Eur Respir J, 1995, 8, 349–356
DOI: 10.1183/09031936.95.08030349
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European Respiratory Journal
ISSN 0903 - 1936

Prospective study of risk factors for early and persistent wheezing in childhood

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Prospective study of risk factors for early and persistent wheezing in childhood. S. Lewis, D. Richards, J. Bynner, N. Butler, J. Britton. ©ERS Journals Ltd 1995.

ABSTRACT: The object of this study was to determine the relative importance of low birth weight, preterm birth, low maternal age, household size, exposure to maternal smoking, personal smoking at 16 yrs of age, early termination of breast-feeding and socioeconomic status in the aetiology of wheezing illness in the first 5 yrs of life, and on the persistence of this illness at 16 yrs of age.

In 15,712 children born in Britain during one week of April 1970, the occurrence of wheezing by 5 yrs of age, and of wheezing in the past year at 16 yrs of age within this group were analysed in multivariate logistic regression against each potential risk factor.

The independent determinants of wheezing by 5 yrs of age were male sex, maternal smoking during pregnancy (odds ratio (OR) for 15+ cigarettes·day^{-1} =1.39; 95% confidence interval (95% CI) 1.22–1.58) and low birthweight (OR for birthweight <2.5 kg=1.26; 95% Cl 1.07–1.50). Of children who had wheezed by 5 yrs of age, 15% reported wheezing in the past 12 months at 16 yrs of age. The persistence of symptoms at 16 yrs of age was independently related to low maternal age (OR for 20 *vs* 40 yrs of age = 1.96; 95% CI 1.08–3.45) and to high social status (OR for most *vs* least advantaged=1.95; 95% CI 1.13–3.38).

We conclude that low birth weight and maternal smoking in pregnancy are independent risk factors for early childhood wheezing, but in 85% of children with early wheezing it resolves by 16 yrs of age. Persistence of wheeze at 16 yrs of age is related to low maternal age and high socioeconomic status. Therefore, the factors involved in the aetiology of early childhood wheezing may be different from those associated with wheezing which persists into adolescence.

Eur Respir J., 1995, 8, 349–356.

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Keywords: Childhood wheeze
low birth weight
maternal age
passive smoking
socioeconomic status

Received: April 18 1994
Accepted after revision December 23 1994

This study was funded by the National Asthma Campaign

Asthma is a major public health problem in most economically developed countries, and several studies have suggested that the prevalence of diagnosed asthma, and of wheezing illness in childhood and adolescence is increasing [1–4]. Although the aetiology of childhood wheezing illness is not fully understood, recent evidence suggests that susceptibility to wheezing, and more specifically to asthma, may be determined by exposures or events occurring very early in life. The occurrence of wheezing or diagnosed asthma in childhood and adolescence has been shown to be increased in relation to low birth weight [5, 6], preterm birth [7], low maternal age [6, 8, 9], and maternal smoking both before and after birth [10–12]. Maternal smoking and low birth weight have been shown to be associated with reduced lung function during childhood [7, 13–15], whilst maternal smoking, low maternal age and early bottle feeding are associated with lower respiratory tract illness in the first 2 years of life [16–18], which, in turn, is linked with the development of asthma in childhood [19, 20]. A child with few older siblings may be more susceptible to the occurrence of hayfever and to the development of atopy [21, 22], which, in turn, is related to the onset of asthma. Collectively this evidence, therefore, suggests that exposures occurring during pregnancy and early childhood can influence the risk of childhood and adolescent asthma.

However, low birth weight, preterm birth, low maternal age, household size, maternal smoking, infant feeding practices, and socioeconomic status are all closely interrelated with each other, and with socioeconomic status, making it difficult to distinguish which of these factors are the important independent determinants of wheeze. Furthermore, whilst wheezing in infancy is common, it appears to have a favourable prognosis, since the majority of children who wheeze in early childhood are free of symptoms by adolescence or early adulthood [9, 23–25]. At present, it is not understood why wheezing illness persists in some children, when in most it resolves spontaneously. Nor is it clear whether wheezing illness that resolves in early childhood and wheezing which persists into adolescence represent variations in presentation of

the same disease, or whether they are manifestations of aetiologically distinct disease processes [23, 26, 27].

