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### **RESEARCH PAPER**

# Parental smoking and children's respiratory health: independent effects of prenatal and postnatal exposure

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**Objectives:** Adverse effects have been reported of prenatal and/or postnatal passive exposure to smoking on children's health. Uncertainties remain about the relative importance of smoking at different periods in the child's life. We investigate this in a pooled analysis, on 53 879 children from 12 cross-sectional studies—components of the PATY study (Pollution And The Young).

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Received 10 November 2005 Accepted 24 May 2006 **Methods:** Effects were estimated, within each study, of three exposures: mother smoked during pregnancy, parental smoking in the first two years, current parental smoking. Outcomes were: wheeze, asthma, "woken by wheeze", bronchitis, nocturnal cough, morning cough, "sensitivity to inhaled allergens" and hay fever. Logistic regressions were used, controlling for individual risk factors and study area. Heterogeneity between study-specific results, and mean effects (allowing for heterogeneity) were estimated using meta-analytical tools.

**Results:** There was strong evidence linking parental smoking to wheeze, asthma, bronchitis and nocturnal cough, with mean odds ratios all around 1.15, with independent effects of prenatal and postnatal exposures for most associations.

**Conclusions:** Adverse effects of both pre- and postnatal parental smoking on children's respiratory health were confirmed. Asthma was most strongly associated with maternal smoking during pregnancy, but postnatal exposure showed independent associations with a range of other respiratory symptoms. All tobacco smoke exposure has serious consequences for children's respiratory health and needs to be reduced urgently.

onsiderable attention has focused recently on the harmful effects of involuntary or "passive" smoking. Many studies have reported adverse effects of prenatal and/or postnatal exposure on children's respiratory health, with much of the literature summarised in a number of reviews.<sup>1-4</sup> Within a broad picture of harmful effects, uncertainties remain, including the relative importance of exposure at different periods in the child's life.

There is some evidence that prevalence of wheeze in childhood is associated more strongly to prenatal (intrauterine) exposure than with current parental smoking.<sup>5-9</sup> In the Italian study of Agabiti *et al*, the effect of current parental smoking on wheeze was evident only in adolescents but not among younger children, while the effect of maternal smoking during pregnancy was greater in children.<sup>10</sup> A Polish study found current exposure a stronger predictor than prenatal exposure,<sup>11</sup> while a study in Chicago found a protective association with current maternal smoking.<sup>12</sup> Similar inconsistencies have been seen for effects of tobacco exposure on child's asthma and other respiratory outcomes.<sup>2</sup> <sup>4</sup>

Several studies have shown protective effects of current parental smoking on atopy, or on atopic-related conditions such as eczema or hay fever.<sup>13–16</sup> Yet Lam *et al* found increased risks of hay fever related to passive smoking,<sup>15</sup> and passive smoking was also associated with allergic rhinoconjunctivitis and hay fever among Swedish and Turkish schoolchildren.<sup>17 18</sup>

The Pollution And The Young (PATY) project assembled data on exposures and health for 58 561 children, from crosssectional studies carried out in 12 countries with comparable questionnaires. PATY was established primarily to investigate associations between air pollution and respiratory health. Here we use that subset of 53 879 children with information on parental smoking. This pooled analysis, on extensive, original data (with only three of the 12 studies as yet published on this topic),<sup>19–21</sup> gives a powerful opportunity to examine critical periods of exposure to cigarette smoke, to address the problems of co-linearity between prenatal and postnatal passive smoking and to assess independent effects of three exposures: maternal smoking during pregnancy, passive smoking during the first two years of the child's life, and current passive smoking. Associations found in this large dataset between prenatal and postnatal passive smoking on children's lung function have already been reported.<sup>22</sup>

#### **METHODS**

Comparable cross-sectional studies were sought (published or otherwise), which assessed respiratory symptoms and individual risk factors at elementary school age by comparable parent's questionnaires,<sup>23</sup> included cough and wheeze as primary outcomes, and (since a primary objective was to assess effects of ambient air pollution) allowed calculation of annual mean particulate matter. To improve comparability further, data were restricted to children aged 6–12 years. Table 1 describes the contributing studies, detailed in individual reports.<sup>10</sup> <sup>19</sup> <sup>20</sup> <sup>24–29</sup>

