



Urban background particulate matter and allergic sensitization in adults of ECRHS II

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Abstract

Background: Epidemiological studies have shown weak or inconsistent associations between ambient air pollutants and allergic sensitization. The aim of this study was to evaluate whether regional urban air pollution may partly explain the large variation in the prevalence of allergic sensitization across cities of the European Community Respiratory Health Survey (ECRHS) II.

Methods: ECRHS is a cross-sectional survey initiated in 29 countries across Europe in the 1990s (ECRHS I) with a follow-up conducted 10 years later (ECRHS II). Subject characteristics were measured by questionnaires and blood tests conducted for the measurement of specific immunoglobulin E. Fine particle mass (PM_{2.5}, <2.5 µm) and sulphur on PM_{2.5} were measured in 21 centres and annual averages of urban regional background air pollution were calculated. Results were scaled by an interquartile range increase in ambient PM_{2.5} (6.03 µg/m³) and sulphur (1336 ng/m³). Generalized estimating equations were applied to compute population average effect estimates with adjustment for age, gender, smoking habit, education and number of siblings.

Results: A notable variation in pollution level and prevalence of allergic sensitization was observed. Moreover, exposure to urban regional background air pollution was not associated with allergic sensitization; adjusted odds ratios and 95% confidence interval were 1.02 (0.95–1.09) for PM_{2.5} and 1.08 (0.86–1.31) for sulphur. These statistically non-significant associations were sensitive to model specification.

Conclusions: The study suggests that regional air pollution measured at fixed sites is not associated with allergic sensitization among adults in ECRHS II.

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Keywords: Air pollution; Allergy; Allergic sensitization; Asthma; Atopy; Diesel exhaust particles

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Introduction

According to growing empirical evidence, the prevalence of atopic diseases and allergy has increased in a number of developed countries among children and adults (Upton et al., 2000; Maziak et al., 2003) although atopic diseases and asthma prevalence may have plateaued in recent years, particularly among adults (von Hertzen, 2005; Braun-Fahrlander et al., 2004). The rise in allergy is generally attributed to the western life style and environmental factors and does not seem to reflect changes in genetic factors (von Hertzen and Haahtela, 2004; Ronchetti et al., 2001). Although, a number of factors are assumed to be responsible for the increased prevalence of atopy and allergic diseases, an association with increased exposure to traffic-related pollution has been proposed besides life-style changes in microbial stimulation of the immune system. Since allergic diseases are important public health problems, the need to identify causes and contributing factors is irrefutable.

Epidemiological research, human and animal experimental studies have demonstrated a diverse role of pollutants in relation to allergy. However, the underlying mechanisms by which pollutants exert effects are still unclear. A number of experimental and toxicological studies in humans and animals using different methods have shown a variety of inflammatory and immunological reactions to short exposure to particulate matter (PM) and diesel exhaust particles (Heinrich et al., 2005a; Diaz Sanchez, 1997; Nel et al., 1998; Riedl and Diaz-Sanchez, 2005). Pollutants may have a role as triggers for new onset of allergy or in exacerbating existing allergic disease. In addition, they have been suggested to be adjuvant for immunoglobulin E (IgE) and contributing to the increased global allergen production (Riedl and Diaz-Sanchez, 2005; Bernstein et al., 2004).

Numerous epidemiological studies have documented an association between air pollutants and allergic diseases, although these associations were at times inconsistent (Heinrich and Wichmann, 2004). Studies from different countries have shown that both adults and children living close to main and busy roads have an increased risk of allergic disease and respiratory symptoms (Kramer et al., 2000; Venn et al., 2001; Wyler et al., 2000). Other studies have not found such an association (Livingstone et al., 1996; Nicolai et al., 2003). Epidemiological air pollution studies have used a variety of exposure assessment methods such as subjective proxy measures of self-reported distance from heavy traffic and traffic density as well as objective traffic counts, geographical information systems (GIS) and measurement of ambient pollutants from central sites (Heinrich and Wichmann, 2004). Several studies have shown that for regional air pollution such as fine

particle mass concentration, and in particular sulphate and sulphur mass concentration on PM, fixed site monitors can serve as good proxy for personal exposure across the community (Oglesby et al., 2000; Brunekreef et al., 2005).

The European Community Respiratory Health Survey (ECRHS) is a cross-sectional multi-centre study of adults originally aged 20–44 years (ECRHS I) (Burney et al., 1994) that were followed for nearly 10 years (ECRHS II) (Jarvis, 2002). Both surveys included initial screening questionnaires, extensive interviewer led questionnaires, blood test for IgE, spirometry, methacholine challenge tests and skin prick tests. The objective of the current analysis is to investigate the prevalence of allergic sensitization and its relation to regional air pollutants in the follow-up of cohorts of ECRHS II in 21 participating centres where additional air pollution measurement were made.