The present analysis was conducted to determine the extent and relative aetiological importance of the effects of exposures during pregnancy or early childhood on the occurrence of early wheeze, and of persistent wheeze, using data from a nationally representative British birth cohort.

Materials and methods

Study subjects

Subjects for the study comprised all children documented in the 1970 British Cohort Study (BCS70), which included all children born in Britain between 5th and 11th April, 1970.

Study design

Details of maternal age, birth weight, gestational age, and maternal smoking during pregnancy were collected by midwives who visited the child within 3 months of birth, and the majority within 10 days of birth. Information on maternal smoking, socioeconomic status, the number of older and younger children in the household, and duration of breast-feeding was collected by maternal questionnaire at 5 yrs of age, and lifetime and 12 month period prevalence of wheezing at 5 and 16 yrs of age. At 16 yrs of age, the children completed questionnaires which included information on their current personal cigarette consumption. Socioeconomic status was expressed in terms of a derived variable, the "social index", which was calculated at 5 yrs of age and combined information on parental occupation, educational qualifications, and housing and income measures into a variable graded from 1–5 according to increasing social disadvantage [28]. Initially known as the Child Health and Education Survey (CHES), full details of the cohort at birth and 5 yrs of age have been documented previously [29].

Analysis

We have defined wheeze by 5 yrs of age as a positive response to the question, "Has the child ever wheezed?" at age 5. In a data set restricted to those children who had a first occurrence of wheezing before the age of 5 yrs, we have defined persistent wheeze as wheezing that was present in the past 12 months at 16 yrs of age, and also examined possible differential response bias at 16 yrs of age, according to gender and social class. Univariate analyses and cross tabulations of wheeze by 5 yrs of age, and persistent wheeze at 16 yrs of age in those children who wheezed before 5 yrs of age, against sex, social index, birth weight, maternal age, number of older and younger children in the household, gestational age, breast-feeding categories, categories of maternal cigarette consumption during pregnancy and at 5 yrs of age, and child's personal cigarette consumption at 16 yrs of age were carried out using Statistical Package for the Social Sciences (SPSS)-PC [30]. The independent effects of these variables on the occurrence of childhood wheezing were assessed by multiple logistic regression in EGRET [31]. All exposures were fitted initially as categorical variables to determine independent effects, but were subsequently introduced as binary or continuous variables, where examination of odds ratios showed these to be more applicable. In the multivariate analysis of factors predicting persistent wheeze, categories of exposure were combined as appropriate to eliminate empty cells.

Results

Of an initial 17,196 children in the cohort at birth, 629 were resident in Northern Ireland and were not followed up at any subsequent occasion, and a further 563 are known not to have survived to 5 yrs of age. Of the remainder, 13,135 mothers were surveyed and provided wheezing information when the child was 5 yrs of age, 13,871 at 10 yrs of age and 9,600 at 16 yrs of age. Information on wheezing was available at 5, 10 or 16 yrs of age in a cumulative population of 15,712 children, and at birth, 5 and 16 yrs of age in 7,359 children. Wheezing at any time in the past was reported by 20.8% at 5 yrs of age, 20.5% at 10 yrs of age and 16.7% at 16 yrs of age, and, in the cumulative population surveyed at 5, 10 or 16 yrs of age, a history of wheezing was reported on one or more of these occasions in a total of 30.4% by 16 yrs of age (table 1). Of all wheezing illness occurring before 16 yrs of age, therefore, 57% was reported by 5 yrs of age. Of those 2,703 children who wheezed before 5 yrs of age, 1,518 (56%) responded to the wheezing questions at 16 yrs of age, this response rate being slightly higher in females than males (60 and 53%, respectively), and in high socioeconomic groups (62 and 48% from the most and least advantaged groups, respectively). Of those children who wheezed before 5 yrs of age, 222 (15%) reported wheezing at 16 yrs of age; after adjustment for the differential response rates according to social index, the percentage remaining symptomatic at 16 yrs of age was virtually unchanged at 14.5%.

In univariate analyses, wheeze by 5 yrs of age was more frequent in relation to low maternal age, low birth weight, maternal smoking during pregnancy and at 5 yrs of age, low social index, and in children who were not breast-fed and lived in a household with more older children (table 2). Wheeze by 5 yrs of age was also more frequent in boys. There was no significant association with preterm birth, number of younger children in the household, or to paternal smoking for children of nonsmoking mothers.