All studies collected data on the children's health and individual/household risk factors (including exposure to tobacco smoke) via questionnaires, distributed in schools and filled in by the parents. Care was taken to select or construct variables which were as comparable as possible.<sup>23</sup>

Eight outcomes were analysed: wheeze in the last 12 months, "woken by wheeze in the last 12 months", asthma ever, bronchitis in the last 12 months, nocturnal

 Table 1
 Participating studies: geographic units, period of data gathering, and number of children, aged 6–12 years, with information on age, sex, and parental smoking

Study	Number of study areas	Data collection	Number of children	Age range (years)
Austria, Linz Survey	8 areas in 1 town	Jan 1996–Dec 1998	3776	6–8
Bulgaria, CESAR study	4 areas in 3 towns	Feb-May 1996	2973	7–11
Czech Republic, CESÁR study	4 areas in 1 town	Feb-May 1996	2962	7–11
Germany, Bitterfeldt study	3 areas in 3 towns	Aug 1992–Jul 1993	1972	6-12
Hungary, CESAR study	5 areas in 5 towns	Feb-May 1996	3031	7–11
Italy, Sidria study	29 areas in 22 towns	Oct 1994–Mar 1995	9073	6–10
Holland, 24 school study	24 areas in 19 towns	Apr 1997–Jul 1998	1913	7–12
North America, 24 city study	24 areas in 24 towns	Sep-Nov in 1988-90	14845	8–11
Poland, CESAR study	4 areas in 4 towns	Feb-May 1996	2643	7–11
Russia, 10-city study	13 areas in 10 towns	Apr-May 1999	5412	8-12
Slovakia, CEŚAR study	4 areas in 3 towns	Feb-May 1996	2531	7–11
Switzerland, Scarpol study	10 areas in 10 towns	Oct 1992–Mar 1993	2748	6-12
Total	132 areas in 105 towns		53879	

dry cough in the last 12 months, morning cough, "sensitivity to inhaled allergens", and hay fever ever. Detailed wordings are reported elsewhere.<sup>23</sup> Three "parental smoking" measures were defined: mother smoked during pregnancy, child lived with a smoker during the first two years of life (unavailable for Austria and Switzerland, in Germany "first year of life"), and child currently lives with a smoker. The latter included all smokers in the household, in all countries. Passive smoking during the first two years was restricted to parental smoking in Italy, Switzerland and the CESAR (Central European Study on Air pollution and Respiratory health) countries.

Only the exposures relate to different periods of the child's life. Health questionnaires were administered only once per child.

#### Statistical analyses

Analyses were done using STATA v8. A two-stage approach was used. In stage 1, study-specific parental smoking effects were estimated using logistic regression (on individual level records). Three models were used: The first ("confounder adjusted") controlled for potential confounders (listed below), but not for the other smoking variables. The second and third models additionally adjusted for one and then both other smoking variables. In stage 2, the study specific results were entered into a meta-analysis, to obtain forest plots of the estimates, a mean estimate (a weighted mean of the study specific estimates), and a measure and Cochran  $\chi^2$  test of between-study heterogeneity. Study specific estimates were assumed to follow a random distribution about a mean, and the estimation of this mean and its confidence interval took into account both variation among study-specific estimates and uncertainty (due to sampling variability) related to each study-specific estimate.30

We controlled for age, sex, maternal education, paternal education, nationality, household crowding, gas for cooking, unvented gas/oil/kerosene heater, mould, birth order, "ever had a pet", and study area. Adjusting for study area accounts for risk factors such as ambient air pollution, climate, and neighbourhood socioeconomic differences.

Meta-regressions assessed associations between studyspecific estimates and study-characteristics. These potential sources of heterogeneity between estimates were: season of data collection; study period; proportion of younger children (6–8 years old); response rate (above/below 80%); Western or former "Eastern Block" countries.

We tested robustness of results to controlling for parental illness (a potentially problematic variable, since parental smoking may cause both parent's and child's illness), attendance at kindergarten, and breastfeeding. We also assessed effect modification by age ( $6-8 \nu 9-12$ ), breastfeeding, household crowding and, since a recent study found that associations between maternal smoking during pregnancy and asthma were restricted to girls,<sup>31</sup> for effect modification by the child's sex.

#### RESULTS

Table 2 shows study characteristics, frequency of exposure to passive smoking, and prevalences of respiratory and allergic disorders. Bronchitis was reported most frequently, prevalences exceeding 30% in four of the studies. Hay fever and "woken by wheeze in the last 12 months" were reported least frequently, with prevalences under 10% in most studies.