Materials and methods

Study design

ECRHS is a multi-centre survey conducted in 29 centres in Europe. Its protocol has been extensively described elsewhere (Burney et al., 1994; Jarvis, 2002) and additional information is also accessible on www.ecrhs.org. The cross-sectional survey was initiated in 22 countries in 1990 as ECRHS I and follow-up was conducted in 2000/01 as ECRHS II. The current analysis relates to participants in ECRHS II.

Study population

Subjects for the present study were defined as all those participants of ECRHS II who responded to the stage II (main questionnaire). These subjects were invited to complete a detailed questionnaire and to provide a blood sample. Inclusion criteria were (1) presence of air pollution measurement in the particular centre and (2) presence of IgE measurement. Accordingly, this analysis includes 6470 participants from 21 centres.

Questionnaires

In both surveys in the first stage the study participants received a short postal screening questionnaire that inquired about symptoms of asthma, use of asthma medications and presence of hay fever and allergies. In the second stage, a randomly selected sample of respondents to stage I received an extensive interviewer led questionnaire. Included were, among other items, respiratory symptoms, history of asthma and allergy, smoking habits, use of medication for asthma and home

environment. Respondents to the screening questionnaire with symptoms of asthma and asthma attack, and who had not been identified in the random sample were also recruited for the main questionnaire.

Blood tests for IgE

In all centres blood samples were collected to assess specific IgE against *D. pteronyssinus*, *timothy grass*, cat, *C. herbarum* allergens and total IgE. Collection, handling and measurement of blood followed identical standard procedures and analyses were conducted by the ECRHS Central Laboratory at King's College London, using the Pharmacia CAP system (Sweden Diagnostics, Uppsala, Sweden). Allergic sensitization was defined as any elevation of specific IgE to a level of 0.70 kU/l or greater.

Exposure assessment

The air pollution module included 21 centres. One fixed monitoring site was selected at each centre, which was considered representative of urban regional background air quality. In all centres mass concentration of PM_{2.5} and sulphur were measured for almost 1 year and annual averages of the pollutants were calculated. The methods have been described elsewhere (Hazenkamp-von Arx et al., 2003, 2004; Kuenzli et al., 2004; Gotschi et al., 2002). Standardized technique and similar equipments were used in all centres and a single central laboratory and one technician was responsible for weighing the filters. Elemental composition of PM_{2.5} was analysed for different chemical elements using dispersive X-ray fluorescence spectrometry (ED-XRF).

Statistical analysis

The association between allergic sensitization and annual average PM_{2.5} mass concentration and sulphur mass on PM_{2.5} was estimated by using a population-averaged (marginal) logistic regression procedure adjusting for the following covariates: age (in 3 groups), gender, smoking status, socio economic status, (as expressed by the level of education), number of siblings, and study centre. Each centre was considered as a cluster and to account for possible correlations in each study centre a generalized estimating equations (GEEs) method was used. The population-averaged effect estimate was computed using the GENMOD procedure in SAS.

The following sensitivity analyses were conducted: (1) exclusion of all centres in a country after another, (2) varying the cut off point for the specific IgE levels used to define sensitized and non-sensitized categories and (3) modelling the association between air pollution and specific sensitization to pollen allergen alone.

Results are reported as adjusted odds ratios (OR) together with 95% confidence intervals (CI) scaled to interquartile range (IQR) of pollutants as follows: for PM_{2.5} = 6.03 µg/m³ and for sulphur = 1336 ng/m³ increment. All computations were made by SAS 8.2 (SAS Institute, NC, USA).

Results

General characteristics of the study population

Table 1 shows the number of participants at different stages of ECRHS II by centre. 12,940 subjects were eligible for ECRHS II out of which 10,051(77.68%) responded to the screening questionnaire, 8367(64.66%) to the main questionnaire. Half of the subjects (50.03%) had gone through blood tests for IgE measurement. Characteristics about the study participants and sensitization status are shown in Table 2. The mean age ± SD of the study population was 42.78 ± 7.20 years. The F:M sex ratio was 1.08:1. About 1/3 of the study population was sensitized to one or more of the tested allergens. More males were sensitized to allergens than females ($p < 0.001$). More than 1/3 of the participants were smokers at the time of the study and about 1/4 were ex-smokers. Participants with no siblings were more likely to be sensitized than those with one or more siblings. There were no significant differences in participation rates in ECRHS II by gender, age, and sensitization status at ECRHS I. Response was; however, related to smoking and education. There was some difference in response for IgE measurement in ECRHS II in participants eligible for ECRHS II by centre (38.8–81.4%).

Ambient air pollution

Table 3 shows average annual concentration of pollutants. There is considerable variation in the annual average mean concentration of pollutants across Europe. The highest concentrations of pollutants were reported from Turin, Verona and Pavia and the lowest concentrations of all measured pollutants were from Reykjavik. Moreover, the two Swedish centres, Umea and Uppsala, had low concentrations of both pollutants too. There was a 12–13-fold difference between centres with lowest annual average concentration and highest concentration of pollutants. Two Belgian centres located not far apart had differing air pollutant concentration: Antwerp City had high concentrations of all measured pollutants whereas Antwerp South had concentrations which were in the lower third.

