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PM_{10}, and children's respiratory symptoms and lung function in the PATY study

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ABSTRACT: Studies of the impact of long-term exposure to outdoor air pollution on the prevalence of respiratory symptoms and lung function in children have yielded mixed results, partly related to differences in study design, exposure assessment, confounder selection and data analysis.

We assembled respiratory health and exposure data for >45,000 children from comparable cross-sectional studies in 12 countries. 11 respiratory symptoms were selected, for which comparable questions were asked. Spirometry was performed in about half of the children. Exposure to air pollution was mainly characterised by annual average concentrations of particulate matter with a 50% cut-off aerodynamic diameter of 10 μm (PM_{10}) measured at fixed sites within the study areas.

Positive associations were found between the average PM_{10} concentration and the prevalence of phlegm (OR per 10 $\mu g \cdot m^{-3}$ 1.15, 95% CI 1.02–1.30), hay fever (OR 1.20, 95% CI 0.99–1.46), bronchitis (OR 1.08, 95% CI 0.98–1.19), morning cough (OR 1.15, 95% CI 1.02–1.29) and nocturnal cough (OR 1.13, 95% CI 0.98–1.29). There were no associations with diagnosed asthma or asthma symptoms. PM_{10} was not associated with lung function across all studies combined.

Our study adds to the evidence that long-term exposure to outdoor air pollution, characterised by the concentration of PM_{10}, is associated with increased respiratory symptoms.

KEYWORDS: Child, lung function, nitrogen dioxide, particulate matter, respiratory symptoms

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Short-term increases in outdoor air pollution have been associated with respiratory symptoms and temporary lung function decreases [1, 2]. The impact of long-term exposure to outdoor air pollution on prevalence of respiratory symptoms and lung function in children has been investigated in studies around the world [3–15]. Results concerning symptoms have been mixed, with more evidence for significant effects of outdoor air pollution on bronchitis or symptoms such as cough and phlegm than on asthma or asthmatic symptoms such as wheeze. Results from cross-sectional studies of lung function in children were also mixed [14]. Several prospective studies documented significant effects of outdoor air pollution on lung function development, *e.g.* the Californian Children's Health Study [14, 15]. Some of the inconsistencies in reported associations between air pollution and lung function may be due to differences in study design [14]. Studies differ in their study area (air pollution exposure contrasts between communities *versus* within a community), measured pollutants (particulate matter, sulphur dioxide, nitrogen dioxide and ozone), wording of symptom questions, study population (either population based or high risk), inclusion of potential confounders and statistical methods. Particulate matter air pollution has been represented with various indices, including total suspended particulate matter (TSP), particulate matter with a 50% cut-off aerodynamic diameter of 10 μm (PM_{10}) or 2.5 μm ($PM_{2.5}$). Some studies have reported higher air pollution effect estimates on lung function for females [7, 12], but the evidence is currently not convincing [14]. In the Children's Health study, air pollution effects on symptoms were stronger in males [8], whereas the effects on lung function were stronger in females [7]. Interpretation of subgroup analysis in single studies is difficult as the power to detect significant interactions is limited.

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To overcome some of these shortcomings, the Pollution and the Young (PATY) project assembled health and exposure data for 58,561 children from comparable cross-sectional studies in 12 countries on children's respiratory health. Pooling original data allowed harmonisation of data analysis and definition of confounders, pursuit of research questions not addressed originally, and inclusion of unpublished studies. We made further use of the large dataset to assess effect modification with more precision than single studies. We already published on associations between outdoor NO_2 and respiratory symptoms in a subset of the five PATY studies with NO_2 exposure data [16]. In the current article, we examine the association between ambient fine particulate matter (PM_{10}) in all PATY studies and prevalence of respiratory symptoms and lung function.

METHODS

Study design

Cross-sectional studies of children were sought that assessed respiratory symptoms and individual risk factors by questionnaire, included cough and wheeze as outcomes, and allowed calculation of annual mean particulate matter measures by study area. We included all cross-sectional studies that were available at the onset of the study. From the USA and the Netherlands, we included only the most recent and largest study, excluding the Six City and Six School studies [14]. Table 1 describes the studies contributing to this paper. More details on the individual studies can be found elsewhere [4, 10, 11, 13, 16, 18–20]. The studies from Russia, Central and Eastern Europe and Italy have not previously published results of air pollution analysis in the English language. The study areas were of substantially different magnitude. The Austrian and Czech study was performed in one city, and the North American study included a very large area in the USA and Canada. We therefore anticipated some heterogeneity in effects, which was taken into account in the analysis. All studies had obtained permission from the relevant medical ethical committees.

Health data

Original questionnaires were translated into English and critically examined for comparability of wording. 11 comparable symptom outcomes were identified: wheeze in the past 12 months, asthma ever, bronchitis in the past 12 months, phlegm, nocturnal dry cough in the past 12 months, morning cough in the past 12 months, sensitivity to inhaled allergens, hay fever ever, itchy rash ever, woken by wheeze in the past 12 months and allergy to pets. The exact wording of the symptom questions in all studies has been reported previously [21].