Numbers living with a reported current smoker ranged from 45.8% in Germany to 70.9% in Bulgaria. Passive smoking during the first two years of life ranged from 18.7% in Germany (first year of life only), then from 46.3% in Russia, to 74.8% in Poland. Reported prenatal exposure tended to be rarer in Eastern countries and ranged from 4.4% in Russia to 28.7% in Holland.

The exposures were correlated, as anticipated. Coefficients of correlation (r) between current exposure and exposure during the first two years ranged from 0.22 in Germany to 0.75 in the Czech Republic. Between prenatal exposure and exposure in the first two years, r ranged from 0.16 in Bulgaria to 0.42 in North America and the Netherlands, and between current and prenatal exposure, r ranged from 0.14 in Bulgaria to 0.42 in North America.

#### Confounder adjusted results

Wheeze and nocturnal cough were associated with all three smoking measures, with harmful effects seen in nearly all studies (fig 1). Mean odds ratios for wheeze ranged from 1.17 (95% confidence interval (CI) 1.02 to 1.33) for the effect of smoking during the first two years, to 1.25 (95% CI 1.14 to 1.37) for smoking during pregnancy (table 3).

There was evidence of heterogeneity (within a strong predominance of positive results) among results for both current smoking and smoking during the first two years. Mean odds of nocturnal cough were raised by around 12% for all three smoking variables, with no evidence of heterogeneity.

Asthma was clearly related to smoking during pregnancy, with a mean odds ratio of 1.18 (95% CI 1.08 to 1.28). Odds ratios for the other periods of exposure were also above one in nine of the 12 countries, with no evidence of heterogeneity.

Associations between current smoking and "woken by wheeze" were predominantly positive, with a mean odds ratio of 1.12 (95% CI 0.99 to 1.25). For the other two smoking

	Austria	Bulgaria	Czech	Germany	Hungary	Italy	Holland	N America	Poland	Russia	Slovakia	Switz
East/West (E or W)	>	ш	ш	ш	ш	>	>	>	ш	ш	ш	≥
2/3 questionnaires in spring. $1 = yes$ , $0 = no$	0	_	-	0	-	0	0	0	-	0	_	0
Post 1995 study. 1 = yes, 0 = no	-	-	-	0	-	0	-	0	-	-	-	0
Response rate <0.8. 1 = yes, 0 = no	0	0	-	0	-	0	_	0	-	0	-	-
% of children in age range 6–8 years	98	44	34	32	30	61	33	5	37	17	34	55
Frequencies of exposures (%):												
Maternal smoking during pregnancy	17.5%	6.4%	8.9%	4.9%	12.7%	17.2%	28.7%	26.6%	25.3%	4.4%	6.0%	17.0%
Smoking during first 2 years of life	I	70.1%	62.0%	18.7%	62.9%	57.6%	60.7%	63.4%	74.8%	46.3%	54.9%	I
Current smoker in household	62.5%	70.9%	57.4%	45.8%	55.9%	58.2%	58.1%	50.4%	64.9%	46.1%	48.4%	48.2%
Prevalences of symptoms (%):												
Wheeze in last 12 months	13.67	16.41	19.76	10.21	9.92	6.76	9.45	19.40	11.84	13.29	9.37	10.32
Asthma ever	8.49	16.50	9.72	8.52	22.35	8.99	8.06	9.69	10.21	1.86	6.88	9.00
Bronchitis in the last 12 months	I	23.69	41.12	I	32.57	12.40	7.82	6.19	34.60	14.71	30.94	18.26
Nocturnal dry cough	10.40	5.35	18.54	18.57	9.42	15.66	21.74	I	13.55	I	12.83	21.57
Morning cough	5.28	16.02	25.61	13.82	6.17	I	I	6.02	45.71	11.35	14.40	11.83
Sensitivity to inhaled allergens	12.85	12.37	16.67	I	14.02	10.92	15.17	21.00	13.90	6.44	14.65	13.70
Hay fever ever	5.32	I	I	4.55	I	7.78	7.19	14.34	I	1.20	I	10.10
Wóken by wheeze in the last 12 months	I	7.07	14.78	I	8.37	1.87	4.92	5.18	8.62	4.25	8.58	4.59

measures results were less clear—mean associations were positive, but with considerable heterogeneity.

