

Study of the aetiology of wheezing illness at age 16 in two national British birth cohorts

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Abstract

Background - Data from two national British birth cohorts were used to measure the increase in prevalence of wheezing illness at age 16 between 1974 and 1986, and to investigate the role of several potential risk factors in the increase.

Methods - The occurrence of self-reported asthma or wheezy bronchitis within the past year, and the frequency of attacks of wheezing illness at age 16, were compared in 11 262 and 9266 children born in one week of 1958 and 1970, respectively. The effects of several putative risk factors for asthma - including birth weight, maternal age, birth order, breast feeding, maternal smoking in pregnancy, child's personal smoking, and father's social class - on the change in occurrence of wheezing illness at age 16 were assessed by multiple logistic regression.

Results - The annual period prevalence of asthma or wheezy bronchitis at age 16 increased from 3.8% in 1974 to 6.5% in 1986 (prevalence ratio (PR) = 1.71, 95% CI 1.52 to 1.93). The proportion of children experiencing attacks more than once a week increased from 0.2% to 0.7% (PR = 3.77, 95% CI 2.28 to 6.23). The prevalence of self-reported eczema and hayfever within the past year doubled between 1974 and 1986, suggesting that the increase in asthma was part of a general increase in the prevalence of atopic disease. However, in the complete dataset, after adjustment for the effects of the risk factors studied, the prevalence odds ratio for asthma or wheezy bronchitis in 1986 compared with 1974 was virtually unchanged from the unadjusted value at 1.77 (95% CI 1.46 to 2.15). **Conclusion** - The prevalence of wheezing illness in British teenagers increased by approximately 70% between 1974 and 1986. This increase appears to have occurred in the context of a general increase in atopic disease and was largely unexplained by changes in the distribution of maternal age, birth order, birth weight, infant feeding, maternal smoking, active smoking by the child, or father's social class.

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An increase in the prevalence of wheezing illness and diagnosed asthma has been reported in children and adults in the UK and in several other countries.¹⁻⁹ The factors contributing to

this increase are unknown, but increases in exposure to maternal cigarette smoke, an increased rate of survival of very low birth weight babies, an increase in bottle rather than breast feeding, an increasing proportion of children born to younger mothers, changes in air pollution levels, increased exposure to environmental allergen, and changes in dietary intake have all been implicated.¹⁰⁻¹⁴ To date, however, there have been few prospective population studies of the effects of these exposures.

We have used data on the prevalence of asthma or wheezy bronchitis at age 16 in two national British birth cohorts studied in 1974 and 1986 to determine whether asthma prevalence increased during this period in this age group, to determine whether the increase occurred in association with an increase in other atopic diseases, and to explore the roles of birth weight, maternal age, maternal smoking in pregnancy, breast feeding, birth order, father's social class, and teenage smoking in any change.

Methods

The 1958 and 1970 British birth cohorts, known respectively as the National Child Development Study (NCDS) and the British Cohort Study (BCS70), originated in studies of perinatal mortality amongst all children in England, Scotland and Wales born during one week of March 1958 and April 1970, respectively. The surviving children were followed up at ages seven, 11, and 16 in the NCDS cohort, and at five, 10, and 16 in the BCS70 cohort. In both cohorts, midwives collected information at birth on birth weight, father's occupational social class,¹⁵ maternal age, and maternal smoking during pregnancy, and at each subsequent follow up in both cohorts interviewers collected a wide range of social, family and health data from parents which included, at age 16, data relating to the occurrence of wheezing and/or diagnosed asthma (appendix). In addition, the children in both cohorts provided details of personal current smoking at age 16.

At age 16, parents were asked a question on wheezing illness which was worded virtually identically in both cohorts: "If your child ("teenager" in 1986) has had asthma or wheezy bronchitis in the past 12 months, did this occur at least once a week, usually less than once a week, less than once a month, or frequency unknown?", although it was differentially nested within previous questions. In both cases we have taken any positive response to the question on the occurrence of asthma and/or

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wheezy bronchitis at age 16 to indicate that the child had experienced symptoms of one of these wheezing illnesses in the past year at that age, and we have defined frequent wheeze as wheeze which occurred more than once a month. At age 16, parents were also asked identical questions concerning absence from school for one week or more due to asthma or wheeziness in the past year, and the presence of hayfever or eczematous rashes in the past 12 months.