However, maternal smoking during pregnancy and at 5 yrs of age were closely associated with each other, and also with low birth weight, preterm birth, low maternal age, more older children in the household, low social index and bottle rather than breast-feeding. The effects

Table 1. – Cross-sectional 12 month period prevalance, reported lifetime prevalence at each age, and lifetime prevalence of wheeze in the cumulative population to 16 yrs of age in the 1970 birth cohort

Age at interview yrs	Cross-sectional prevalence of wheeze		Reported lifetime prevalence of wheeze		Lifetime prevalence of wheeze in the cumulative population	
	%	n	%	n	%	n
5	9.9	12402	20.8	12973	20.8	12973
10	7.6	13575	20.5	13626	27.5	13997
16	6.6	9006	16.7	9333	30.4	15712

n: number responding to question. The cumulative population includes all those surveyed up to and including the given age.

Table 2. – Univariate percentages and odds ratios for occurence of wheezing by 5 yrs of age against potential risk factors in pregnancy and early childhood, and p-value for a Chi-squared test across all catagories of each variable

	Children n	Reported wheezing by 5 yrs of age %	OR (95% CI) for wheezing by 5 yrs of age	p-value for Chi-squared test	p-value for test of trend
Social index					
Most advantaged	1246	18.5	1		
Advantaged	3507	19.5	1.07 (0.91–1.26)		
Average	4783	21.1	1.18 (1.01–1.39)	0.003	<0.001
Disadvantaged	1968	22.4	1.28 (1.07–1.52)		
Most disadvantaged	1461	23.1	1.32 (1.10–1.60)		
Birth weight g					
>4000	1089	21.7	1		
3500–4000	3403	19.5	0.88 (0.74–1.04)		
3000–3500	4901	20.3	0.92 (0.79–1.08)	0.003	0.004
2500–3000	2407	21.9	1.02 (0.85–1.21)		
2000–2500	599	25.2	1.22 (0.96–1.54)		
<2000	178	27.0	1.34 (0.93–1.92)		
Sex					
Male	6713	23.5	1		
Female	6260	18.0	0.71 (0.66–0.78)	<0.001	NA
Maternal age yrs					
<20	1106	21.4	1		
20–24	4527	20.7	0.96 (0.82–1.13)		
25–29	3966	21.4	1.00 (0.85–1.17)	0.37	0.27
30–34	1913	21.3	0.99 (0.83–1.19)		
35–39	771	18.9	0.86 (0.68–1.08)		
≥40	235	16.6	0.73 (0.50–1.06)		
Breast-feeding months					
Never	8086	21.8	1		
<1	2077	19.5	0.87 (0.77–0.98)	0.003	<0.001
1–3	1281	19.8	0.89 (0.76–1.03)		
>3	1391	18.0	0.79 (0.68–0.91)		
Gestation weeks					
39+	8253	20.3	1		
37–38	1452	21.3	1.06 (0.93–1.22)	0.39	0.15
35–36	310	20.6	1.02 (0.77–1.35)		
<34	154	25.3	1.33 (0.92–1.92)		
Maternal smoking during pregnancy cigs·day^{-1}					
None	7437	18.9	1		
1–4	855	20.6	1.12 (0.94–1.33)		
5–14	2628	24.0	1.36 (1.22–1.52)	<0.001	<0.001
≥15	1610	25.0	1.44 (1.27–1.63)		
Maternal smoking at 5 yrs of age cigs·day^{-1}					
None	7337	18.9	1		
1–4	460	21.5	1.17 (0.93–1.48)	<0.001	<0.001
5–14	1727	22.9	1.27 (1.12–1.44)		
≥15	2990	24.4	1.38 (1.25–1.53)		
Older children in household n					
0	4950	19.9	1		
1	4494	20.7	1.05 (0.95–1.17)	0.07	0.03
2	2125	23.0	1.20 (1.06–1.36)		
3	900	21.4	1.10 (0.92–1.31)		
4+	496	21.0	1.07 (0.85–1.34)		

OR: odds ratio; 95% CI: 95% confidence interval; NA: not applicable.