Bronchitis was related to current smoking, and to smoking during the first two years, with mean odds ratios of about 1.10 (fig 2). Associations of bronchitis with smoking during pregnancy were heterogeneous, within no clear pattern.

For all three exposures, effect estimates for hay fever were predominantly negative, with Russia the main exception (fig 2). Mean odds ratios for both the effect of smoking during the first two years and of smoking during pregnancy were around 0.90. The Russian estimate for current smoking was large, giving rise to some between study heterogeneity (p = 0.10).

Effect estimates of current smoking on "sensitivity to inhaled allergens" showed some apparently protective effect, with mean odds ratio of 0.96 (95% CI 0.91 to 1.02). For smoking during pregnancy, and smoking during the first two years, estimates tended to be small and mean odds ratios essentially null.

Mean effect estimates for morning cough were positive for all exposures, up to 1.12 (95% CI 0.99 to 1.27) for smoking during the first two years, but with heterogeneity between studies within unclear patterns of association.

Few consistent associations were seen between study specific results and potential sources of heterogeneity tested, and differences between groups of studies were generally small. Odds ratios tended to be inversely related to the proportion of younger children in the study. For smoking during pregnancy, estimates were higher in the later studies for most outcomes, and also in the studies with lower response rates (categorisations which overlapped considerably).

#### Independent effects of the exposure periods

For most of the outcomes strongly associated with smoking during pregnancy (wheeze, asthma, hay fever), associations remained robust to all adjustments. For nocturnal cough, the association became of borderline statistical significance. Mean, fully-adjusted odds ratios were 0.89 (95% CI 0.80 to 1.00) for hay fever, and around 1.15 for these other four outcomes (table 3).

Of those outcomes most strongly associated with smoking during the first two years of life (wheeze, asthma, bronchitis, nocturnal cough, hay fever), associations with bronchitis, wheeze and nocturnal cough were independent of smoking during pregnancy (data not shown), but were weakened in the fully adjusted model.

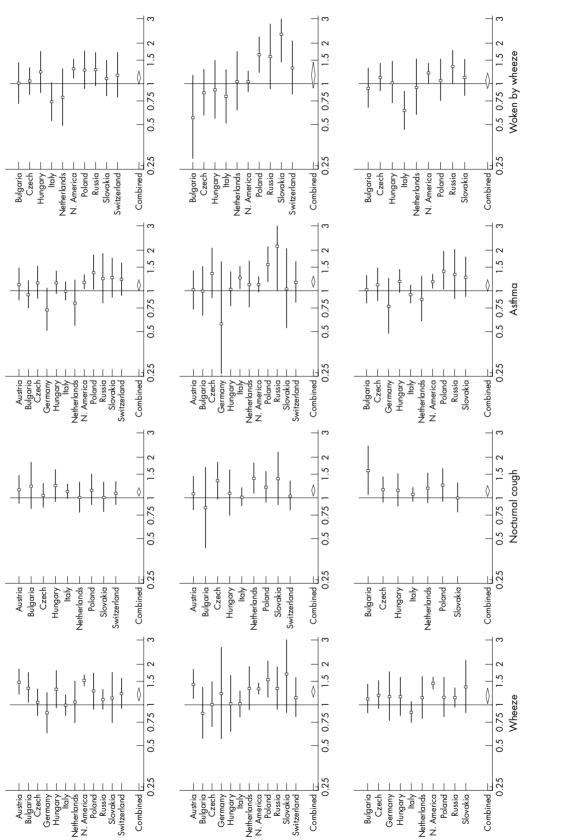
For current smoking, associations with bronchitis and "woken by wheeze" remained robust after all adjustments (table 3). Those for wheeze and nocturnal cough were independent of smoking during pregnancy (data not shown), and odds ratios remained raised after all adjustments, albeit not statistically significant. The mean odds ratio for asthma was considerably reduced by these adjustments.

#### Sensitivity analyses

There was no consistent effect modification by age within the individual studies.

In more crowded households than less crowded ones mean effects were greater for wheeze, bronchitis, and both coughs, but lower for asthma and sensitivity to inhaled allergens. The strongest interaction was found for morning cough: a mean odds ratio 17% higher (95% CI -1% to 39%) in crowded households than in less crowded ones.