Several of the studies also performed spirometry (table 1). All studies used equipment that fulfilled either the 1987 criteria of the American Thoracic Society (ATS) or the 1993 European Respiratory Society (ERS) criteria. Spirometry was performed using the 1987 protocol of the ATS (North American, German and Austrian studies) or the 1993 ERS (CESAR study and the Netherlands). Further details have been published previously [17]. The main lung function measures of interest were forced vital capacity (FVC), forced expiratory volume in 1 s (FEV_1), peak expiratory flow and the forced expiratory flow at 25–75% of the FVC ($FEF_{25–75\%}$).

Exposure assessment methods

The main exposure of interest was the annual mean concentration of PM_{10} in the corresponding study area. Data on the gaseous pollutants NO_2 and SO_2 were also obtained. In all studies, air pollution concentrations were measured at fixed monitoring sites in the study area. To assess the comparability of monitoring sites and monitoring methods, a standard questionnaire was discussed with the investigators of the studies (online supplementary material pages 2 and 3 and tables S1 and S2). Briefly, PM_{10} was directly measured specifically for the study with Harvard impactors in Switzerland, the CESAR study, and for Russia and North America. In the Netherlands, Austria and Germany, particulate matter measurements were converted to gravimetric PM_{10} using co-located measurements with a standard particulate matter sampler in the study area. In the Italian study, multiple particulate matter monitoring methods were used and there was insufficient co-location with standard PM_{10} equipment to allow calculation of a consistent PM_{10} concentration. The evaluation further resulted in a few modifications of the original exposure estimates and exclusions of a few areas because of unrepresentative monitoring sites (online supplementary material pages 2 and 3).

Data analysis

A priori, we assessed that air pollution exposure contrasts between countries could not be exploited, as differences in language and (unmeasured) major risk factors were likely to be more dominant determinants for the health outcomes (especially with regards to symptoms). Hence, a two-stage analysis approach was used. In stage one, study-specific PM_{10} effects were estimated using logistic regression for symptoms and linear regression for lung function. This approach also has the advantage that systematic differences in PM_{10} sampler performance between studies do not affect the results. An area-level random intercept was included to account for clustering within the study areas. The CESAR study was conducted in five countries and, although common methods were used, the study was analysed per country. In stage two, effect estimates and standard errors were entered into a meta-analysis, obtaining a mean estimate, and a measure and Cochran Chi-squared test of heterogeneity using the STATA (StataCorp, College Station, TX, USA) metan command. Estimation of this mean and its confidence interval takes into account both between-study variation in effects and uncertainty of study-specific estimates [22]. In the first stage, we controlled for age, sex, maternal education, paternal education, household-crowding, current parental smoking, mother smoking during pregnancy, gas cooking, unvented gas/oil/kerosene heater, mould, nationality, birth order and ''ever had a pet'' [16]. Lung function analyses were additionally adjusted for age, height, weight, technician, instrument, season of testing and reported infection on the day of the test. The natural logarithm of lung function variables was used as the dependent variable to allow for non-normal distribution and nonlinear associations with anthropometric variables [17]. The natural logarithm of age, weight and height (sex-specific using an interaction term) were included as predictors following the North American study [13]. We further calculated predicted values for FVC, FEV_1 and $FEF_{25–75\%}$ using recently published prediction equations and used the % predicted lung function as the dependent variable in an additional analysis [23].

TABLE 1 Overview of design, respiratory health and exposure data of studies included in the Pollution and the Young (PATY) project

Study name, location [ref.]	Study areas	Main age range yrs	Health end-points	Health data collection	Exposure data collection	PM_{10}# µg·m^{-3}	NO_2# µg·m^{-3}	SO_2# µg·m^{-3}
Scarpol, Switzerland [11]	10 communities, major cities (Bern, Geneva, Zürich) and small towns	6–12	Symptoms	October 1992–March 1993	1992¶	24 (10–33)	32 (16–50)	13 (2–23)
Linz, Austria [17]	Schools assigned to 8 monitors in the city of Linz	6–8	Symptoms, lung function	January 1996–December 1998	1996–1998	32 (24–42)	26 (20–31)	6 (4–14)
CESAR, Central and Eastern Europe [18]	3 areas in 3 towns in Bulgaria	9–12	Symptoms, lung function	Spring 1996	October 1995–October 1996	67 (62–71)	NA	NA
	4 areas in the city of Ostrava, Czech Republic	9–12	Symptoms, lung function			76 (65–89)	NA	NA
	5 towns spread throughout Hungary	9–12	Symptoms, lung function			61 (56–72)	NA	NA
	4 towns spread throughout Poland	9–12	Symptoms, lung function			74 (60–85)	NA	NA
	4 areas in three towns in Slovakia	9–12	Symptoms, lung function			49 (41–57)	NA	NA
Germany [5]	3 towns former East Germany (Hettstedt, Zerbst, Bitterfeld)	6–12	Symptoms, lung function	September 1992–July 1993	1991–1993	43 (33–53)	NA	60 (46–75)
SIDRIA, Italy [19]	46 areas in 22 towns including major cities (Rome, Turin) and small towns	6–10	Symptoms	October–December 1994	October 1993–October 1994	NA	52 (14–93)	13 (2–32)
24-school, the Netherlands [10]	24 schools located within 400 m of a major road in mid-west Netherlands	7–12	Symptoms, lung function	April 1997–July 1998	April 1997– May 1998	34 (30–39)	35 (27–44)	NA
10-city, Russia [20]	13 areas in 10 towns of different size (largest Ekaterinburg) and industrialisation	8–12	Symptoms	April–May 1999	November 1998–November 1999	24 (20–28)	20 (13–35)	26 (7–65)
24-city, USA [4, 13]	24 medium-sized communities in the USA and Canada	8–12	Symptoms, lung function	September–May 1988–1991+	Year prior to health evaluation	24 (15–33)	NA	12 (1–34)

