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Parental education and lung function of children in the PATY study

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ABSTRACT

Studies of the relationships between low socio-economic status and impaired lung function were conducted mainly in Western European countries and North America. East-West differences remain unexplored. Associations between parental education and lung function were explored using data on 24,010 school-children from 8 cross-sectional studies conducted in North America, Western and Eastern Europe. Parental education was defined as low and high using country-specific classifications. Country-specific estimates of effects of low parental education on volume and flow parameters were obtained using linear and logistic regression, controlling for early life and other individual risk factors. Meta-regressions were used for assessment of heterogeneity between country-specific estimates. The association between low parental education and lung function was not consistent across the countries, but showed a more pronounced inverse gradient in the Western countries. The most consistent decrease associated with low parental education was found for peak expiratory flow (PEF), ranging from -2.80 % to -1.14 %, with statistically significant associations in 5 out of 8 countries. The mean odds ratio for low PEF (<75 % of predicted) was 1.34 (95% CI 1.06–1.70) after all adjustments. Although social gradients were attenuated after adjusting for known risk factors, these risk factors could not completely explain the social gradient in lung function.

Key words: lung function, parental education, combined analysis, East-West differences, PATY study, children

ABBREVIATIONS

A	Austria
BMI	body mass index
CI	confidence interval
CZE	Czech Republic
FEV1	forced expiratory volume in the first second
FVC	forced vital capacity
GER	Germany
HUN	Hungary
LBW	lower birth weight
LRI	low respiratory tract infection
MMEF	maximal mean expiratory flow
NL	the Netherlands
OR	odds ratio
PATY	Pollution and the Young (<i>project</i>)
PEF	peak expiratory flow
POL	Poland
SES	socioeconomic status
SLO	Slovakia
US/USA	North America

INTRODUCTION

Socioeconomic status (SES) has been found an important predictor of health within developed countries. Publication of the Whitehall study results [1], reporting differences in all-cause mortality between social classes, was followed by an increased interest in the issue of social health inequalities in epidemiological research [2-3].

Only a limited number of studies have investigated the SES effect on impaired lung function or chronic obstructive pulmonary disease. Studies on adults found evidence that the level of education was associated with airways disorders independently of smoking [4-5]. A review by Hegewald and Crapo [6] found significantly negative correlations between lung function and SES both in children and adults.

The CARDIA study [7] on young adults found a decline of lung function over time due to lower childhood SES. A British study [8] confirmed that childhood poverty was associated with poorer lung function in women aged 60-79.

American studies with large sample size [9-10] also brought evidence that low SES was associated with lower lung function in children.

An Austrian study of school age children [11] found that most of lung function measures were negatively associated with a lower birth weight (LBW), lower maternal education, smaller gestational age, and larger family size.

Associations between low SES and impaired lung function both in children and adults were detected mainly in Western European countries and North America. East-West differences have not yet been explored.

The PATY project (Pollution and the Young) offers a unique opportunity to investigate the relationship between lung function in school-age children and their socioeconomic status in a large international dataset.

MATERIAL AND METHODS

Study design and study population

The present study is a combined analysis of questionnaire and lung function data from 8 cross-sectional studies in which the lung function measurements were part of the original studies. The study sample contained 24,010 school-children aged 6-12 years from the North American 24-cities study [12], the East European CESAR study countries [13], and data from Austria (Linz study [14]), Germany (Bitterfeldt, Hettstedt and Zerbst study [15]), and the Netherlands (24-schools study [16]). The number of children derived from the original studies into a current analysis is slightly smaller due to missing data – only those with a full set of data were taken into the analysis. The studies were conducted across the 1990s. Some studies were conducted in several areas of one country, whereas others (CESAR and the 24-cities study) were conducted in more than one country.

The combined analyses used original data including measures of lung function, and questionnaire information on a wide range of potential risk factors including sources of indoor air pollution, socio-economic status, family medical history etc.

Definition of parental education status

Parental education was defined as the maximum of the mother's and father's educational level and classified into three categories (low, medium, and high) as described previously [17]. This classification was done at country level, taking frequency distributions into account to make sure that every country had a sufficiently large number of subjects with low and high parental education, respectively [17]. Nevertheless, for the present analyses the frequency of "low lung function" (see below) was found to be too small in low parental education category (as defined by Gehring et al. [17]) in some countries and therefore, the low and medium parental education categories were joined and defined as "low". Only subjects with a defined parental education were included in the analysis.