PM_{2.5} was fairly well correlated with sulphur with a spearman correlation coefficient at $r = 0.77$ across cities (Table 4).

Table 2. Basic description of the study participants in 21 centres of ECRHS II

	Sensitized to any allergen ^a (n = 1995)	Non-sensitized (n = 4469)	Total
	Frequency (%)	Frequency (%)	
Gender			
Male	1101 (35.46)	2004 (64.54)	3105
Female	894 (26.62)	2465 (73.38)	3359
Age			
Age 26–39	875 (35.76)	1572 (64.24)	2447
Age 40–49	766 (29.03)	1873 (70.79)	2639
Age 50–59	354 (25.69)	1024 (74.31)	1378
Smoking history			
Current smokers	540 (27.62)	1415 (72.38)	1955
Ex-smokers	501 (29.32)	1208 (70.68)	1709
Non-smokers	950 (34.06)	1839 (65.94)	2789
Education			
Completed at age 20	1054 (28.11)	2695 (71.89)	3749
Completed after age 20	941 (34.66)	1774 (65.34)	2715
No. of siblings			
No. siblings	260 (39.63)	396 (60.37)	656
1 Sibling	650 (34.26)	1247 (65.74)	1897
2 Siblings	497 (31.70)	1071 (68.03)	1568
3 Siblings	276 (27.74)	719 (72.26)	995
4 or more Siblings	303 (22.87)	1022 (77.13)	1325

^a Any sensitization against one of the following: *D. pteronyssinus* (d1), cat (e1), timothy grass (g6) and *Cladosporium* (m2) using 0.70 kU/l as a cut off point.

Prevalence of allergic sensitization

Table 5 shows the crude and adjusted prevalence rate. The crude prevalence of allergic sensitization was markedly different across the study centres ranging from 13.5 in Reykjavik to 41.5 in Ipswich. Adjustment was made for gender, age, smoking habit, education and number of siblings. Adjustment altered the crude prevalence only marginally. Fig. 1 shows the scatter plot of adjusted prevalence and ambient pollutants. There was no obvious association between prevalence, allergic sensitization and any single pollutant overall. The highest prevalence of allergic sensitization was observed in the two centres in England with PM_{2.5} concentrations in the lower third of the distribution. Conversely, Turin, a centre with one of the highest concentration of PM_{2.5} and sulphur level is placed 14th out of 21 centres in regard to prevalence. As shown in Fig. 1, the Italian centres form a cluster of the three most polluted cities.

In logistic regression, all pollutants were weakly but positively associated with any sensitization and pollen sensitization, as shown in Table 6. However, the sizes of estimates were far from being significant. Table 7 shows the relation between ambient pollutant level and any

allergic sensitization and pollen only sensitization calculated by excluding centres of one country at a time. This sensitivity analysis demonstrated substantial instability of the point estimates. Exclusion of Italian centres has resulted in OR of 1.18 (0.99–1.41) for PM_{2.5} and 1.19 (0.96–1.48) for sulphur. On the other hand, analyses without Iceland led to point estimates less than unity. Exclusion of the two centres with the lowest participation rates only marginally changed the estimates of the association (data not shown).

Discussion

This follow-up cohort of a large population based survey has investigated the relation between allergic sensitization and ambient air pollutants in 21 centres across Europe. The study has found no clear association between air pollutants and allergic sensitization measured by specific IgE. The small observed association was not statistically significant and rather unstable in the sensitivity analyses. Exclusion of Italy (i.e. the three locations with the highest pollution) and analyses without Reykjavik (i.e. the centre with the lowest concentration of all pollutants) led to particularly strong

Table 3. Annual average concentration of pollutants for each center

	PM _{2.5}	Sulphur
Centre		
Antwerp South	20.8	3460.6
Antwerp City	24.1	3487.3
Erfurt	16.3	2724.5
Barcelona	22.2	3304.6
Galdakao	16.3	3772.7
Albacete	13.1	2401.3
Oviedo	15.9	2812.5
Huelva	17.3	3709.1
Grenoble	19.0	2113.6
Paris	17.8	2572.7
Pavia	35.3	4244.4
Turin	44.9	4351.0
Verona	41.5	4798.0
Ipswich	16.5	2377.7
Norwich	16.2	2327.2
Reykjavik	3.7	369.9
Gothenburg	12.6	2150.9
Umea	5.6	987.6
Uppsala	10.4	1790.7
Basel	17.4	2473.6
Tartu	14.8	2123.7
Total		
Mean	16.6	2519
Std. dev.	8.5	1050
Minimum	3.7	369.9
Maximum	44.9	4798
Range	41.1	4428
IQR ^a	6.03	1336

^aIQR = Interquartile range measured for PM_{2.5} in µg/m³ for sulphur 1336 ng/m³.