Data are presented as mean (range), unless otherwise stated. PM_{10} was directly measured in Switzerland, Central European Study on Air pollution and Respiratory Health (CESAR) study, Russia and USA; it was estimated using co-located measurements from total suspended particulate matter in Austria and Germany, and from $PM_{2.5}$ in the Netherlands. PM_{10}: particulate matter with a 50% cut-off aerodynamic diameter of 10 µm; NA: not available. #: mean and range of study area-specific annual average concentrations; ¶: 1993 for PM_{10}; +: study in three consecutive years including eight, nine and seven cities, respectively. SIDRIA: Studi Italiani sui Disturbi Respiratori nell'Infanzia e l'Ambiente.

Meta-regressions assessed associations between study-specific estimates and study characteristics. These *a priori*-defined potential sources of heterogeneity between estimates were study period, design type (between-city, within-city or mixed design), location of monitoring station, proportion of younger children (6–8 yrs), questionnaire-date variability across study areas, high response rate (>80%) and response-rate variability across study areas.

Subgroup analyses were conducted in the first stage to assess individual subject characteristics as a source of heterogeneity. We stratified by sex, age and reporting of wheeze, and sensitisation (the latter for lung function only).

All analyses were performed using STATA version 8 (StatCorp).

RESULTS

Associations between air pollution and respiratory symptoms

Data were available from 11 studies on PM10 and symptoms (table 1). The highest PM10 concentrations were measured in the Central and Eastern European areas. The range in concentration within a study was largest in the North American and Swiss studies (ratio of maximum to minimum larger than two) (fig. 1).

Complete information on health and covariates was available for 45,788 children. About one-third of the children were from the North American study (table 2). Several-fold differences in symptom prevalence were found between countries, probably partly related to cultural differences and subtle differences in wording of the question.

After adjustment for confounders, PM10 was significantly associated with phlegm and morning cough (table 3 and fig. 2). Associations between PM10 and a doctor diagnosis of bronchitis, nocturnal cough and hay fever were borderline significant. Significant heterogeneity between study-specific estimates was found for most outcomes. The most consistent pattern was found for phlegm and hay fever, for which most study-specific effect estimates were either positive or slightly negative (fig. 2). For bronchitis and the two cough variables, both positive and negative effect estimates were found. A diagnosis of asthma and the symptoms wheeze and being woken by wheeze were not associated with PM10. Meta-regression could not identify significant factors at the study level explaining the observed

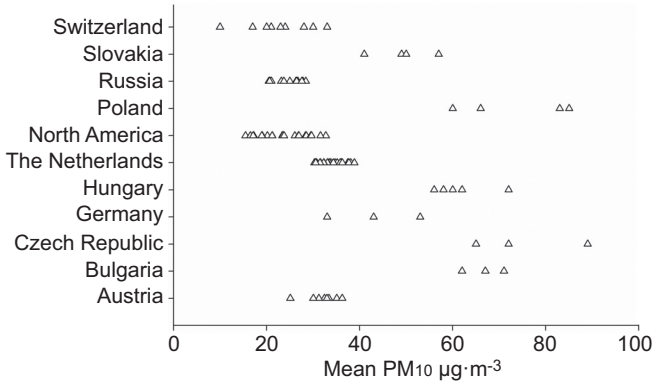

FIGURE 1. Annual average concentrations of particulate matter with a 50% cut-off aerodynamic diameter of 10 µm (PM10) per study area, within each country.

TABLE 2 Prevalence (%) of respiratory symptoms in each country

	Children[#] n	Wheeze[¶]	Asthma	Bronchitis	Phlegm	Nocturnal cough	Morning cough	Sensitivity to inhaled allergens	Hay fever	Itchy rash	Woken by wheeze	Allergy to pets
Austria	3904	13.6	8.6	[+]		10.4	5.3	12.8	5.2	8.2		5.8
Bulgaria	2765	15.8	15.9	23.7	4.0	5.3	16.3	11.3		9.3	6.6	4.7
Czech Republic	3356	20.6	9.8	41.5	18.5	19.6	26.8	17.3		10.8	15.5	4.6
Germany	1903	10.1	8.5				13.8		4.5	15.0		2.1
Hungary	3460	9.6	22.2	32.9	2.3	9.3	6.4	14.0		6.9	8.2	5.0
The Netherlands	1916	9.5	8.1	7.9	9.5	21.6		15.2	7.2	22.3	4.9	9.3
North America	14496	19.4	9.7	6.2	5.9		5.9	20.7	14.1		5.1	
Poland	2821	12.3	10.5	34.9	11.0	13.7	46.3	13.9		7.4	8.9	6.2
Russia	5453	13.4	1.9	14.7	7.2		11.4	6.4	1.2		4.4	
Slovakia	2975	9.9	6.7	31.3	5.4	13.7	14.6	14.4		9.7	8.9	3.2
Switzerland	2739	10.4	9.0	18.3		21.5	11.9	13.7	10.2	13.3	4.6	4.6
Total	45788	14.9	9.7	18.6	7.3	13.9	12.7	15.3	9.3	10.7	6.8	5.0