Lung function outcomes

Lung function testing was performed according to the protocol of the American Thoracic Society [18], except for the minimum exhalation time of 6 s (not feasible for children) and except for the Dutch study, which followed the protocol of the European Respiratory Society [19].

We analyzed the following volume and flow parameters: forced vital capacity (FVC), forced expiratory volume in the first second (FEV1), peak expiratory flow (PEF) and maximal mean expiratory flow (MMEF). MMEF data were not available from Germany.

In addition, “low lung function” was analyzed, specified by low FVC (defined as less than 85 % of predicted by age, gender, height, and weight from all study participants from the same country), low FEV1 (less than 85 % of predicted), low PEF (less than 75 % of predicted) and low MMEF (less than 75 % of predicted) [20]. These cut-off levels were based on a priori clinical experience. Effect on poor lung function was analyzed by logistic regression.

Potential confounders

A set of a-priori confounders was prepared based on the literature. Confounders were divided into two groups: early life factors such as maternal smoking during pregnancy, premature birth (< 36 weeks), low birth weight (less than 2.3 kg), breastfeeding (less/more than 3 months), attendance of kindergarten, low respiratory tract infection (LRI) in first 2 years of life, and parental history of asthma; and other potential confounders like body mass index (BMI) [21], the presence of any smoker in the household, pet ownership ever, overcrowding, presence of mould/moisture in the child’s home, use of gas for cooking or gas/kerosene/oil heater and infection prior to test.

Statistical analysis

Since lung growth during childhood is not linear, the lung function variables were log-transformed for calculation of predicted values, i.e. the linear (for continuous outcomes)

regression models used the natural logarithm of each lung function variable as the dependent variable and the relationship with body parameters were described using the natural logarithm of age and weight including an interaction between sex and natural logarithm of height.

Data were analyzed in two stages. In stage one, country-specific estimates of effects of low parental education were estimated using linear regression for the continuous outcomes and logistic regression for the binary outcomes. The models included random effects at area level allowing for geographic clustering of outcomes.

In stage two, these country specific effect-estimates and their standard errors were pooled using meta-analytic methods, obtaining a mean estimate and a measure and Cochran ² test of heterogeneity. Country-specific effects are assumed to follow a random distribution about a mean, and the estimation of this mean (and confidence interval) takes into account variations both within and between studies [22].

All country-specific and pooled estimates were produced in three models – Model 1 controlled for age, sex, weight, height, and technician (technician who performed the lung function testing). In Model 2 early life factors were added; and in the third model the other potential confounders were considered (Table 1).

The magnitude of the effect of each confounder was tested separately. The final set of confounders was selected for all potential confounders that change odds ratios (OR) for any of the low lung function indicators by more than at least 10 % in one country (Table 1).

As indicated, not all potential confounding variables were available for all studies - sensitivity analyses were conducted to assess the impact of unavailability of covariates, by comparing results between studies with full set and restricted sets of confounders. As the US data represents the largest group further sensitivity analysis was performed on the restricted data set without American data.

Meta-regressions were used to assess whether the following study characteristics could explain heterogeneity between country-specific estimates: East/West differences based upon a hypothesis of different health status in Western countries and former Eastern block (Germany was coded Eastern country as the study was conducted in the Eastern part of Germany), response rate lower than 80 %; earlier studies (arbitrary stated cut-point 1995); proportion of young children (6-8 years versus 9-12 years); proportion of high parental education, and study design: whether the study was conducted within-towns, between-towns or a mixture.

All analyses were performed in STATA version 8.

RESULTS

The distribution of parental education, confounders and potential sources of heterogeneity across countries are summarized in Table 1. The prevalence of higher education differed between countries, ranging from 13.7 % in Germany to 67.1 % in North America.

Final set of confounders

The final set of early life factors (Model II) included mother smoking during pregnancy (highest change of OR for low MMEF -11.4 % in the Netherlands and for low PEF -13.8 % in Poland), premature birth, low birth weight, attendance of kindergarten and breastfeeding. Other a-priori confounders did not meet the set criteria and therefore they were not used for analysis. Controlling for these risk factors changed odds ratios only slightly, e.g. LRI in first 2 years of life with the greatest change being -6.6 % for low MMEF in Poland. A still weaker impact was made by controlling for parental history of asthma.