In those studies for which parental illness data were available, parental allergy did not confound associations between child's "sensitivity to inhaled allergens" and parental smoking, nor parental lung disease for nocturnal cough, nor parental asthma for child's asthma. For hay fever,





Kposure to:         Exposure to:           Current smoking         Smoking in pregnancy         Smoking in pregnancy         Smoking in pregnancy           Current smoking         Confounder adjusted         Fully adjusted         Fully adjusted         Fully adjusted         Fully adjusted           Weeze         1.20 (1.06 to 1.35) <sup>1++</sup> 1.12 (0.98 to 1.27) <sup>1+</sup> 1.26 (1.14 to 1.37) <sup>++</sup> 1.17 (1.02 to 1.33) <sup>1++</sup> 1.06 (0.95 to 1.19)           Weeze         1.11 (1.05 to 1.18) <sup>1+</sup> 1.03 (0.92 to 1.16) <sup>1+</sup> 1.03 (0.92 to 1.12) <sup>1+</sup> 1.04 (0.95 to 1.12) <sup>1+</sup> 1.03 (0.92 to 1.12) <sup>1+</sup>		Fully adjusted	Smaking in pregnancy			
$ \begin{array}{c c c c c c c c c c c c c c c c c c c $		Fully adjusted	Smoking in preductory			
$ \begin{array}{ c c c c c c c c c c c c c c c c c c c$		Fully adjusted	Annowing in Pricylind		Smoking in first 2 years	
$ \begin{array}{c ccccccccccccccccccccccccccccccccccc$			Confounder adjusted	Fully adjusted	Confounder adjusted	Fully adjusted
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$			1.25 (1.14 to 1.37)**	1.12 (1.04 to 1.22)**	1.17 (1.02 to 1.33) <sup>H</sup> *	1.06 (0.95 to 1.19)
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$			1.18 (1.08 to 1.28)**	1.17 (1.04 to 1.31)*	1.10 (1.00 to 1.21)*	1.04 (0.95 to 1.14)
ough     1.11 (1.03 to 1.19)**     1.05 (0.94 to 1.17)     1.13 (1.03 to 1.24)**     1.15 (1.00 to 1.32)     1.11 (1.03 to 1.21)**       1.07 (0.98 to 1.16)     1.04 (0.95 to 1.13)     1.12 (0.97 to 1.30) <sup>H</sup> 1.14 (0.94 to 1.39) <sup>H</sup> 1.12 (0.99 to 1.27) <sup>H</sup> aled allergens     0.96 (0.91 to 1.02)     0.96 (0.88 to 1.04)     0.98 (0.91 to 1.05)     0.98 (0.91 to 1.07)     1.02 (0.94 to 1.12) <sup>H</sup> 0.92 (0.81 to 1.04)     0.99 (0.81 to 1.20) <sup>H</sup> 0.87 (0.77 to 0.96) <sup>H*</sup> 0.89 (0.91 to 1.07)     1.02 (0.93 to 1.12) <sup>H</sup> 22 (0.81 to 1.04)     0.99 (0.81 to 1.20) <sup>H</sup> 0.87 (0.77 to 0.96) <sup>H*</sup> 0.89 (0.80 to 1.00) <sup>*</sup> 0.91 (0.83 to 0.98) <sup>*</sup> 22 (0.81 to 1.04)     0.99 (0.81 to 1.20) <sup>H</sup> 0.87 (0.77 to 0.96) <sup>H*</sup> 0.89 (0.80 to 1.00) <sup>*</sup> 0.91 (0.83 to 0.98) <sup>*</sup> 22 (0.81 to 1.04)     0.99 (0.81 to 1.20) <sup>H</sup> 0.87 (0.77 to 0.96) <sup>H*</sup> 0.89 (0.80 to 1.00) <sup>*</sup> 0.91 (0.83 to 0.98) <sup>*</sup> 22 (0.81 to 1.04)     0.99 to 1.25)     1.16 (1.03 to 1.30) <sup>**</sup> 1.15 (0.93 to 1.43) <sup>H</sup> 1.13 (0.88 to 1.45) <sup>H</sup> 1.04 (0.91 to 1.20) <sup>H</sup>	-		1.03 (0.92 to 1.16) <sup>H</sup>	0.98 (0.86 to 1.11) <sup>H</sup>	1.08 (1.02 to 1.14)*	1.03 (0.94 to 1.12)