Data are presented as %, unless otherwise stated. [#]: number with no missing covariates; [¶]: symptoms for the past 12 months, except asthma, hay fever and itchy rash, for which the questions referred to lifetime (ever); [+]: some outcomes not included in the questionnaire of all countries.

TABLE 3 Association between prevalence of respiratory symptoms and long-term average concentration of particulate matter with a 50% cut-off aerodynamic diameter of 10 μm (PM_{10})

	Mean OR (95% CI)	
	Age-sex adjusted	Fully adjusted#
Wheeze	1.03 (0.95–1.11)¶	1.01 (0.95–1.09)
Asthma	0.99 (0.92–1.08)	1.03 (0.97–1.10)
Bronchitis	1.06 (0.94–1.21)¶	1.08 (0.98–1.19)¶
Phlegm	1.16 (1.02–1.31)¶	1.15 (1.02–1.30)¶
Nocturnal cough	1.15 (1.00–1.32)¶	1.13 (0.98–1.29)¶
Morning cough	1.16 (1.02–1.32)¶	1.15 (1.02–1.29)¶
Sensitivity to inhaled allergens	1.01 (0.90–1.13)¶	1.02 (0.93–1.11)
Hay fever	1.18 (0.96–1.44)	1.20 (0.99–1.46)
Itchy rash	1.04 (0.98–1.11)	1.07 (0.96–1.19)¶
Woken by wheeze	1.04 (0.94–1.14)¶	1.01 (0.92–1.12)
Allergy to pets	1.18 (0.95–1.46)¶	1.18 (0.96–1.45)¶

Odds ratios (ORs) are combined effect estimates from single pollutant models calculated from country-specific estimates using random effects model. Mean ORs and 95% confidence intervals are given per 10 $\mu g \cdot m^{-3}$ increase in PM_{10}. #: adjusted for age, sex, maternal education, paternal education, household-crowding, current parental smoking, mother smoking during pregnancy, gas-cooking, unvented gas/oil/kerosene heater, mould, nationality, birth order and ''ever had a pet''; ¶: evidence of between-study heterogeneity ($p<0.10$).

heterogeneity in effect estimates. Table S3 presents the data for the symptom phlegm.

Two-pollutant models were employed for symptoms showing (borderline) significant associations with PM_{10} in the single-pollutant model (table 4). Adjustment for SO_2 made little difference to the PM_{10} effect estimates with the exception of bronchitis, which showed a substantial decrease (single *versus* two pollutant PM_{10} estimates table 4). Adjustment for NO_2 made little difference to the PM_{10} effect estimates for bronchitis, phlegm, morning cough and hay fever. For the symptoms of nocturnal cough, sensitivity to inhaled allergens, itchy rash and allergy to pets, after inclusion of NO_2, the PM_{10} effect estimates were reduced. Correlations (r) between the annual average concentration of NO_2 and PM_{10} in the studies with $\geqslant 10$ study areas ranged from 0.48 to 0.84. Correlations between SO_2 and PM_{10} ranged from 0.36 to 0.82.

PM_{10} effect estimates did not differ significantly between males and females, or between the younger and older children in the study population (table S4). Associations for hay fever and allergy to pets were stronger in the older children, but the difference with the younger children was not significant. Effect of PM_{10} on nocturnal cough and allergy to pets were stronger in boys than in girls but the differences did not reach statistical significance.

Associations between air pollution and lung function

Valid lung function data were available for 22,809 children (table S5). About 60% of the children with a valid lung function test were from the North American study. While in the North American, German, Austrian and Dutch studies, the percentage of children with a valid lung function test was well over 80%, it ranged from between 26 and 60% for the four CESAR study countries. This was related to too early termination of the test, resulting in too low FVC values. In all studies except the Austrian study, the mean percentage predicted lung function using the Stanojevic equations was close to 100.

On average, no association was found between the average PM_{10} concentration of the study area and lung function (fig. 3). In individual studies, both increases (Slovakia) and decreases (North America and Poland) in lung function were found with increasing PM_{10}. Removing the CESAR countries from the analysis did not change the associations substantially (table S6). Analysis of the data using the recent Stanojevic prediction equations also resulted in no significant associations between PM_{10} and lung function (table S6).

There were no significant differences in PM_{10} effect estimates between males and females or younger and older children (table 5).

DISCUSSION

Statistically (borderline) significant positive associations were found between PM_{10} and the prevalence of phlegm, morning cough, hay fever, bronchitis and nocturnal cough. There were no associations with diagnosed asthma and asthma symptoms. PM_{10} effect estimates did not differ between males and females. PM_{10} was not associated with lung function.