Table 4. Spearman correlation coefficients between annual concentrations of pollutants of the 21 study centres of ECRHS II

Pollutant	PM _{2.5}	Sulphur
PM _{2.5}	1.00	
Sulphur	0.77	1.00

All spearman correlation coefficients are statistically significant.

changes in the associations, ranging from 0.95 up to 1.19 (in case of sulphur and any sensitization).

We have found large variation in the adjusted prevalence of allergic sensitization across the study centres ranging from 13.5 in Reykjavik to 41.5% in Ipswich. The variation in concentration of regional urban pollutants was also considerable and substantially larger than in other cross-community air pollution studies. Despite this ideal setting of large diversities in

Table 5. Adjusted and crude prevalence of allergic sensitization for each centre in ECRHS II^a

Centre	Prevalence (%)		
	Crude	Adjusted (95% CI) ^b	
Antwerp South	25.2	24.7	(20.1–29.8)
Antwerp City	27.4	26.1	(21.0–32.1)
Erfurt	20.7	20.2	(15.8–25.4)
Barcelona	22.2	21.8	(16.8–27.8)
Galdakao	23.7	23.1	(19.1–27.7)
Albacete	16.0	15.6	(12.1–20.0)
Oviedo	23.8	23.8	(18.9–29.4)
Huelva	29.3	29.2	(24.0–34.9)
Grenoble	31.6	31.8	(26.8–37.3)
Paris	25.4	26.0	(21.4–31.1)
Pavia	21.3	21.1	(14.3–30.1)
Turin	24.2	23.7	(17.6–31.0)
Verona	25.4	25.0	(19.2–31.9)
Ipswich	40.8	41.5	(35.6–47.8)
Norwich	37.4	39.1	(33.4–45.2)
Reykjavik	14.4	13.5	(10.8–16.7)
Gothenburg	26.6	25.9	(21.8–30.6)
Umea	26.1	24.3	(20.3–28.9)
Uppsala	34.8	31.3	(27.3–35.7)
Basel	39.3	37.6	(33.2–42.3)
Tartu	17.3	15.5	(11.9–20.0)

^aAdjusted for gender, age, number of siblings, smoking habit and education.

^bCI = confidence interval.

exposure and outcome, we were unable to explain the differences in sensitization across Europe by the level of regional urban background pollution. Some centres with comparatively high concentration of ambient pollutants like Turin had midrange prevalence. Conversely, the two UK centres with intermediate range concentration of pollutants had the highest prevalence of sensitization.

Our study is a large population based survey that has used an extensive data set based on the same methods from several centres. In addition, the study has applied standardized and identical exposure estimation and IgE measurement. Exposure and outcome were analysed centrally by one laboratory and this would reduce the possibility of misclassification of exposure and outcome. Furthermore, IgE measurements are not subject to reporting and information bias. Thus, we consider non-differential misclassification of outcomes and covariates an unlikely explanation of these null findings.

We have used one fixed central monitoring site to assess the exposure of subjects whose residential addresses are spread over a large metropolitan area in most of the study centres. The use of ambient PM_{2.5} and, in particular, sulphur on PM_{2.5} guarantees an optimal characterization of the citywide level of these pollutants. Studies have shown that fixed site monitors of fine particles are valid surrogates for regional air