1.07         0.08 to 1.16         1.04         0.05 to 1.13         1.12         0.09 to 1.27         1.12         0.09 to 1.07         1.12         0.09 to 1.07         1.02         0.09 to 1.07         0.091         0.012         0.09 to 1.02         0.091         0.012         0.094 to 1.12         0.091         0.010         0.01         0.031         0.031         0.091         0.011         0.091         0.091         0.091         0.091         0.091         0.091         0.091         0.091         0.091         0.091         0.091         0.091         0.091         0.091         0.091         0.091         0.091         0.091         0.091         0.091         0.091         0.091         0.091         0.091         0.091         0.091         0.091         0.091         0.091         0.0	-		1.13 (1.03 to 1.24)**	1.15 (1.00 to 1.32)	1.11 (1.03 to 1.21)**	1.05 (0.94 to 1.18)
aled allergens         0.96 (0.91 to 1.02)         0.96 (0.98 to 1.04)         0.98 (0.91 to 1.05)         0.98 (0.91 to 1.07)         1.02 (0.94 to 1.12) <sup>H</sup> 0.92 (0.81 to 1.04)         0.97 (0.77 to 0.96) <sup>H</sup> 0.87 (0.77 to 0.96) <sup>H</sup> 0.89 (0.90 to 1.00) <sup>H</sup> 0.91 (0.83 to 0.98) <sup>H</sup> 2.2         0.97 to 1.02         0.79 to 0.96 (0.91 to 1.20) <sup>H</sup> 0.87 (0.77 to 0.96) <sup>H+</sup> 0.89 (0.80 to 1.00) <sup>H+</sup> 0.91 (0.83 to 0.98) <sup>H+</sup> 2.2         1.12 (0.99 to 1.25)         1.16 (1.03 to 1.30) <sup>H+</sup> 1.15 (0.93 to 1.43) <sup>H+</sup> 1.13 (0.88 to 1.45) <sup>H+</sup> 1.04 (0.91 to 1.20) <sup>H+</sup>			1.12 (0.97 to 1.30) <sup>H</sup>	1.14 (0.94 to 1.39) <sup>H</sup>	1.12 (0.99 to 1.27) <sup>H</sup>	1.09 (0.96 to 1.25) <sup>H</sup>
0.92 (0.81 to 1.04) 0.99 (0.81 to 1.20) <sup>H</sup> 0.87 (0.79 to 0.96) <sup>**</sup> 0.89 (0.80 to 1.00) <sup>*</sup> 0.91 (0.83 to 0.98) <sup>*</sup> 1.12 (0.99 to 1.25) 1.16 (1.03 to 1.30) <sup>**</sup> 1.15 (0.93 to 1.43) <sup>H</sup> 1.13 (0.88 to 1.45) <sup>H</sup> 1.04 (0.91 to 1.20) <sup>H</sup>	aled allergens		0.98 (0.91 to 1.05)	0.98 (0.91 to 1.07)	1.02 (0.94 to 1.12) <sup>H</sup>	1.06 (0.94 to 1.20) <sup>H</sup>
wheeze 1.12 (0.99 to 1.25) 1.16 (1.03 to 1.30)** 1.15 (0.93 to 1.43) <sup>H</sup> 1.13 (0.88 to 1.45) <sup>H</sup> 1.04 (0.91 to 1.20) <sup>H</sup>	-		0.87 (0.79 to 0.96)**	0.89 (0.80 to 1.00)*	0.91 (0.83 to 0.98)*	0.97 (0.87 to 1.07)
	wheeze		1.15 (0.93 to 1.43) <sup>H</sup>	1.13 (0.88 to 1.45) <sup>H</sup>	1.04 (0.91 to 1.20) <sup>H</sup>	0.98 (0.85 to 1.12)
	Unterences berween estimates from the two models may include the <sup>H</sup> Heteroaqeneity between study specific results (p<0.10).	e loss or up to two stuales when aajusti	ig tor smoking during the tirst tw	o years or lire.		
Differences between estimates from the two models may include the loss of up to two studies when adjusting for smoking during the first two years of life. <sup>H</sup> Heterogeneity between study specific results (p<0.10).	Odds ratios are from confounder adjusted models, and from fully adjusted (for previous covariates plus both other smokina variables)	adiusted (for previous covariates plus b	oth other smoking variables).			