The main strength of our study is the large number of children (45,000) taken from studies in 12 countries. This reduces the risk of finding spurious associations due to, for example, unmeasured confounding at the study area level as in single studies. The large study size also allowed for analyses of subgroups with more precision. Compared with a standard meta-analysis of studies, our study offers several advantages related to having the original data of all the studies available instead of only the air pollution effect estimates. First, we selected end-points for a common analysis that were considered sufficiently similar in wording. Secondly, the same data analysis procedures were used, including a common set of confounders. Thirdly, the comparability of exposure data collection could be assessed in detail, which resulted in the removal of some study areas from the epidemiological analysis. Finally, several unpublished studies were included in the analysis.

Comparison with previous studies

Our findings of significant associations between PM_{10} and respiratory symptoms and no associations with lung function are in agreement with the Harvard Six City study and two German studies, which were not included in the current analysis [3, 9, 24]. In contrast, other studies not included in the PATY study did find associations between long-term average air pollution exposure and lung function [14]. For the studies included in the PATY study the large North American study found associations with both lung function and bronchitis [13], whereas the Dutch, German and CESAR studies [5, 10, 18] did not find lung function associations.

The effect of air pollution may have been too modest to be reflected in detectable changes of lung function. The (asthma)

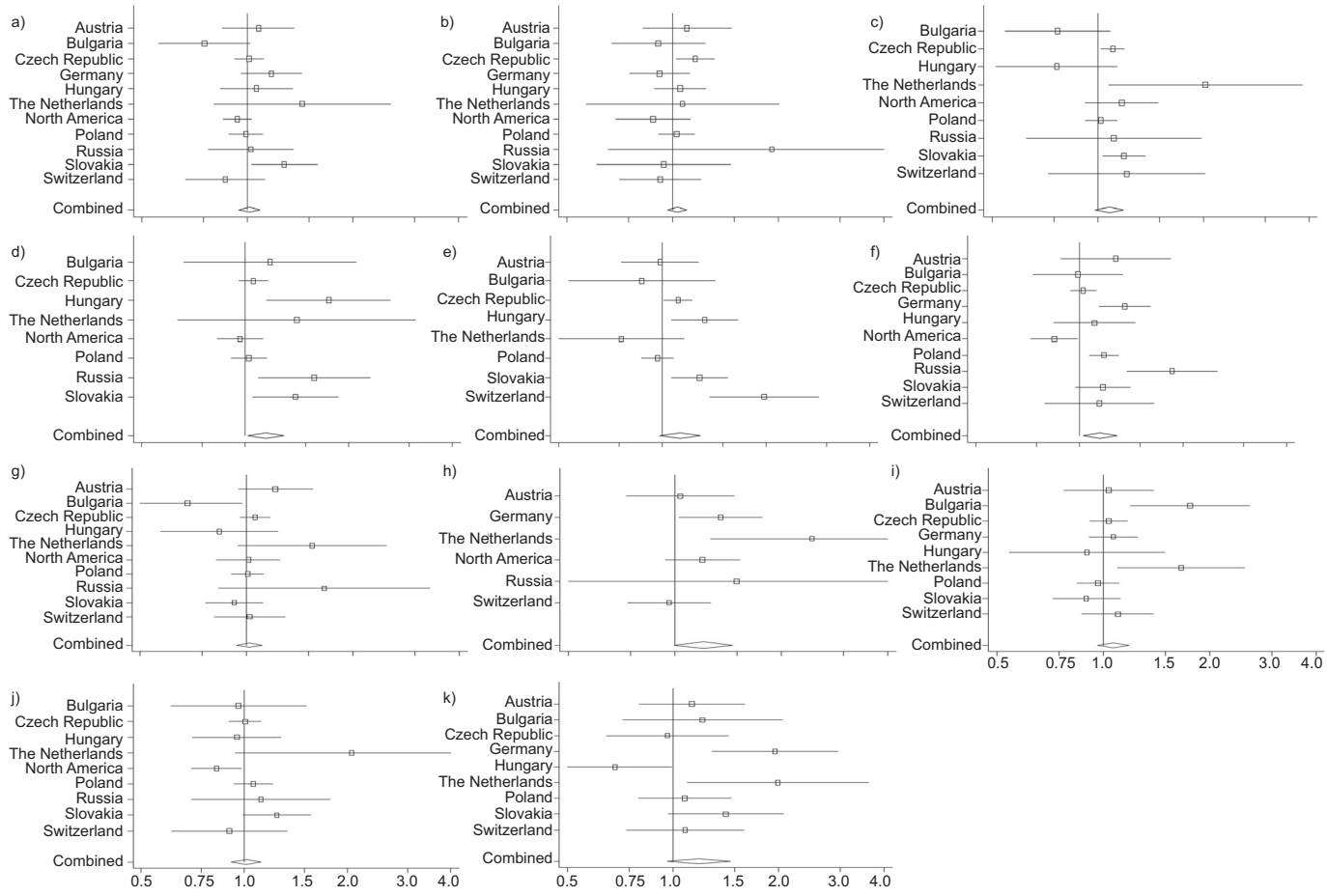

FIGURE 2. Forest plots of study-specific and mean odds ratios for effects of particulate matter with a 50% cut-off aerodynamic diameter of 10 μm (PM_{10}) on a) wheeze, b) asthma, c) bronchitis, d) phlegm, e) nocturnal cough, f) morning cough, g) sensitivity to inhaled allergens, h) hay fever, i) itchy rash, j) being woken by wheeze and k) allergy to pets. Odds ratios per 10 $\mu g \cdot m^{-3}$ increase in PM_{10} are from single pollutant models, adjusted for individual risk factors. The vertical line indicates odds ratio of 1 and horizontal lines represent 95% confidence intervals of estimates. The diamond shape at the bottom of each graph indicates position, and confidence interval, of the mean of the estimates. Symptoms are for the past 12 months, except asthma, hay fever and itchy rash, which refer to lifetime (ever).

symptoms related to the largest deficits in lung function were also not associated with outdoor air pollution. Alternatively, different biases in the analysis of symptoms and lung function may explain the inconsistencies. First, the typically small effects of air pollution on lung function may have been masked by factors such as variability in coaching and judgement by the technician, instrument, subtle shifts in instrument calibration, short-term weather factors and (past) infections [10]. In the CESAR study, good-quality tests were only obtained in <50% of the children, despite a rigorous quality assurance/quality control protocol. Exclusion of the CESAR study countries from the analysis, however, did not change our results. Secondly, reporting bias of symptoms may explain some of the positive associations in studies