The final set of other risk factors to be adjusted for in Model III were BMI (highest change of OR for low FEV1 by 15.7 % in Poland), presence of a smoker in the household (highest change of OR for low FVC -20.3 % in the Czech Republic), pet ownership (changed OR for low PEF by -14.8 % in Hungary) and overcrowding (highest change of OR for low PEF -20.0 % in Poland). Presence of mould/moisture in the child's home, use of gas for cooking or

gas/kerosene/oil heater and infection prior to test modified the relationship between low parental education and health outcomes only little, so that were not included into the final set of confounders.

Continuous lung function analyses

The association between continuous lung function parameters and low parental education was not consistent across the countries (Fig. 1). The results of the fully adjusted linear regression model varied between countries, ranging for FEV1 and FVC from changes of -1.09 % and -1.08 % respectively in Germany to changes of +1.43 % and +1.33 % respectively in Poland; and MMEF changes ranged from -1.66 % in Slovakia to +1.70 % in Poland. The most consistent decrease was found for PEF, ranging from -2.80 % in the USA to -1.14 % in Hungary and the results were statistically significant in 5 out of 8 countries.

In the basic model low parental education was associated with a significant overall mean decrease of PEF (-2.2 %) and MMEF (-1.4 %) with no indication of heterogeneity between studies (Table 2). No association with FVC and a borderline significant association with FEV1 were found in Model I with evidence of heterogeneity ($p < 0.10$) for both these outcomes – Table 2. After controlling for early life factors the effect of low parental education on lung function parameters slightly decreased except for PEF. Further adjustment for all other potential risk factors confirmed the only significant association between low education and PEF (-2.4 %) and still borderline significance with MMEF (-0.8 %).

Low lung function analyses

The overall distribution of low lung function varied modestly between countries. The mean distribution of low FEV1 reached 6.5 %, low FVC 6.1 %, low PEF 5.2 % and low MMEF 10.6 % across the countries (Table 3).

The mean odds ratios describing the association between parental education and prevalence of low lung function were statistically significant for FVC, PEF and MMEF and ranged from

1.18 for MMEF to 1.38 for PEF in the baseline Model I (Fig. 2). The associations with parental education persisted after additional adjustment for early life factors and other potential confounders, but were statistically significant only for PEF in Model III (Fig. 2). Mean odds ratios for FEV1 were not statistically significant, with considerable between-country heterogeneity. The fully adjusted model gave slightly lower mean odds ratios for FVC and MMEF compared with the basic model. For PEF, where the largest adverse effects were seen, the mean OR changed only slightly after adjustment from 1.38 (95% CI 1.08-1.76), to 1.34 (95% CI 1.06-1.70). The results indicate that the association with parental education could not be fully explained by the additional studied risk factors.

Analysis of heterogeneity of results

Country-specific results tended to be heterogeneous. We explored this heterogeneity, focussing on the low lung function measures. The significant source of heterogeneity of the results was the differences between the Western and Eastern countries for FEV1, and differences between countries with higher (more than 80 %) and lower response-rate for PEF (Table 4).

The association between low FEV1 and low parental education appears to be confined to Western countries (OR=1.28; 95% CI 1.10-1.49), where the ORs varied from 1.20 (95% CI 1.01-1.43) in North America to 1.56 (95% CI 0.96-2.53) in the Netherlands (Table 4, Fig. 2).

The same East-West difference was not apparent for low FVC, MMEF or PEF.

All other study characteristics (proportion of young children, proportion of high parental education, and study design) could not explain heterogeneity between country-specific estimates.

Sensitivity analysis

The impact of missing confounding variables in some studies on the meta-analysis results was explored in sensitivity analyses. Study results for each of the health outcome were compared

between groups of studies with the full availability of covariates, studies with 5 items missing (early life factors and overcrowding in Austria) and 3 items missing (breastfeeding, attendance of kindergarten and presence of pets in a household in North America). The sensitivity analyses indicated that the missing confounders in some studies did not significantly change the results.

Excluding the US data lead to broader confidence intervals, decreased % change of lung function parameters (FEV1, FVC, MMEF) and loss of heterogeneity of results for FEV1. Indication of heterogeneity of results in the restricted data set has still been confirmed for FVC. Other results were found out regarding PEF – the point estimates for the percentage difference in fully adjusted models decreased from -2.4 % in the full dataset to -1.9 % in the restricted data set and heterogeneity decreased practically to zero. All the models for PEF (full data set, restricted data set and US data set itself) provided statistically significant results with narrow confidence intervals.