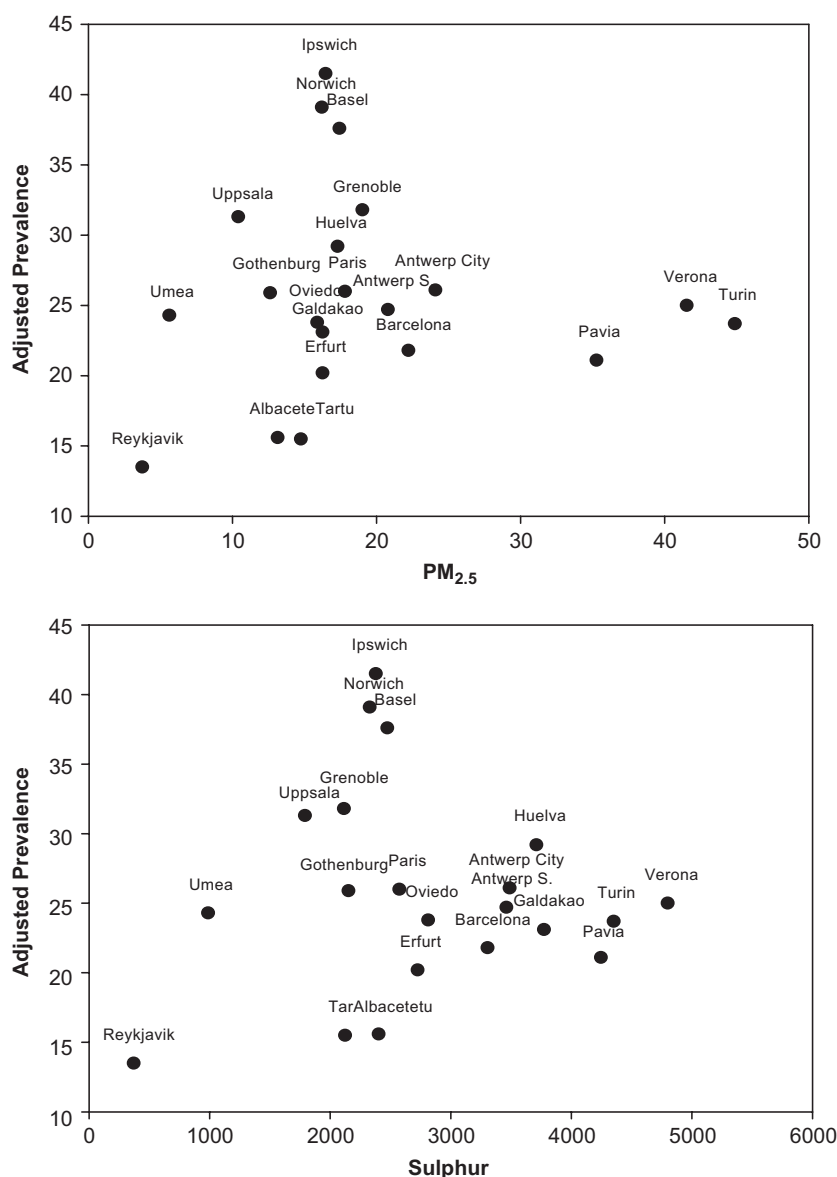


Fig. 1. Adjusted prevalence of allergic sensitization versus annual mean concentration of pollutants.

Table 6. Adjusted and crude prevalence of allergic sensitization for each centre in ECRHS II

Pollutant	Any allergic sensitization ^b			Pollen sensitization		
	OR ^c	LCI	UCI	OR ^c	LCI	UCI
PM _{2.5} ^a	1.02	0.9461	1.0859	1.04	0.97391	1.11337
Sulphur ^a	1.08	0.8850	1.3130	1.04	0.8395	1.2774

^aIQR: PM_{2.5} = 6.03 µg/m³, sulphur 1336 ng/m³.

^bAny sensitization against one of the following: *D. pteronyssinus* (d1), cat (e1), timothy grass (g6) and *Cladosporium* (m2) using 0.70 kU/l as a cut off point.

^cAdjustment was made for gender age, smoking, education and number of siblings.

pollution (Oglesby et al., 2000; Cyrus et al., 1998; Roosli et al., 2000; Sarnat et al., 2002). In line with EXPOLIS and other studies, a recent investigation by Brunekreef

et al. (2005) published by the Health Effects Institute has shown a very high correlation between outdoor, indoor and personal concentration of PM_{2.5} and in particular

Table 7. Adjusted odds ratios for the association between any allergic and pollen sensitization and urban air pollutants after exclusion of one country in sequence

Excluded country	Pollutant	Any sensitization			Pollen sensitization		
		OR	LCL	UCL	OR	LCL	UCL
Belgium	PM _{2.5}	1.02	0.95	1.08	1.04	0.98	1.09
	Sulphur	1.09	0.89	1.34	1.05	0.84	1.31
Germany	PM _{2.5}	1.01	0.94	1.09	1.04	0.98	1.10
	Sulphur	1.08	0.88	1.33	1.05	0.85	1.29
Spain	PM _{2.5}	1.01	0.90	1.13	1.04	0.94	1.15
	Sulphur	1.03	0.84	1.27	1.07	0.90	1.28
France	PM _{2.5}	1.01	0.95	1.08	1.04	0.98	1.10
	Sulphur	1.10	0.90	1.34	1.06	0.85	1.31
Italy	PM _{2.5}	1.18	0.99	1.41	1.10	0.90	1.33
	Sulphur	1.19	0.96	1.48	1.02	0.74	1.40
England	PM _{2.5}	1.03	0.96	1.11	1.06	0.99	1.14
	Sulphur	1.12	0.94	1.33	1.08	0.89	1.31
Iceland	PM _{2.5}	0.98	0.92	1.04	1.01	0.95	1.08
	Sulphur	0.95	0.80	1.13	0.92	0.72	1.17
Switzerland	PM _{2.5}	1.02	0.94	1.10	1.04	0.98	1.11
	Sulphur	1.08	0.90	1.30	1.03	0.86	1.25
Sweden	PM _{2.5}	1.01	0.96	1.07	1.04	0.99	1.08
	Sulphur	1.12	0.87	1.44	1.08	0.84	1.40
Estonia	PM _{2.5}	1.01	0.92	1.10	1.03	0.96	1.11
	Sulphur	1.05	0.85	1.29	1.01	0.81	1.25

Abbreviations: OR: odds ratio, LCL: lower confidence limit, UCL: upper confidence limit.

sulphur mass concentrations. The authors propose that central site monitors of PM_{2.5} are a reasonable surrogate for personal and indoor exposure of adults in Helsinki, Finland and Amsterdam, The Netherlands. Thus, we are confident that our markers of exposure are not prone to within-city misclassification of personal exposure in our study centres, and between-community difference in sulphur mass concentrations are far larger than what can be expected for within-community spatial variation. Consequently, we conclude that misclassification of exposure to secondary regional pollution is also an unlikely explanation of these findings.