where parents of the children are aware of high air pollution exposures. This is an unlikely explanation, especially in the North American study where none of the included cities was highly polluted by local sources, and the Dutch study where all schools were located within 400 m from a major road. The pattern of associations, with bronchitis but not asthma, also makes reporting bias unlikely. Thirdly, lung function data were available for a smaller subset of children, but the precision of estimated effects on lung function was good because of pooling data from a large number of children. Fourthly, pollution levels were moderate. Air pollution may affect lung function at higher pollution levels, such as in many developing countries. Longitudinal studies in highly polluted Mexico City support this [14]. Fifthly, spirometry was performed with now updated guidelines. The updates in performance of testing are probably not sufficiently major to explain the lack of overall associations in our study. We further showed that the use of recent prediction equations for spirometry also resulted in no association between PM_{10} and lung function. Finally, we only included cross-sectional studies. Several prospective studies have found associations between air pollution and lung function growth, although a series of Austrian studies did not find consistent effects of particulate matter [14].

Heterogeneity of effects

Despite the efforts to select symptoms with similar wording and harmonise confounder data and data analysis, significant heterogeneity was present in both the symptom and lung function country-specific effect estimates. *A priori*-defined study-level factors could not explain this heterogeneity, possibly related to the relatively small number of studies.

TABLE 4 Combined effect estimates of particulate matter with a 50% cut-off aerodynamic diameter of 10 μm (PM_{10}) on respiratory symptoms from single- and two-pollutant models

	Studies n	Mean OR (95% CI)#	
		Single-pollutant model	Two-pollutant model
Bronchitis			
In studies with SO_2 data	3	1.17 (0.93–1.48)	0.81 (0.44–1.51)¶
In studies with NO_2 data	3	1.35 (0.96–1.91)	1.49 (0.85–2.61)
Phlegm			
In studies with SO_2 data	2	1.23 (0.81–1.89)¶	1.24 (0.80–1.94)¶
In studies with NO_2 data	2	1.55 (1.11–2.18)	1.55 (1.01–2.38)
Nocturnal cough			
In studies with SO_2 data	2	1.41 (0.68–2.93)¶	1.43 (0.61–3.36)¶
In studies with NO_2 data	3	1.14 (0.68–1.91)¶	0.79 (0.53–1.19)
Morning cough			
In studies with SO_2 data	5	1.25 (0.93–1.67)¶	1.24 (0.90–1.70)¶
In studies with NO_2 data	3	1.42 (1.04–1.92)	1.36 (0.87–2.13)
Hay fever			
In studies with SO_2 data	5	1.13 (0.98–1.31)	1.19 (1.01–1.40)
In studies with NO_2 data	4	1.22 (0.84–1.78)¶	1.18 (0.70–1.97)
Itchy rash			
In studies with SO_2 data	3	1.05(0.93–1.19)	1.13 (0.97–1.33)
In studies with NO_2 data	3	1.18 (0.94–1.50)	0.91 (0.48–1.71)¶
Allergy to pets			
In studies with SO_2 data	3	1.31 (0.90–1.90)¶	1.16 (0.88–1.52)
In studies with NO_2 data	3	1.25 (0.92–1.70)	0.87 (0.42–1.80)¶

Combined effect estimates calculated from country-specific estimates using random effects model. #: adjusted for age, sex, maternal education, paternal education, household crowding, current parental smoking, mother smoking during pregnancy, gas cooking, unvented gas/oil/kerosene heater, mould, nationality, birth order, and ''ever had a pet'' and expressed per 10-$\mu g \cdot m^{-3}$ increase in PM_{10}; ¶: evidence of between study heterogeneity ($p<0.10$).