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some odds ratios changed a little towards the null on adjusting for parental allergy, and similarly for bronchitis and morning cough, on adjusting for parental lung disease (data not shown). Neither attendance at kindergarten nor breastfeeding had any confounding effect.

Child's sex was not a strong modifier of effects of maternal smoking in pregnancy. Contrary to Alati's findings,<sup>31</sup> the mean odds ratio for asthma was higher in boys: 1.24 (95% CI 1.12 to 1.38) versus 1.10 (95% CI 0.95 to 1.27) in girls. However, outcome- and country-specific interactions were generally small and varied in direction. There was little evidence of breastfeeding modifying the effect of either postnatal exposure, particularly for smoking in the first two years of life. For current exposure, the strongest evidence was seen for wheeze where, in six of nine countries, stronger effects of exposure were seen among children who were breastfed (the great majority of the children) than in those who were not. (This pattern was little changed by controlling for other smoking measures, or the interaction between breastfeeding and smoking in the first two years of life.) The interaction was statistically significant in Bulgaria and Germany, and the mean of the nine interaction terms was also statistically significant. In the German dataset, the existing, apparently protective effect became more pronounced among children not breastfed, with a null effect among breastfed children. We tested these results by restricting the analysis to children who were breastfed, and testing for a trend in environmental tobacco smoke (ETS) effect across length of breastfeeding. The resulting interaction terms bore no correspondence to the interactions seen with the yes/no breastfeeding variable.

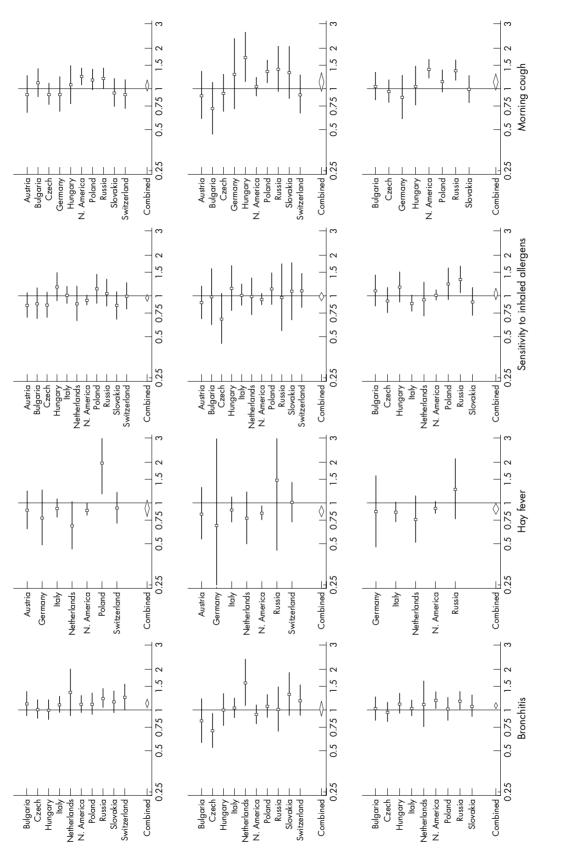
#### DISCUSSION

Adverse effects of parental smoking were seen with considerable consistency for several health outcomes, in particular asthma, wheeze, bronchitis, and nocturnal cough. By contrast, negative effects predominated for hay fever, though results were available for fewer studies, and based on fewer cases.

Correlations between exposures hamper efforts to distinguish between their effects. But generally, odds ratios for our three exposure periods remained raised (if with reduced statistical significance) after mutual adjustment, demonstrating some independence of effect. Maternal smoking during pregnancy showed independent effects particularly on wheeze, asthma, nocturnal cough and (inversely) hay fever. Distinguishing between effects of early-life and current exposure proved harder. But estimated effects of postnatal exposure on wheeze, bronchitis and nocturnal cough were independent of smoking during pregnancy.