However, our assignment of exposure does not capture exposure to fresh exhaust or tail pipe pollutants. As shown in several studies, fresh tail pipe pollutants such as CO, NO, ultrafine particles and others show very strong spatial gradients in proximity to streets (Zhu et al., 2002), thus, fixed site monitors may substantially under or overestimate the conditions at residential locations. Studies have shown that traffic emission, particularly diesel, is an important source of pollution in urban areas and its surroundings and there is a growing concern regarding its public health consequences (Kuenzli et al., 2000).

Cross-community comparisons like ours are not designed to investigate the association between fresh exhaust and sensitization. In fact, our findings are consistent with two large Swiss epidemiologic studies (Braun-Fahrlander et al., 1997; Wüthrich et al., 1999) which have found no association between community level air pollution and allergic diseases and symptoms. Those studies that examined local traffic-related pollution and sensitization report conflicting results. Some studies have reported a positive association (Kramer et al., 2000; Wyler et al., 2000) while others did not find any association (Nicolai et al., 2003; Hirsch et al., 1999; Heinrich et al., 2005b). Our results are also in line with our recent analyses of the associations between regional pollution and bronchitis symptoms (Sunyer et al., 2006). Although, evidence for effects of air pollution on symptoms is rather compelling, we found no association of PM_{2.5} or S on PM_{2.5} and bronchitis symptom rates across the 21 communities.

Another potential explanation of null findings may be related to the exposure time window considered in this study among adults. It should be noted that the majority of these traffic-related epidemiological studies were conducted in children and pupils in Europe and the

few studies that have investigated both children and adults have found strongest associations between respiratory allergic problems and traffic exposure among children (Lercher et al., 1995; Oosterlee et al., 1996) which suggest that children are differentially vulnerable to the adverse effects of traffic-related pollution. Moreover, development of sensitization later in life may require several years of exposure. ECRHS did not measure ambient pollutants in the past and pollution levels were much higher 10–20 years ago in some centres.

If local unmeasured factors related to cultural factors (e.g., diet) or climate contribute to sensitization, cross-city comparisons face also major difficulties to control such factors that may determine the background rates of sensitization in each city, region, or country. One ECRHS study has shown a wide variation in atopy and its association with asthma between participating centres and even within centres of the same country which supports the role of lifestyle factors in allergy (Sunyer et al., 2004).

In an Italian ISAYA study, de Marco et al. (2004), investigated the relationship between climate, outdoor NO₂ and asthma prevalence in different parts of Italy and found a higher asthma prevalence in those regions with Mediterranean climate. Likewise studies from Germany have shown the possible influence of lifestyle factors on the risk of allergy (Wichmann, 1996). In spite of the high level of ambient air pollution in former East Germany, the prevalence of allergic sensitization was conspicuously low (von Mutius et al., 1994; Nowak et al., 1996). However, studies conducted many years after re-unification have found a striking increase in sensitization to common allergens (von Mutius et al., 1998; Heinrich et al., 2002) while air quality substantially improved over the same years (Kreyling et al., 2003; Ebel et al., 2001).

In conclusion, our study has shown no association between allergic sensitization and regional air pollutants in adults in Europe. Thus, regional air pollution cannot explain the substantial difference in the prevalence of allergic sensitization observed across Europe. To clarify the possible contribution of tail pipe exhaust in the development of sensitization, exposure assessment strategies are required that capture within-community contrasts and personal exposure to this important source of toxic emissions.