DISCUSSION

This study found positive associations between low lung function and low parental education. Significant risk increases of low lung function parameters (PEF OR=1.38, FVC OR=1.28, and MMEF OR=1.18) were associated with low parental education before inclusion of potential risk factors. Odds ratios for low FVC and MMEF were reduced and became statistically non-significant after adjustment for other risk factors, but the risk of low PEF remained persistent after adjustment, decreasing only slightly to OR=1.34. The overall effect of SES over LF parameters was found. That only PEF remained significant is mostly due to the fact that PEF shows the smallest chance variation. So here the power to detect small effects is greatest.

Our study results support findings from other studies on socio-economic differences of lung function [5, 9-10] mostly being carried out in the Western countries and showed that the social gradient is less pronounced in Eastern European countries.

In a previous analysis of the PATY data [17], adverse effects of low parental education were observed on prevalences of wheeze and nocturnal dry cough. The association with wheeze was mainly restricted to children from Eastern Europe, and the authors commented that different distributions of atopy and different patterns of link between wheeze, atopy, and SES in Eastern and Western countries might have played a role [17]. The East-West effect modification for lung function, reported in the current paper, is in the opposite direction, with higher effects of low education occurring in the Western countries. We speculate that this may be partly due to a more pronounced link in Western countries between individual-level socioeconomic status and area-level deprivation, with the latter – acting perhaps via factors such as housing quality, ambient air pollution, etcetera – having its own adverse effects on lung function [23].

Explanation of associations with education by other risk factors

The study results might be conservative. Inclusion of other risk factors may result in over-adjustment as part of the behaviours, e.g. smoking, or living conditions, e.g. mould in the home, may be in the causal chain from socio-economic conditions and health.

Low respiratory tract infection in early childhood had been hypothesized to be one of the risk factors [11], but in our multi-country study controlling for this risk factor changed odds ratios only slightly. The impact of early life factors on lung function data in our study confirmed the results of previous studies – maternal smoking during pregnancy [20], day-care attendance [24], and low-birth weight and premature birth [11].

Passive smoking is one of the most important confirmed risk factor of impaired lung function [20, 25-26]. This was again confirmed in this study.

Brunekreef et al. [27] reported dampness and moulds to be a strong predictor of impaired lung function. But in our study mould/moisture did not relevantly affect the relationship between education and health outcomes.

Some studies reported SES differences in outdoor/indoor air pollution [28-31]. However adverse effects on lung function are reversible with the improvement of air quality [14, 32]. In spite of these reported class-specific differences of indoor exposure, the impact of gas use for cooking or use of unvented gas/kerosene/oil (water) heater had only a weak impact on relationships being investigated in our study.

Some studies reported racial differences to be a cause of different lung function outcomes [33-34]. The information on race of children was not available in most of component studies. For the Austrian, the Netherlands and the US datasets the information on nationality/race was available, but it concerned only minorities representing around 3.5 % of the study sample in the US and the Netherlands. In the Austrian data nationality was based on „child’s language“ and minorities varied from 2.3 - 8.4 %. To avoid confounding of effect estimates caused by genetic aspects relating with the different race (in the US data) and ethnic differences probably interacting both with SES and culturally determined life-style only data on major population was analysed.

No comparative data on physical activity was available. Instead BMI was included into a set of potential confounders as the association between lung function parameters and overweight in children was confirmed by several studies [35-37].

We have to acknowledge that our variable ‘low education’ may not be fully equivalent across all countries, and that quantitative results from pooling country-specific effect estimates may be seen as indicative rather than as numeric absolutes. Gehring et al., reporting on parental education and respiratory symptoms in the PATY study [17], expressed a confidence that parental education really reflected the children's SES, based on consistency of the association

between parental education and crowding. Furthermore, our analyses of heterogeneity did not find differences of results between countries with different proportions of high parental education. However, the country-specific effect estimates themselves and the patterns of association seen across them, remain important results, besides the mean estimates presented. It is worthy to notice that education as previously defined (Gehring et al.) (17) is a proxy of SES for a broader range of possible risk factors for low lung function that can be modified, including quality of housing, poor sanitation, air pollution in a living area, ETS exposure, diet, physical activities, access to health care etc. Even when a range of these risk factors that are linked to SES (mother smoking in pregnancy, premature birth/low birth weight, breastfeeding, attending kindergarten, presence of current smoker in a household, pet ownership ever and overcrowding) are included in the model there remains an effect of low parental education that is not explained by these specific risk factors. That proxy SES measures, such as low education, can explain more variation in ill-health than the sum of the known individual risk factors, illustrates precisely the strength of SES as a concept of health relevance.