All analyses were carried out using SAS¹⁶ and SPSS-PC Version 4.1¹⁷ for univariate analyses within the 1958 and 1970 cohorts, respectively, and SAS and EGRET¹⁸ for multiple logistic regressions on the combined cohort. Potential bias in response at age 16 was investigated in both cohorts in relation to sex, father's social class at birth, and in children with and without a reported history of wheeze at previous follow ups. Where appropriate, estimates of prevalence were adjusted for differential response rates by combining the weighted prevalence estimates for each level of factors associated with response.

The potential risk factors investigated were birth weight, maternal age, father's social class, birth order, breast feeding, maternal smoking during pregnancy, and child's personal smoking. Details of maternal smoking in pregnancy were available for both cohorts as a derived categorical variable according to levels of cigarette consumption: 0, 1-4, 5-14, and 15 or more cigarettes per day and, in 1958 only, an additional category defined as "variable smoking". In the derivation of a binary indicator of maternal smoking in pregnancy (ever versus never) a response in this latter category was taken to indicate smoking in pregnancy, and in dose-response analyses such a response was defined to be missing. The relationship between

each of these factors and asthma and/or wheezy bronchitis in the past year, frequent wheeze, or school absence due to asthma/wheeziness were examined univariately within each cohort, and univariately between cohorts in the combined dataset after adjustment for a binary cohort term using multiple logistic regression. The cohort odds ratios (1986/1974) for asthma and/or wheezy bronchitis in the past year were compared before and after adjustment for each risk factor, and the attributable risk calculated by the method of Breslow and Day.¹⁹ To investigate whether the relationship between each risk factor and disease prevalence was similar in 1986 to 1974, each multiple logistic model was augmented with a term describing the statistical interaction between cohort and each risk factor.

Having examined the effects of individual risk factors, the combined effects of all risk factors were examined in a dataset restricted to those individuals with complete data on all of the aetiological factors investigated. The unadjusted odds ratio (1986/1974) for asthma and/or wheezy bronchitis in the past year was calculated as before, and then each of the factors birth weight, maternal age, father's social class, birth order, breast feeding, maternal smoking during pregnancy, and child's personal smoking at age 16 were added to the model to obtain the odds ratio adjusted for all of these risk factors in order to assess the proportion of the excess risk in 1986 which may be attributed to the overall change in exposure to these risk factors. Since the response rate to child's personal smoking was substantially lower, particularly in 1986, than for all other questions, the inclusion of child's smoking greatly reduced the size of the available dataset so further logistic regression models were fitted excluding child's personal cigarette consumption and the unadjusted and adjusted odds ratio examined as before.

Relationships between the other two measures of asthma - frequent wheeze and school absence due to asthma or wheeziness - and each of the aetiological variables were examined in a similar way.

Results

A response to the question concerning the occurrence of asthma and/or wheezy bronchitis was provided at age 16 by 11 262 of the 1958 cohort in 1974 and 9266 of the 1970 cohort in 1986, whilst 11 243 and 8592, respectively, provided information on school absence. In both cohorts the response rate at age 16 was independent of the wheezing history reported at previous follow ups (table 1) and, in 1974, response rates were consistent in males and females and across social class groups, but in 1986 males and the lowest social class groups were slightly under-represented. The response rates to the question on asthma/wheezy bronchitis for males and females in 1974 were 67% and 68% of those responding at age 7, and in 1986 were 56% and 63%, respectively of those responding at age 5, and the response rate for those in non-manual compared with manual

Table 1 Summary of non-response bias at age 16, presented as the percentage responding to questions on asthma/wheezy bronchitis at age 16, by response to related questions at age 5 and 10 (1970 cohort) or 7 and 11 (1958 cohort)

	1958		1970	
	Total	Response to wheeze question at age 16	Total	Response to wheeze question at age 16
Asthma/wheezy bronchitis ever by age 7 (1958) and wheeze ever by age 5 (1970)				
Yes	2665	(66%)	2703	(58%)
No	11860	(68%)	10274	(60%)
Asthma/wheezy bronchitis in the past 12 months at age 11 (1958) and wheeze in past 12 months at age 10 (1970)				
Yes	664	(68%)	1045	(59%)
No	12760	(71%)	12599	(61%)