References

- Bernstein, J.A., Alexis, N., Barnes, C., et al., 2004. Health effects of air pollution. *J. Allergy Clin. Immunol.* 114 (5), 1116–1123.
- Braun-Fahrlander, C., Vuille, J.C., Sennhauser, F.H., et al., 1997. Respiratory health and long-term exposure to air pollutants in Swiss schoolchildren. *Am. J. Respir. Crit. Care Med.* 155 (3), 1042–1049.
- Braun-Fahrlander, C., Gassner, M., Grize, L., et al., 2004. No further increase in asthma, hay fever and atopic sensitisation in adolescents living in Switzerland. *Eur. Respir. J.* 23 (3), 407–413.
- Brunekeef, B., et al., 2005. Personal, indoor, and outdoor exposures to PM in cardiovascular patients. <<http://www.healtheffects.org/Pubs/Brunekeef.pdf>> 2005.
- Burney, P.G., Luczynska, C., Chinn, S., Jarvis, D., 1994. The European Community Respiratory Health Survey. *Eur. Respir. J.* 7 (5), 954–960.
- Cyrys, J., Heinrich, J., Brauer, M., Wichmann, H.E., 1998. Spatial variability of acidic aerosols, sulfate and PM₁₀ in Erfurt, Eastern Germany. *J. Exposure Anal. Environ. Epidemiol.* 8 (4), 447–464.
- de Marco, R., Pattaro, C., Locatelli, F., Svanes, C., 2004. Influence of early life exposures on incidence and remission of asthma throughout life. *J. Allergy Clin. Immunol.* 113 (5), 845–852.
- Diaz Sanchez, D., 1997. The role of diesel exhaust particles and their associated polyaromatic hydrocarbons in the induction of allergic airway disease. *Allergy*, 5252–5256.
- Ebel, S., Brauer, M., Cyrys, J., et al., 2001. Air quality in postunification Erfurt, East Germany: associating changes in pollutant concentrations with changes in emissions. *Environ. Health Perspect.* 109 (4), 325–333.
- Gotschi, T., Oglesby, L., Mathys, P., et al., 2002. Comparison of black smoke and PM_{2.5} levels in indoor and outdoor environments of four European cities. *Environ. Sci. Technol.* 36 (6), 1191–1197.
- Hazenkamp-von Arx, M.E., Gotschi, T., Ackermann-Lieblich, U., Gislason, T., Heinrich, J., Jarvis, D., Luczynska, C., Manzanera, A.J., Modig, L., Norback, D., Pfeifer, A., Poll, A., Ponzio, M., Soon, A., Vermeire, P., Kunzli, N., 2003. PM_{2.5} assessment in 21 European study centers of ECRHS II: method and first winter results. *J. Air Waste Manage. Assoc.* 53 (5), 617–628.
- Hazenkamp-von Arx, M.E., Gotschi, T., Ackermann-Lieblich, U., et al., 2004. PM_{2.5} and NO₂ assessment in 21 European study centres of ECRHS II: annual means and seasonal differences. *Atmos. Environ.* 38 (13), 1943–1953.
- Heinrich, J., Wichmann, H.E., 2004. Traffic related pollutants in Europe and their effect on allergic disease. *Curr. Opin. Allergy Clin. Immunol.* 4 (5), 341–348.
- Heinrich, J., Hoelscher, B., Frye, C., Meyer, I., Wjst, M., Wichmann, H.E., 2002. Trends in prevalence of atopic diseases and allergic sensitization in children in Eastern Germany. *Eur. Respir. J.* 19 (6), 1040–1046.
- Heinrich, J., Schwarze, P.E., Stilianakis, N.I., et al., 2005a. Studies on health effects of transport-related air pollution. In: Krzyzanowski, M., Kuna-Dibbert, B., Schneider, J. (Eds.), *Health Effects of Transport-Related Air Pollution*. World Health Organization Regional Office for Europe, pp. 125–183.
- Heinrich, J., Topp, R., Gehring, U., Thefeld, W., 2005b. Traffic at residential address, respiratory health, and atopy in adults: the National German Health Survey 1998. *Environ. Res.* 98 (2), 240–249.
- Hirsch, T., Weiland, S.K., von Mutius, E., et al., 1999. Inner city air pollution and respiratory health and atopy in children. *Eur. Respir. J.* 14 (3), 669–677.