East-West differences

Analysis of heterogeneity confirmed East-West differences in study results for low FEV1 and low FVC and differences between groups of countries according the response-rate (below/above 80 %) for low PEF. Considering that higher response rates were seen in the US, Austria, and German studies, and East-West and response-rate differences greatly overlapped, it can be assumed that the differences are caused more likely by East-West than response-rate differences.

East-West differences were also found in analyses of wheeze and low parental education in the earlier paper [17]. The opposite East-West pattern was seen in the present analysis - higher risks of low FEV1 and low FVC were seen in children from less educated families in

the Western countries. The observed East-West differences in relationship between low education and lung function might be ascribed to differences in factual status [38-39] regarding occupational class, material resources, life-style and behavior patterns, with education in Eastern countries not necessarily a good indicator of affluence due to low consistency of socio-economic status. This speculation is supported by Davey-Smith et al. [40] who argued that material resources related to occupational social class rather than culturally based sources related to education should be key determinants of socio-economic differentials. However, information on occupational social class of parents was not available for most studies.

Although the data were acquired in the period from 1988 to 1998, the authors are confident of its relevance. Such large datasets, especially for the US population have not been collected since that period. The East-West differences in social health inequalities might have changed since that time. Education is having a much more important role in socio-economic status in the Eastern countries. But the argument of material conditions as key determinant of socio-economic health differences remains, and this still persists between Western and Eastern countries.

CONCLUSIONS

The results of the study confirmed a higher risk of low lung function in children from less educated families. The associations with parental education were more pronounced in the Western countries, while in the Eastern countries the direction of the association was not consistent, which might be explained by the low consistency of socio-economic status in the former socialist countries. Although social gradients were attenuated after adjusting for several known risk factors, these risk factors could not completely explain the social gradient in lung function.

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ETHICS COMMITTEE APPROVAL

The paper combines the data from the 8 previous cross-sectional studies - all of them were approved by the Ethics Committees.

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FIGURES

Figure 1 Forest plots for the effect estimates of low parental education

Figure 2 Forest plots for the association between low FEV1, FVC, PEF and MMEF and low parental education

Table 1. Description of the studies and the study sample (in total 24,010 children)

Country abbreviation *	POL	HUN	SLO	CZE	NL	GER	A	US	All
Number of study-areas	4	5	4	4	24	3	8	24	76
Number of towns	4	5	3	1	19	3	1	24	60
Year(s) of questionnaires & lung function	96	96	96	96	97/98	92/93	96-98	88-90	88-98
Number of children (n)	1 472	1 613	970	806	1 734	1 788	2 898	12 729	24 010
Male sex (n)	726	768	519	455	859	902	1 544	6 497	12 270
% from country sample	(49.3)	(47.6)	(53.5)	(56.5)	(49.5)	(50.4)	(53.3)	(51.0)	(51.1)
Age range selected for lung function testing	9-12	9-12	9-12	9-12	7-12	6-12	6-11	8-12	6-12
Age group 9-12 (n)	1 472	1 613	970	806	1 225	1 230	73	12 057	19 446
% from country sample	(100.0)	(100.0)	(100.0)	(100.0)	(70.6)	(68.80)	(2.5)	(94.7)	(81.0)
High parental education (n)	259	418	400	205	704	233	999	8 207	11 425
% from country sample	(17.6)	(25.9)	(41.2)	(25.4)	(40.6)	(13.0)	(34.5)	(64.5)	(47.6)
Early life factors (Model II)									
Mother smoking during pregnancy (n)	371	201	63	72	464	86	511	3 296	5 064
% from country sample	(25.2)	(12.5)	(6.5)	(8.9)	(26.8)	(4.8)	(17.6)	(28.9)	(21.1)
Premature birth (n)	150	134	78	65	170	132	-	588	1 317
% from country sample	(10.2)	(8.3)	(8.0)	(8.1)	(9.8)	(7.4)	-	(4.6)	(5.5)
Low birth weight < 2.3 kg (n)	162	145	85	67	189	149	-	591	1 388
% from country sample	(11.0)	(9.0)	(8.8)	(8.3)	(10.9)	(8.3)	-	(4.6)	(5.8)
Breastfeeding (n)	997	1 196	860	691	1 098	1 387	-	-	6 229
% from country sample	(67.7)	(74.1)	(88.7)	(85.7)	(63.3)	(77.6)	-	-	(25.9)
Attendance kindergarten (n)	221	329	390	242	160	1 221	-	-	2 563
% from country sample	(15.0)	(20.4)	(40.2)	(30.0)	(9.2)	(68.3)	-	-	(10.7)
Other potential confounders (Model III)									
Current smoker in a household (n)	983	913	521	471	982	823	1 690	6 282	12 665
% from country sample	(66.8)	(56.6)	(53.7)	(58.4)	(56.6)	(46.0)	(58.3)	(49.4)	(52.7)
Pet ownership ever (n)	939	749	441	477	1 301	1 161	1 317	-	6 385
% from country sample	(63.8)	(46.4)	(45.5)	(59.2)	(75.0)	(64.9)	(45.4)	-	(26.6)
Crowding (n)	258	211	111	87	221	267	-	2 123	3 278
% from country sample	(17.5)	(13.1)	(11.4)	(10.8)	(12.7)	(14.9)	-	(16.7)	(13.7)
Overweight and obesity (n)	273	254	149	186	291	289	558	4 219	6 219
% from country sample	(18.6)	(15.8)	(15.4)	(23.1)	(16.8)	(16.2)	(19.3)	(33.2)	(25.9)
Variables for exploring heterogeneity									
East_West (East=1, West=0)	1	1	1	1	0	1	0	0	
Response rate < 0.8 (yes=1)	1	1	1	1	1	0	0	0	
Post 1995 study (yes=1)	1	1	1	1	1	0	1	0	
Proportion of young children (< 20%=1, med=2, >80%=3)	2	2	2	2	2	2	3	1	
Proportion high parental education < 30 % (yes=1)	0	0	1	0	1	0	1	1	
Study design within-towns, between-, mixture (W, B, M)	B	B	M	W	M	B	W	B	