Table 3. – Independent odds ratios, p-values for the addition of each factor to the regression, and confidence intervals for the effects of male sex, low birth weight, and maternal smoking during pregnancy on the risk of wheezing up to 5 yrs of age (intercept = baseline category for comparison)

	OR	p-value	95% CI
Intercept (male birth weight >2,500 g, mother nonsmoker, never breast-fed)	0.28		0.26–0.30
Female	0.72	<0.001	0.66–0.78
Birthweight <2,500 g	1.26	0.007	1.07–1.50
Maternal smoking during pregnancy cig·day^{-1}			
1–4	1.10	<0.001	0.92–1.31
5–14	1.34		1.20–1.49
≥15	1.39		1.22–1.58
Breast-fed	0.90	0.027	0.82–0.99

OR: odds ratio; 95% CI: 95% confidence interval.

of these variables are, therefore, likely to be confounded. Multivariate analysis revealed that, of these factors, the independent determinants of wheeze to 5 yrs of age were a birth weight under 2,500 g, maternal smoking during pregnancy, bottle rather than breast-feeding and male sex (table 3). After allowing for these independent effects, there was no further significant effect of maternal age, number of older children in the household, social index, or gestation. The effects of either smoking during pregnancy or at 5 yrs of age were similar, both exhibiting a dose-related association with cumulative wheeze, but in mothers for whom both of these smoking measures were known, smoking during pregnancy was slightly more significantly related. Although there was no significant independent effect of social index in multiple logistic regression, social index was an important confounder in the relationship between breast-feeding and wheeze to 5 yrs of age, since the effect

Table 4. – Univariate percentages, and odds ratios for occurence of persistent wheezing at 16 yrs of age against potential risk factors in pregnancy and early childhood, and p-value for Chi-squared test across all catagories of each variable

	Children n	Those wheezing before age 5 yrs, who wheezed in past 12 months at 16 yrs of age %	OR (95% CI) for persistent wheezing at 16 yrs of age	p-value for Chi-squared test	p-value for test of trend
Social index					
Most advantaged	142	18.3	1		
Advantaged	410	17.3	0.93 (0.57–1.54)	0.08	0.03
Average	591	12.7	0.65 (0.40–1.06)		
Disadvantaged	212	15.6	0.82 (0.47–1.45)		
Most disadvantaged	162	10.5	0.52 (0.27–1.01)		
Birth weight g					
>3000	1075	13.8	1		
2500–3000	290	16.6	1.24 (0.87–1.77)	0.21	0.08
<2500	117	18.8	1.45 (0.88–2.38)		
Sex					
Male	837	13.7	1		
Female	681	15.7	1.17 (0.88–1.56)	0.28	NA
Maternal age yrs					
<20	126	17.5	1		
20–24	530	16.0	0.90 (0.54–1.51)	0.29	0.03
25–29	472	15.5	0.86 (0.51–1.46)		
30–34	235	10.6	0.56 (0.30–1.04)		
35–39	94	11.7	0.63 (0.29–1.37)		
≥40	23	8.7	0.45 (0.00–2.06)		
Breast-feeding					
Never	984	14.2	1		
Ever	520	15.5	0.91 (0.67–1.22)	0.48	NA
Gestation weeks					
<37	62	17.1	1		
>37	1143	14.1	0.76 (0.39–1.49)	0.42	NA
Maternal smoking during pregnancy cigs·day^{-1}					
None	820	15.6	1		
1–4	106	15.1	0.96 (0.55–1.69)	0.41	0.45
5–14	351	12.0	0.73 (0.51–1.07)		
≥15	200	16.0	1.03 (0.67–1.57)		
Childs smoking at 16 yrs of age cigs·week^{-1}					
None	590	16.3	1		
1–5	47	14.9	0.90 (0.39–2.07)		
6–40	81	8.6	0.49 (0.22–1.09)	0.27	0.03
41–100	55	9.1	0.51 (0.20–1.32)		
≥100	11	9.1	0.51 (0.07–4.07)		
Number of older children in household at 5 yrs of age					
0	554	16.8	1		
1	551	13.2	0.76 (0.54–1.06)		
2	260	14.6	0.85 (0.56–1.28)	0.42	0.13
3	99	12.1	0.68 (0.36–1.30)		
4+	53	11.3	0.63 (0.26–1.52)		

OR: odds ratio; 95% confidence interval; NA: not applicable.

