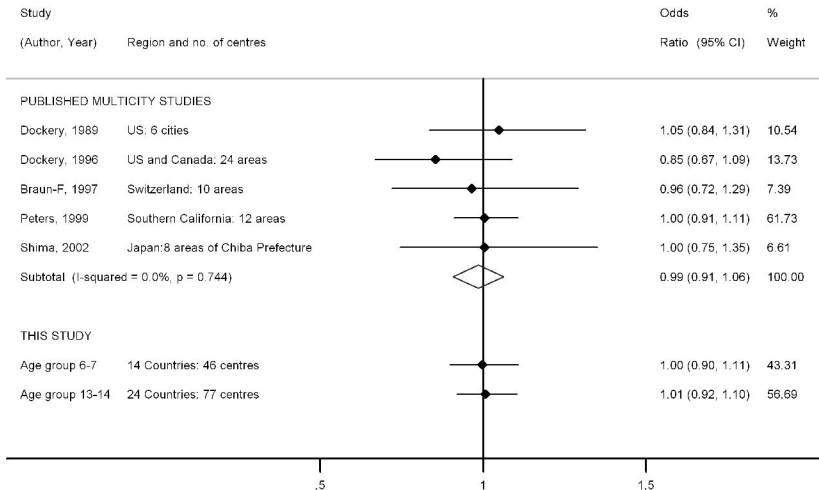


Age group 13-14

Spearman rho= -0.36
p<0.001, Obs=105







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 (PM) since this is associated with a range of respiratory outcomes and associations have been observed with proximity to traffic pollution.
- 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 urban background PM₁₀
- The results suggest that community levels of ambient PM are unlikely to explain international variations in prevalence.
- Future studies of differences in prevalence between communities will benefit from improved exposure assessment and control for confounding factors at the individual level.