* Country abbreviation Study

POL Poland (CESAR study) Leonardi et al. 2002 [13]

HUN Hungary (CESAR study) Leonardi et al. 2002 [13]

SLO Slovakia (CESAR study) Leonardi et al. 2002 [13]

CZE Czech R (CESAR study) Leonardi et al. 2002 [13]

NL 24 school study, Netherlands Janssen et al. 2003 [16]

GER Bitterfeldt study, Germany Heinrich et al. 1999 [15]

A Linz Study, Austria Neuberger et al. 2002 [14]

US 24 city study, North America Raizenne et al. 1996 [12]

Table 2. The mean percentage change of lung function parameters in association with low parental education for each outcome from the basic (adjusted for age, sex, height, weight and technician), early life factors and all confounder adjusted models. P-values for evidence of heterogeneity between study-specific results.

	Model I Basic model change % (95% CI)	Model II Early life factors adjusted change % (95% CI)	Model III Confounder adjusted change % (95% CI)
FEV1			
Estimate (Random)	-0.4 (-1.0; 0.1)	-0.3 (-1.0; 0.3)	-0.4 (-0.9; 0.2)
p-Heterogeneity	0.061	0.054	0.112
FVC			
Estimate (Random)	-0.1 (-0.7; 0.5)	-0.1 (-0.9; 0.6)	-0.2 (-0.8; 0.4)
p-Heterogeneity	0.013	0.017	0.028
PEF			
Estimate (Random)	-2.2 (-2.7; -1.7)	-2.2 (-2.7; -1.6)	-2.4 (-2.9; -1.8)
p-Heterogeneity	0.600	0.915	0.688
MMEF			
Estimate (Random)	-1.4 (-2.2; -0.6)	-1.1 (-2.0; -0.2)	-0.8 (-1.6; 0.04)
p-Heterogeneity	0.862	0.835	0.604