Table 5. – Independent odds ratios, p-values for the addition of each factor into the regression, and confidence intervals for the effects of maternal age, and social index on wheeze in the past year at 16 yrs of age, for wheezing which commenced before 5 yrs of age (intercept=baseline catagory for comparison)

	OR	p-value	95% CI
Intercept (maternal age=15, most disadvantaged)	0.17		0.11–0.26
Maternal age (per year increase)	0.97	0.033	0.94–0.99
Social index (per unit increase)	1.18	0.017	1.03–1.36

OR: odds ratio; 95% CI: 95% confidence interval.

of breast-feeding was only marginally significant (OR for bottle rather than breast-feeding=1.09; p=0.054) after addition of social index to the model.

Univariate analysis of the persistence of wheeze at 16 yrs of age, within those who had wheezed by 5 yrs of age, revealed that the relationships with maternal smoking and low birth weight were less marked than for any wheeze before 5 yrs of age, whilst the linear association with low maternal age was stronger (table 4). The association both with social index and the number of older children in the household were reversed, such that persistent wheeze was more frequent in children from high, rather than low social class backgrounds, and in households with fewer older children. In univariate analysis, none of these effects reached statistical significance when modelled as categorical variables, although the effects of social index and maternal age both exhibited a significance univariate linear trend (p=0.029 and p=0.027 for social index and maternal age, respectively). In univariate analysis, there was a significant linear relationship with the child's personal smoking at 16 yrs of age, such that persistent wheezing was more frequent in nonsmokers, but this effect did not reach statistical significance in multivariate analysis. Multivariate analysis revealed that persistent wheezing was significantly and independently related to increasing social index and low maternal age modelled as continuous variables (table 5). There was no significant relationship between persistent wheeze at 16 yrs of age and any of the factors predicting wheeze by 5 yrs of age, including maternal smoking during pregnancy, maternal smoking up to 5 yrs of age, low birth weight, or bottle-feeding, and no significant relationship with the number of older children in the household, in either univariate or multivariate analysis (table 6).

Table 6. – Independent odds ratios, p-values for the addition of each factor into the regression, and confidence intervals for the effects of maternal age, social index, sex, breast-feeding, maternal smoking in pregnancy, number of older children in the household, and low birth weight on wheeze in the past year at 16 yrs of age, for wheezing which commenced before 5 yrs of age (intercept = baseline category for comparison)

	Odds ratio	p-value	95% CI
Intercept (maternal age = 15, most disadvantaged, male, never breast-fed, mother nonsmoker, birth weight >2.5 kg, no older children in the household)	0.17		0.09–0.31
Maternal age (per year increase)	0.97	0.048	0.94–1.00
Social index (per unit increase)	1.17	0.039	1.01–1.35
Female	1.12	0.432	0.84–1.50
Breast fed	1.03	0.858	0.75–1.41
Birthweight <2.5 kg	1.47	0.130	0.89–2.43
Maternal smoking in pregnancy cigs·day^{-1}			
1–4	0.99		0.56–1.75
5–14	0.73	0.363	0.50–1.09
≥15	1.09		0.70–1.68
Number of older children in the household (per child increase)	1.00	0.95	0.85–1.17

Discussion

In this study, we have attempted to identify the independent determinants of wheeze in early childhood, and to establish whether the same or different aetiological factors determine the persistence of wheeze into adolescence. Univariate analyses of the occurrence of wheeze before 5 yrs of age confirmed an association with low maternal age, low birthweight, low socioeconomic status, early termination of breast-feeding, maternal smoking, a greater number of older children in the household, and male sex. However, the major independent predictors of wheeze by 5 yrs of age in this cohort were maternal smoking, low birth weight and male sex, as demonstrated in an earlier analysis of this cohort, which has shown that maternal smoking is an important predictor of wheeze to 5 yrs of age [29]. We were unable to separate the effects of maternal smoking during pregnancy from the effects of passive smoking in infancy, because most mothers who smoked during pregnancy continued to smoke during the neonatal and infant period, but the association between childhood wheeze and maternal cigarette consumption during pregnancy was slightly stronger and more significant than the association between wheezing and maternal smoking at 5 yrs of age. A previous study of this cohort [17] has suggested that smoking during pregnancy also has a greater influence on hospital admission for lower respiratory tract illness in the first 5 yrs of life. Hence, these two studies of the 1970 cohort suggest that exposure *in utero* or the immediate neonatal period may be a more important determinant of wheezing in childhood than passive smoke exposure in infancy.