Smoking in pregnancy has been linked to low birth weight, which in turn is linked to later morbidity.<sup>1 4 32</sup> Details of possible harmful mechanisms of smoking during pregnancy have been discussed elsewhere, including alterations in the pulmonary neuroendocrine system, reduced lung volume, reduced number of lung saccules, and reduced length of elastin fibres in the lung interstitium, resulting in a loss of lung elasticity.<sup>1 33 34</sup>

If respiratory diseases of children or parents lead to smoking cessation, this may result in underestimation of effects of tobacco smoke in cross-sectional studies and could even cause inverse swings in observed associations (the "healthy smoker" effect). Observed effects would combine real exposure effects and inverse behavioural effects and, for outcomes where true effects are small, behavioural effects could predominate. Observed negative associations between smoking and hay fever could be related to these behavioural effects, rather than to some true protective effect. For asthma and respiratory symptoms behavioural effects have to be





assumed as well; however, the adverse effects of tobacco smoke on these outcomes seems to be much larger and therefore are not masked by behavioural effects.

We rely on parents' questionnaire answers, both for exposure and outcome. Prevalences of smoking in pregnancy were noticeably low in Russia and (apart from Poland) Eastern Europe, and we do not have external data by which to check this, though the consistency across these Eastern countries gives some reassurance. Smokers misclassifying themselves as non-smoking would probably cause underestimation of effects (unless parents of healthy children misclassified themselves more). Since all studies were explicitly focused on outdoor air pollution, self-misclassifications may have been few. There is evidence of reasonable validity of parental responses on smoking, and validation studies carried out in several countries have found a strong correlation between passive smoking exposure in children assessed by measuring the level of urinary cotinine and the amount of parental self-report smoking.<sup>1</sup><sup>21</sup> However, parental smokers under-report cough, and among children with asthmatic symptoms, smokers' children are less likely to be diagnosed asthmatic than non-smokers' children.35 36 Such outcome misclassifications would also tend to cause underestimation of effects.

The relative importance of pre- and postnatal exposure is under debate. We were concerned whether our blunt yes/no exposure measures were adequate in teasing apart the effects of different periods. "Maternal smoking in pregnancy", for example, may be thought partly to represent residual effects of heavy current smoking. For three primary outcomes (asthma, wheeze and bronchitis) we repeated analyses for the effects of smoking during pregnancy among the subset of children with no current exposure, and likewise for the effects of current smoking, in children whose mothers did not smoke in pregnancy. All six analyses showed clear adverse effects (data not shown). We were reassured about interpreting our primary results, guided by consistency and relative strength of evidence seen for effects of exposures at different periods. Recent studies-for example, Kharrazi et al<sup>37</sup>—have found harmful effects on the children of the mother's passive smoking during pregnancy. This exposure was not assessed in most of the PATY studies and could not be analysed here. Evidence that breastfeeding might modify the effect of exposure was tenuous. There was not a clear dose-response relationship, suggesting that the variable might only be an indicator for something else, or that apparent modifications were chance findings.

Selected outcomes had similar questionnaire wordings across studies, except for asthma, where, for example, some referred to the doctor's diagnosis, others did not.<sup>23</sup> Study specific results proved independent of reference to diagnosis (data not shown). Lack of power prevented comparisons across other wording differences. We note that, even given identical wordings, interpretation and diagnosis of "asthma" may vary between, even within, studies.<sup>38</sup>

Cross-sectional studies have limitations, but can access far more individuals than is usually feasible in cohort studies. Evidence on independent effects of pre- and postnatal passive smoking from cohort studies is sparse. A recent Norwegian cohort study was the first to show that prenatal and postnatal passive smoking induce lasting vulnerability for developing asthma or respiratory symptoms in adults (significant for exposure to maternal smoking, but not that of other household members).<sup>39</sup> Independent effects of prenatal smoking remained difficult to assess in this cohort because of small numbers.

In conclusion, the large cross-sectional dataset of the PATY study allowed us to assess independent effects of exposures to passive smoking at different times of a child's life, which Many studies have linked parental smoking to respiratory disease in children, but most of them have lacked the power to demonstrate independent effects of intrauterine and postnatal passive smoking at school age.

This pooled analysis finds long-lasting effects of maternal smoking during pregnancy on wheeze, asthma, and nocturnal cough, independent of postnatal exposure. Independent of smoking during pregnancy, bronchitis, wheeze and nocturnal cough are associated with postnatal exposure.

had been proven difficult in earlier studies.<sup>40</sup> The results confirm long-lasting harmful effects of smoking during pregnancy, and, independently, of smoking later in the child's life. Average, conservative effect estimates at school age were not large, but exposures (particularly postnatal) were widespread. The public health consequence for our populations of children—and our future populations of adults—remains a serious one.

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