Table 3. Description of distribution of low lung function across the countries

Abbreviation	POL	HUN	SLO	CZE	NL	GER	A	US	All
low FEV1* (N)	42	66	50	30	102	103	152	802	1 347
% of study sample	6.8	5.3	5.2	3.7	6.3	6.5	6.4	7.0	6.5
low FEV1 in high parental edu (%)	11.0	5.9	6.0	2.9	5.0	4.6	4.9	6.7	6.3
low FEV in low parental edu (%)	5.8	5.1	4.6	4.0	7.3	6.8	7.3	7.8	6.8
low FVC* (N)	38	77	46	29	101	150	140	681	1 262
% of study sample	6.4	6.4	4.7	3.6	6.2	8.6	5.9	6.0	6.1
low FVC in high parental edu (%)	7.2	6.3	5.0	4.4	4.7	4.8	5.0	5.4	5.3
low FVC in low parental edu (%)	6.2	6.4	4.6	3.3	7.4	9.3	6.4	7.2	6.9
low PEF* (N)	20	28	59	32	75	74	127	669	1 084
% of study sample	3.4	2.3	6.1	4.0	4.6	4.3	4.0	5.9	5.2
low PEF in high parental edu (%)	1.7	2.7	6.5	2.9	4.4	1.7	3.8	4.8	4.6
low PEF in low parental edu (%)	3.8	2.2	5.8	4.3	4.8	4.7	6.3	8.1	5.9
low MMEF* (N)	60	104	92	81	166	-	276	1240	2 019
% of study sample	10.1	8.6	9.5	10.0	10.2	-	11.6	10.9	10.6
low MMEF in high parental edu (%)	11.7	6.0	9.0	9.3	8.8	-	10.4	10.4	10.1
low MMEF in low parental edu (%)	9.8	9.6	9.8	10.3	11.3	-	12.3	11.9	11.3

* Low lung function is measured lung function less than 85% (FVC, FEV1) or 75% (PEF, MMEF) of predicted lung function based upon age, sex, height and weight.

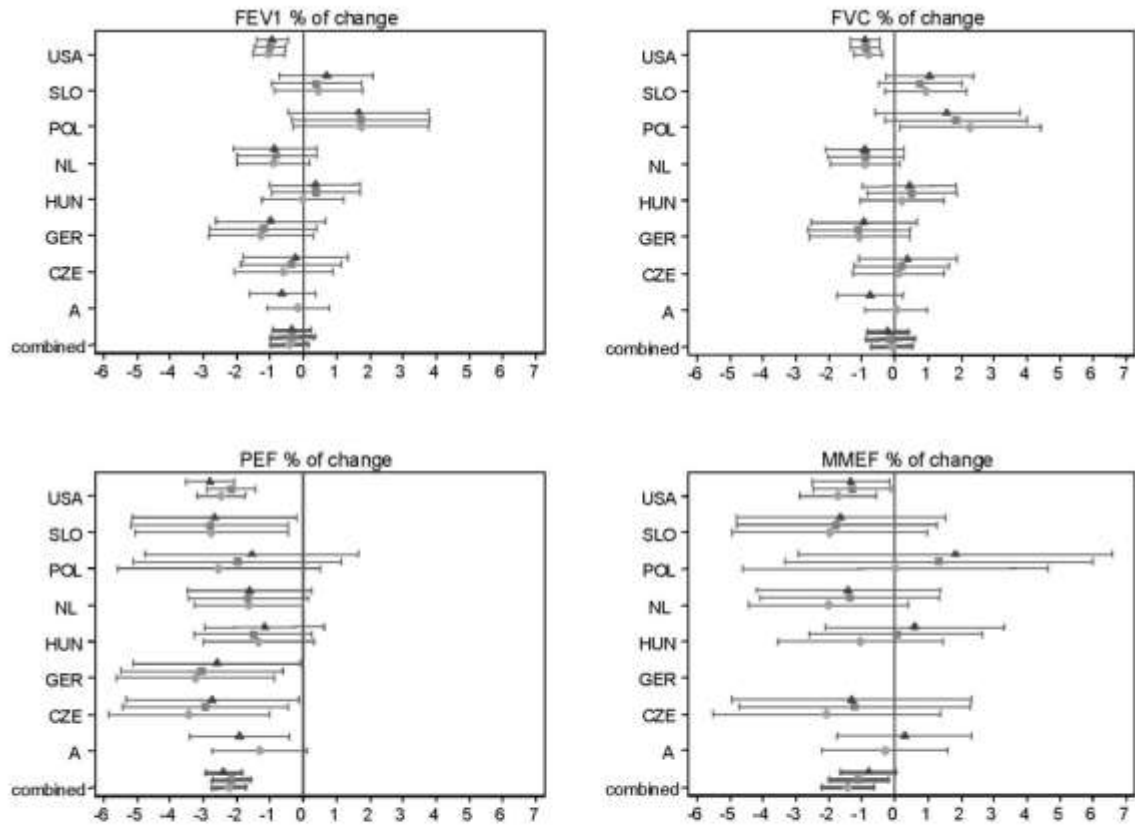
Table 4. Sources of heterogeneity of results - comparison of mean odds ratios for the association between low lung function and low parental education across subgroups of countries.