Several other studies of risk factors for asthma have now produced evidence that childhood wheezing illness is related to exposures occurring in pregnancy and early childhood, and maternal smoking [10–12], low birth weight [5, 6], preterm birth [7], low maternal age [6, 8,

9], and early introduction of bottle-feeding [32] have all been implicated in this respect. It is also well-recognized that most wheezing illness occurring in early childhood resolves by adolescence [9, 23, 24], and although the possibility that symptoms will recur at a later date cannot be excluded, it appears that most childhood wheeze carries a favourable prognosis. It has recently been suggested that childhood wheezing comprises more than one disease, with a majority occurring in response to viral infections, and a minority as a result of allergic asthma [26, 27].

The mechanism by which low birth weight and maternal smoking predispose to wheezing is not known. Maternal smoking has been shown to be associated with a reduction in lung function in the child [13–15, 33], and although no study has been able to distinguish clearly between the effects of smoking before and immediately after birth, evidence from animal studies that passive exposure *in utero* influences lung growth and maturation [34, 35] suggests that exposure to smoke *in utero* in humans may result in small airways at birth. In addition, exposure to maternal cigarette smoke after birth might increase the risk of childhood wheezing by increased sensitization to environmental allergens [36, 37], perhaps through increased mucosal permeability [38], as well as further effects on airway size mediated by inflammation of the airways, or through impaired lung development [14, 39]. Low birth weight children are also known to have lower lung function, so it is possible that the effects of both low birth weight and maternal smoking on the occurrence of wheezing illness are mediated through a predisposition to small airways, and that this increases the likelihood of a wheezing response to viral infections in early childhood [40, 41]. Until relatively recently, wheeze in response to viral infections has tended to be given a diagnostic label of wheezy bronchitis. We have not used maternally-reported diagnoses as outcome measures in this study because of reservations over the potential effects of changes in labelling of wheezing illness in children over time, but the major independent determinants of reported wheezy bronchitis in this cohort were similarly maternal smoking and low birth weight.

A significant univariate association between early childhood wheezing and duration of breast-feeding has been shown in a number of studies, including earlier analyses of this cohort [42]. It is thought that breast feeding might provide immunological protection against infections by transfer of immunoglobulin A and G (IgA and IgG) through breast milk. However, it is also possible that the apparent protective effect of breast-feeding is due to a confounding effect of socioeconomic status, since the effect of bottle rather than breast-feeding is reduced and is no longer significant after adjustment for socioeconomic status.

We have also confirmed previous reports that most children who wheeze before 5 yrs of age are free of wheezing by adolescence [9, 25]. Of the children studied at 16 yrs of age, only 15% of children who wheezed before 5 yrs of age in this cohort had wheezed within the past year at 16 yrs of age, and only 7% of all children seen at 16 yrs of age had wheezed in the past year. Whilst these prevalence estimates are likely to be subject to response bias, adjustment for response in relation to socioeconomic status made virtually no difference to the estimate of persistent wheeze. Irrespective of the effect on the overall prevalence estimates, however, response bias is unlikely to have affected our analysis of the determinants of persistent wheeze at this age, though the fact that the number of children with persistent wheeze at this age was relatively small means that the statistical power of our analysis of effects on persistent wheeze is substantially lower than for wheeze to 5 yrs of age. However, the odds ratio for maternal smoking demonstrated a weaker effect on persistent wheeze than on preschool wheeze, and was not dose-related, and low birth weight was no longer a significant predictor of persistent wheeze, either as a categorical or continuous variable. In contrast, we found that low maternal age was independently significant and had a stronger effect on persistent wheeze than on wheeze to 5 yrs of age. More strikingly, we found that the relationship between persistent wheeze and social index was reversed relative to that between social index and wheeze to 5 yrs of age. Multivariate analysis confirmed that the effects on persistent wheeze of maternal age and social index were independently significant. Thus, persistent wheeze was reported by mothers more commonly in high, rather than low socioeconomic groups, and in children from young mothers.