Table 2 Comparison of prevalence of asthma or wheezy bronchitis and frequency of attacks in the past 12 months at age 16 in 1974 and 1986

	1974		1986		Prevalence ratio (95% CI)
	Total	Number (%)	Total	Number (%)	
Asthma or wheezy bronchitis					
Total	11262	427 (3.8%)	9266	601 (6.5%)	1.71 (1.52 to 1.93)
Male	5759	257 (4.5%)	4552	322 (7.1%)	1.59 (1.35 to 1.86)
Female	5503	170 (3.1%)	4711	279 (5.9%)	1.92 (1.59 to 2.31)
Frequency of attacks of asthma or wheezy bronchitis					
More than once a week	11262	20 (0.2%)	9266	62 (0.7%)	3.77 (2.28 to 6.23)
More than once a month		41 (0.4%)		43 (0.5%)	1.27 (0.83 to 1.95)
Less than once a month		244 (2.2%)		287 (3.1%)	1.43 (1.21 to 1.69)
Frequency unknown		122 (1.1%)		209 (2.3%)	2.08 (1.67 to 2.60)

Table 3 Twelve month period prevalence of asthma/wheezy bronchitis at age 16 and prevalence ratios (1986/1974) for subjects with and without current hayfever and eczema

Eczema in the past 12 months	Hayfever in the past 12 months	1974		1986		Prevalence ratio 1986/1974 (95% CI)
		Total	% prevalence of asthma and/or wheezy bronchitis in the past 12 months at 16	Total	% prevalence of asthma and/or wheezy bronchitis in the past 12 months at 16	
No	No	9294	2.5	6659	3.2	1.27 (1.06 to 1.53)
	Yes	1188	12.1	1858	14.9	1.23 (1.02 to 1.48)
Yes	No	248	6.0	347	7.5	1.24 (0.67 to 2.29)
	Yes	93	19.4	222	35.1	1.82 (1.16 to 2.85)

occupations were 69% and 68%, respectively, in 1974, and 63% and 58%, respectively, in 1986. The lower response rate in males and those in manual occupations in 1986 was generally more marked in those with a wheezing history at age 5 or 10.

The unadjusted period prevalence of reported asthma and/or wheezy bronchitis at age 16 increased from 3.8% in 1974 to 6.5% in 1986 (prevalence ratio (PR) 1.71, 95% confidence interval (CI) 1.52 to 1.93). This increase was slightly greater in females than in males (table 2) but was similar in all levels of father's social class. After adjustment for differential response according to sex and social class, in 1986 the period prevalence of asthma or wheezy bronchitis was 6.3% and the prevalence ratio adjusted for sex and social class effects for 1986 compared with 1974 was virtually unchanged at 1.67 (95% CI 1.49 to 1.87). The proportion of these children experiencing attacks more than once a week increased between 1974 and 1986 from 0.2% to 0.7% (PR = 3.77, 95% CI 2.28 to 6.23), but the proportion of children absent from school in the past year due to asthma or wheeziness increased to a lesser degree from 1.5% in 1974 to 1.7% in 1986 (PR = 1.20, 95% CI 0.96 to 1.49).

The reported period prevalence of eczema and hayfever doubled between 1974 and 1986, eczema from 3.1% to 6.4% (PR 2.04, 95% CI

1.79 to 2.32) and hayfever from 12.0% to 23.3% (PR 1.93, 95% CI 1.82 to 2.06). The proportion of children reporting any one of asthma and/or wheezy bronchitis, hayfever or eczema also increased from 16.3% in 1974 to 29.0% in 1986 (PR 1.78, 95% CI 1.69 to 1.88). Among children with eczema and/or hayfever the period prevalence of asthma and/or wheezy bronchitis increased by 36%, compared with a 27% increase in those children with neither eczema nor hayfever, but this difference was not statistically significant ($p=0.3$). The greatest increase in asthma and/or wheezy bronchitis prevalence occurred in those children who were also reported to have both eczema and hayfever (PR 1.82, 95% CI 1.16 to 2.85, table 3), but there was also no significant difference between the prevalence ratios (1986/1974) for those children with both eczema and hayfever and those with only one or neither of these conditions ($p=0.3$).