- Jarvis, D., 2002. The European Community Respiratory Health Survey II. *Eur. Respir. J.* 20 (5), 1071–1079.
- Kramer, U., Koch, T., Ranft, U., Ring, J., Behrendt, H., 2000. Traffic-related air pollution is associated with atopy in children living in urban areas. *Epidemiology* 11 (1), 64–70.
- Kreyling, W.G., Tuch, T., Peters, A., et al., 2003. Diverging long-term trends in ambient urban particle mass and number concentrations associated with emission changes caused by the German unification. *Atmos. Environ.* 37 (27), 3841–3848.
- Kuenzli, N., Kaiser, R., Medina, S., et al., 2000. Public-health impact of outdoor and traffic-related air pollution: a European assessment. *Lancet* 356 (9232), 795–801.
- Kuenzli, N., Shi, T.M., Goetschi, T., et al., 2004. Beyond the mass: oxidative properties of PM_{2.5} in the European Community Respiratory Health Survey (ECRHS). *Epidemiology* 15 (4), S43.
- Lercher, P., Schmitzberger, R., Kofler, W., 1995. Perceived traffic air pollution, associated behavior and health in an alpine area. *Sci. Total Environ.* 169 (1–3), 71–74.
- Livingstone, A.E., Shaddick, G., Grundy, C., Elliott, P., 1996. Do people living near inner city main roads have more asthma needing treatment? Case-control study. *Br. Med. J.* 312 (7032), 676–677.
- Maziak, W., Behrens, T., Brasky, T.M., et al., 2003. Are asthma and allergies in children and adolescents increasing? Results from ISAAC phase I and phase III surveys in Munster, Germany. *Allergy* 58 (7), 572–579.
- Nel, A.E., Diaz-Sanchez, D., Ng, D., Hiura, T., Saxon, A., 1998. Enhancement of allergic inflammation by the interaction between diesel exhaust particles and the immune system. *J. Allergy Clin. Immunol.* 102 (4), 539–554.
- Nicolai, T., Carr, D., Weiland, S.K., et al., 2003. Urban traffic and pollutant exposure related to respiratory outcomes and atopy in a large sample of children. *Eur. Respir. J.* 21 (6), 956–963.
- Nowak, D., Heinrich, J., Jorres, R., et al., 1996. Prevalence of respiratory symptoms, bronchial hyperresponsiveness and atopy among adults: West and East Germany. *Eur. Respir. J.* 9 (12), 2541–2552.
- Oglesby, L., Kunzli, N., Roosli, M., et al., 2000. Validity of ambient levels of fine particles as surrogate for personal exposure to outdoor air pollution – results of the European EXPOIS-EAS study (Swiss Center Basel). *J. Air Waste Manage. Assoc.* 50 (7), 1251–1261.
- Oosterlee, A., Drijver, M., Lebet, E., Brunekreef, B., 1996. Chronic respiratory symptoms in children and adults living along streets with high traffic density. *Occup. Environ. Med.* 53 (4), 241–247.
- Riedl, M., Diaz-Sanchez, D., 2005. Biology of diesel exhaust effects on respiratory function. *J. Allergy Clin. Immunol.* 115 (2), 221–228.
- Ronchetti, R., Villa, M.P., Barreto, M., et al., 2001. Is the increase in childhood asthma coming to an end? Findings from three surveys of schoolchildren in Rome, Italy. *Eur. Respir. J.* 17 (5), 881–886.
- Roosli, M., Braun-Fahrlander, C., Kunzli, N., et al., 2000. Spatial variability of different fractions of particulate matter within an urban environment and between urban and rural sites. *J. Air. Waste Manage. Assoc.* 50 (7), 1115–1124.
- Sarnat, J.A., Long, C.M., Koutrakis, P., Coull, B.A., Schwartz, J., Suh, H.H., 2002. Using sulfur as a tracer of outdoor fine particulate matter. *Environ. Sci. Technol.* 36 (24), 5305–5314.
- Sunyer, J., Jarvis, D., Pekkanen, J., et al., 2004. Geographic variations in the effect of atopy on asthma in the European Community Respiratory Health Study. *J. Allergy Clin. Immunol.* 114 (5), 1033–1039.
- Sunyer, J., Jarvis, D., Gotschi, T., Garcia-Esteban, R., Jacquemin, B., Aguilera, I., Ackerman, U., de Marco, R., Forsberg, B., Gislason, T., Heinrich, J., Norback, D., Villani, S., Kunzli, N., 2006. Chronic bronchitis and urban air pollution in an international study. *Occup. Environ. Med.* 63 (12), 836–843.
- Upton, M.N., McConnachie, A., McSharry, C., et al., 2000. Intergenerational 20 year trends in the prevalence of asthma and hay fever in adults: the Midspan family study surveys of parents and offspring. *Br. Med. J.* 321 (7253), 88–92.
- Venn, A.J., Lewis, S.A., Cooper, M., Hubbard, R., Britton, J., 2001. Living near a main road and the risk of wheezing illness in children. *Am. J. Respir. Crit. Care Med.* 164 (12), 2177–2180.
- von Hertzen, L.H.T., 2005. Signs of reversing trends in prevalence of asthma. *Allergy* 60 (3), 283–292.
- von Hertzen, L.C., Haahtela, T., 2004. Asthma and atopy – the price of affluence? *Allergy* 59 (2), 124–137.
- von Mutius, E., Martinez, F.D., Fritzsche, C., Nicolai, T., Roell, G., Thiemann, H.H., 1994. Prevalence of asthma and atopy in two areas of West and East Germany. *Am. J. Respir. Crit. Care Med.* 149 (149), 358–364.
- von Mutius, E., Weiland, S.K., Fritzsche, C., Duhme, H., Keil, U., 1998. Increasing prevalence of hay fever and atopy among children in Leipzig, East Germany. *Lancet* 351 (9106), 862–866.
- Wichmann, H.E., 1996. Possible explanation for the different trends of asthma and allergy in east and west Germany. *Clin. Exp. Allergy* 26 (6), 621–623.
- Wüthrich, B., Leuenberger, P., Ackermann-Lieblich, U., et al., 1999. Atopische Sensibilisierung, Luftverschmutzung und respiratorische Erkrankungen in der Schweiz (SAPALDIA Studie). *Allergologie* 22 (5), 267–274.
- Wyler, C., Braun-Fahrlander, C., Kunzli, N., et al., 2000. Exposure to motor vehicle traffic and allergic sensitization. *Epidemiology* 11 (4), 450–456.
- Zhu, Y., Hinds, W.C., Kim, S., Sioutas, C., 2002. Concentration and size distribution of ultrafine particles near a major highway. *J. Air Waste Manage. Assoc.* 52 (9), 1032–1042.