	No. of studies	Mean odds ratio (95% CI)	p-value
FEV1 low			
East*	5	0.86 (0.56 – 1.31)	
West	3	1.28 (1.10 – 1.49)	0.040
PEF low			
Response rate $\geq 80\%$ **	3	1.56 (1.32 – 1.84)	
Response rate $< 80\%$	5	1.01 (0.73 – 1.40)	0.020

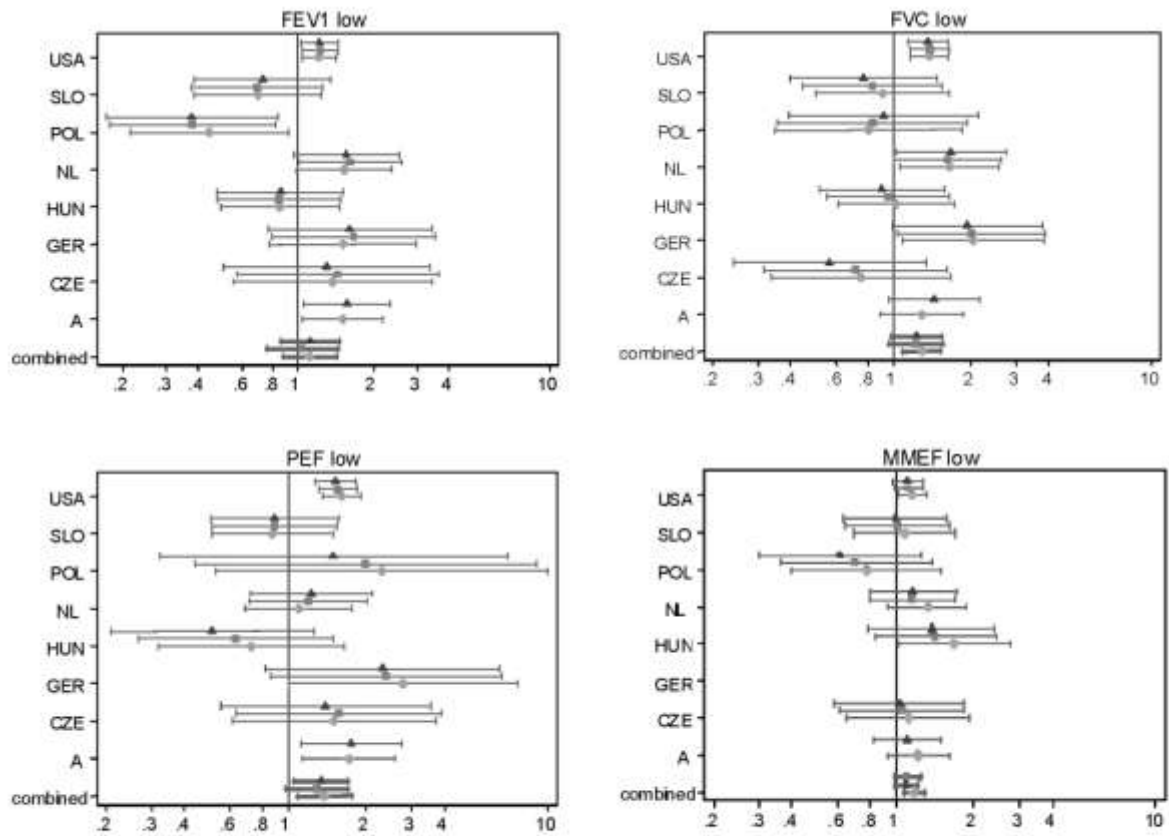
Only factors significantly associated with the size of the effect estimate are presented.

* East=Eastern countries /Poland, Hungary, Slovak Republic, Czech Republic, Germany/
West=Western countries /Netherlands, Austria, US/

** Response rate $< 80\%$ /Poland, Hungary, Slovak Republic, Czech Republic, Netherlands/
Response rate $\geq 80\%$ /Germany, Austria, US/



Effect estimates (% change) of low parental education (◆ basic model, ■ early life factors adjusted model, ▲ fully adjusted model). Vertical lines indicate null position. Horizontal lines represent 95% confidence intervals. Combined indicate random effect summary estimates (% change) and 95% confidence interval.



Effect estimates (Odds ratios) of low parental education (◆ basic model, ■ early life factors adjusted model, ▲ fully adjusted model). Vertical lines indicate null position (OR=1). Horizontal lines represent 95% confidence intervals. Combined indicate random effect summary estimates (OR) and 95% confidence interval.