Although the effect of low birth weight was not statistically significant, the adjusted odds ratio for a birth weight under 2.5 kg was 1.473 (table 6) suggesting that children of a low birth weight may remain at a greater risk of wheezing in later childhood, but that this effect is comparatively less important in persistent wheezing, either because of the relatively small numbers of such children, or because other factors are comparatively more important at this age. Details of the child's own smoking at 16 yrs of age were obtained from a self-completion questionnaire, for which the response rate at 16 yrs of age was somewhat lower than for the maternal questionnaire, though again a better response was obtained from females and those in the higher socioeconomic groups. However, in this dataset, children with persistent wheeze were less likely to smoke.

Since the prevalence of atopy and serum immunoglobulin E (IgE) levels rises steadily during childhood, it is likely that wheezing at 16 yrs of age tends to be due predominantly to allergic asthma. This is supported by the fact that, in this cohort, persistent wheeze at 16 yrs of age was significantly more likely to occur in those children with other signs of atopy at 16 yrs of age (the prevalence of persistent wheeze in those children with and without hayfever or eczema was, respectively, 16 and 3%), and in children of mothers who reported to have asthma, eczema or hayfever (the prevalence of persistent wheeze in children of atopic and nonatopic mothers was, respectively, 20 and 14%); though both of these results rely on parentally-reported atopic conditions which are likely to be biased according to socioeconomic group. Previous studies have shown that positive allergen skin tests, eczema, and hayfever are also more

prevalent in adults and adolescents from high socioeconomic groups [43], and have linked asthma in adolescence with low maternal age [9], so that our findings are consistent with the suggestion that low maternal age and high socioeconomic status may be risk factors for atopic disease. Indeed, a maternally-reported diagnosis of asthma in this cohort was independently related only to high social class and low maternal age.

We suggest that the results of this study support the concept that at least two distinct disease processes are involved in the occurrence of wheezing in childhood, whereby preschool wheezing, associated with maternal smoking in pregnancy and low birth weight, may occur in children with small airways and be precipitated by viral infection [40, 41]; whilst wheeze which persists into adolescence, associated with low maternal age and high socioeconomic status, may be an expression of allergic disease [9, 44–46]. To distinguish more clearly between the relative contribution of atopy to persistent wheezing, and of airway size to wheezing in younger children, we would need lung function and either allergen skin test or serum IgE data, which are so far unavailable for this cohort.

These data were collected in 1986, so that they apply to the situation in Britain as it was 8–9 yrs ago, and other studies have suggested that there may have been a subsequent increase in the prevalence of childhood wheezing illness [47]. A further question which arises from this study is the extent to which the recently reported increase in the prevalence of childhood wheezing is attributable to changes in the prevalence of the risk factors we have identified. Smoking among young women in the UK is reported to have increased in the past two decades [48], and clearly a greater proportion of very low birth weight babies are now surviving into infancy. It is, therefore, possible that both factors have contributed to an increased prevalence of early childhood wheezing. The effects of maternal age as well as a number of environmental exposures associated with high socioeconomic status also need to be explored in relation to the aetiology of atopy, and to the increasing prevalence of wheeze in older children. Also, although the association between low birth weight and wheezing illness which persists into adolescence was not significant in this cohort, the size of the adjusted odds ratio for low birth weight in this cohort in conjunction with recent evidence that low birth weight and lower respiratory illness in infancy are predictors of mortality from chronic obstructive airways disease in adult life [49], suggest that low birth weight, which is itself related to maternal smoking, may still be an influence on the occurrence of wheeze. Further study is also indicated, therefore, to determine whether low birth-weight and maternal smoking are predictors of the development of airflow obstruction in later life in this cohort.

***Acknowledgements*:** The authors thank the National Birthday Trust, University of Bristol, and the International Centre for Child Studies as the source of the BCS70 data. They thank C. Lyn and P. Riley for computing advice and assistance, and the National Asthma Campaign for funding the analysis presented in this study.

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