Differences in study design may have contributed to the observed heterogeneity. Six of the included studies assessed exposure contrasts between communities (Switzerland, Germany, North America, Poland, Hungary and Bulgaria), two studies assessed within-community contrasts (Austria and the Czech Republic), and in the remaining three studies exposure contrasts derived from a mixture of between and within community contrasts. The major common exposure variable PM_{10} is likely to represent different air pollution mixtures in the different studies, with long-range transported particles contributing only in studies with a between-community component and freshly emitted (ultrafine) particles contributing more to the contrast in the within-city studies. However, particles emitted by motorised traffic have contributed to the exposure contrast in all studies. Within the PATY study, there was no consistent pattern of stronger effects for those studies with a strong traffic-exposure component.

We did not find any difference in effect estimates between males and females, either for symptoms or for lung function. In previous single studies, stronger effects were reported for females in some studies [7, 12] and males in other studies [8].

Limitations

The small number of study areas is a limitation in some of our studies, although in Switzerland, Russia, the Netherlands and North America, the number of areas was fairly large ($\geqslant 10$).

The annual average concentration of PM_{10} was the main exposure variable within the PATY study. We also evaluated NO_2 and SO_2 as pollutants representing the urban air pollution mixture, but the number of studies with data on multiple pollutants was limited. Hence, the ability to assess effects of PM_{10} independent of the gaseous pollutants was limited. Two-pollutant models are difficult to interpret, especially when the same source affects both pollutants, as is the case for PM_{10} and NO_2, for which motorised traffic is an important source. We cannot exclude that other pollutants such as the soot or elemental carbon content of particulate matter or the ultrafine particle concentration were associated more strongly with the health outcomes.

Several studies have assessed indicators of motorised-traffic emissions at a fine spatial scale (<100–300 m) [6, 10, 12, 24]. Our central monitoring data do not reflect these fine-scale air pollution variations. Because we did not have access to individual addresses, we were unable to generate individual exposure estimates at the residential address. Hence, our study does not provide information on the role of primary traffic emissions. Although this is a limitation, studies comparing the average concentration across communities remain valuable, as they allow estimation of the potential health effects of more aged pollution mixtures. Furthermore, a large fraction of the population does not live directly on major roads. Personal monitoring studies have shown that the population average

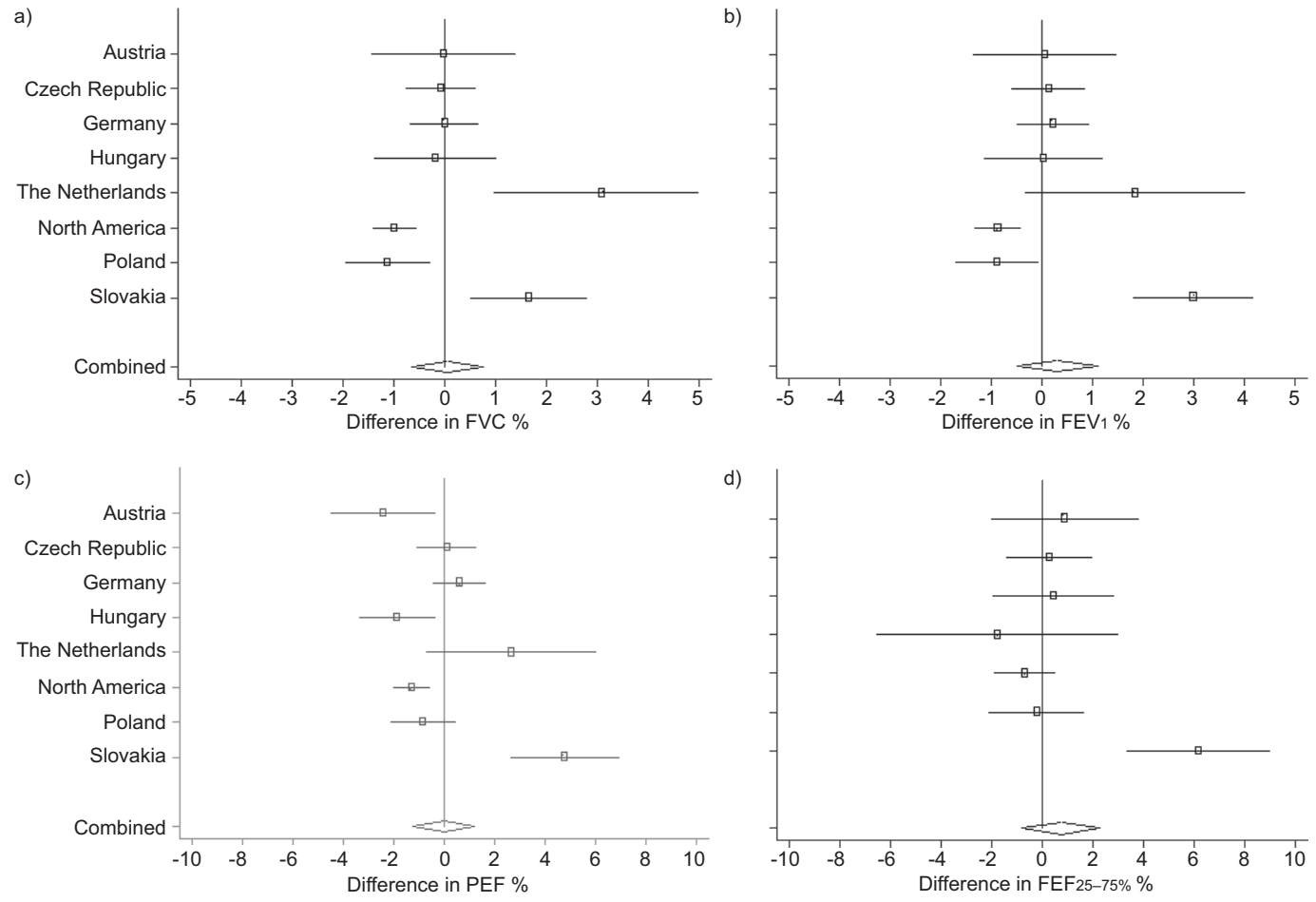

FIGURE 3. Forest plots of study-specific and mean effects of particulate matter with a 50% cut-off aerodynamic diameter of 10 μm (PM_{10}) for a) forced vital capacity (FVC), b) forced expiratory volume in 1 s (FEV_1), c) peak expiratory flow (PEF) and d) forced expiratory flow at 25–75% of the FVC ($FEF_{25–75\%}$). Figures are given as percentage difference in lung function per 10-$\mu g \cdot m^{-3}$ increase in PM_{10} from single pollutant models, adjusted for individual risk factors. The vertical line indicates null, *i.e.* 0% change (no effect), and horizontal lines represent 95% confidence intervals of estimates. ''Combined'' indicates the mean and its confidence interval of the individual estimates.

TABLE 5 Combined estimates for the fully adjusted effect of a 10-$\mu g \cdot m^{-3}$ increase in particulate matter with a 50% cut-off aerodynamic diameter of 10 μm on lung function in different subgroups

	FVC	FEV_1	$FEF_{25–75\%}$	PEF
Sex				
Male	0.1 (-0.8–0.9)	0.3 (-0.6–1.2)	1.0 (-0.8–2.7)	-0.1 (-1.0–0.8)
Female	-0.1 (-0.7–0.6)	0.1 (-0.6–0.8)	0.2 (-1.2–1.7)	-0.3 (-1.8–1.2)
Age yrs				
6–9	0.0 (-1.4–1.4)	0.1 (-1.2–1.4)	0.1 (-2.4–2.6)	-0.3 (-2.3–1.7)
10–12	-0.1 (-0.8–0.6)	0.4 (-0.6–1.4)	1.2 (-0.6–3.0)	0.1 (-1.4–1.6)
Wheeze				
No	0.2 (-0.8–1.2)	0.4 (-0.6–1.4)	1.0 (-0.8–2.8)	-0.1 (-1.7–1.5)
Yes	-0.3 (-1.2–0.5)	-0.4 (-1.3–0.5)	-0.3 (-3.9–3.3)	0.4 (-1.3–2.1)
Sensitivity to inhaled allergens				
No	0.3 (-0.8–1.4)	0.6 (-0.8–2.0)	1.2 (-0.7–1.1)	0.3 (-1.7–2.3)
Yes	-0.4 (-1.1–0.3)	0.0 (-0.9–0.9)	0.6 (-1.8–3.0)	-0.3 (-1.6–1.0)

Data are presented as % difference (95% confidence interval). FVC: forced vital capacity; FEV_1: forced expiratory volume in 1 s; $FEF_{25–75\%}$: forced expiratory flow at 25–75% of the FVC; PEF: peak expiratory flow. Combined effect estimates calculated from country-specific estimates using random effects model.

personal exposure of subjects is strongly related to the outdoor air pollution level measured at a central site in the community [25]. For individual subjects, differences in exposure from the population average may occur. However, much of the measurement error is likely to be Berkson error, which generally does not lead to bias [26]. Finally, the Swiss SAPALDIA (Swiss study on Air Pollution and Lung Disease In Adults) and the Children's Health study study reported an effect of both within and between community contrasts in NO_2 exposure on lung function of adults and children's respiratory symptoms [7, 27, 28]. Chronic bronchitis of adults in the European Community Respiratory Health Survey was associated with individual level variables representing traffic, but not centre level variables such as the central site $PM_{2.5}$ concentration [29]. In that study, the between-community contrast, however, was largely due to differences between countries, a contrast that we specifically decided not to assess because of the potential for too many differences for which we did not have data. Despite the value of assessing community-level pollution, there is a clear need for assessment of the health effects of near-traffic exposures. There is, for example, some evidence that asthma incidence in children and adults may be associated with near-traffic exposures and not with urban background pollution [30].

In conclusion, our study adds to the evidence that long-term exposure to outdoor air pollution, characterised by the concentration of PM_{10}, is associated with increased respiratory symptoms (phlegm and morning cough) in children. We did not find an association between PM_{10} and lung function, possibly due to modest pollution levels and heterogeneity across studies.

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STATEMENT OF INTEREST

None declared.

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