Between the 1958 and 1970 cohorts there was a change in the distribution of several potential risk factors for asthma (figs 1, 2, and 3). In particular, there was a significant increase in the proportion of children with a birth weight under 2 kg ($p=0.001$) and in the proportion of teenage mothers ($p<0.001$). There was also a small but significant increase in the proportion of first born children ($p=0.01$). Significantly more mothers reported smoking

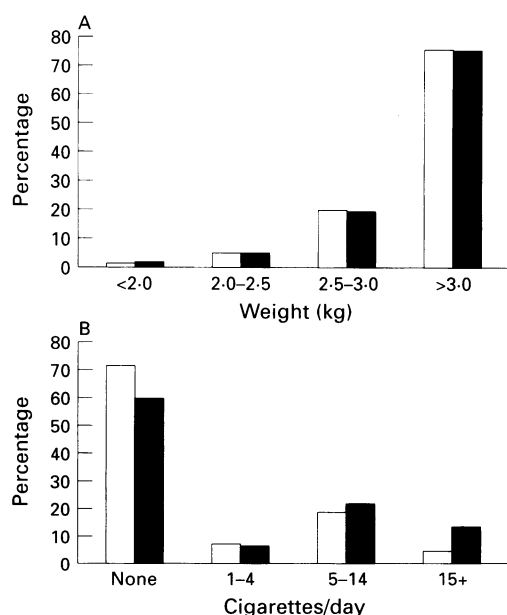


Figure 1 Distribution of (A) birth weight and (B) maternal smoking in pregnancy in the 1958 (□) and 1970 (■) birth cohorts.

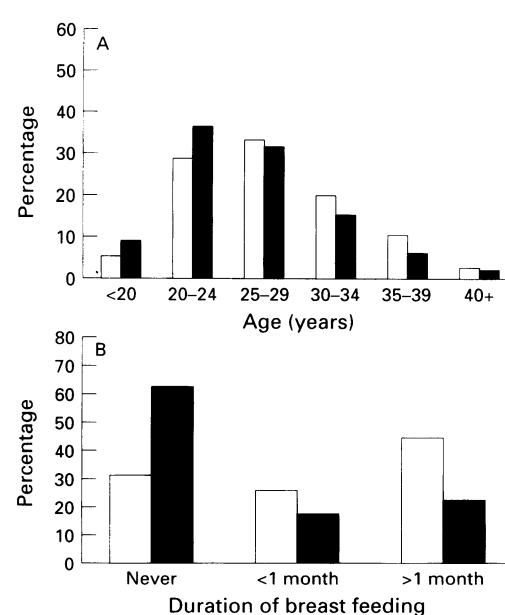


Figure 2 Distribution of (A) maternal age and (B) breast feeding in the 1958 (□) and 1970 (■) birth cohorts.

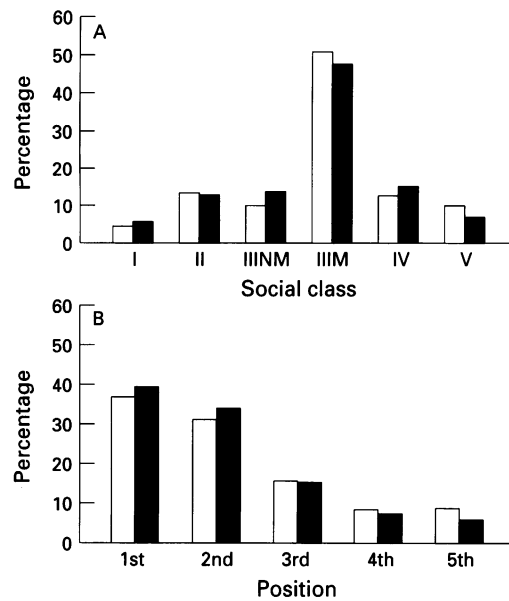


Figure 3 Distribution of (A) father's social class and (B) birth order in the 1958 (□) and 1970 (■) birth cohorts.

during pregnancy in 1970 than in 1958 ($p < 0.001$), with a significant trend towards higher cigarette consumption in 1970 ($p < 0.001$), and there was also a significant

trend towards bottle feeding and bottle feeding at an earlier stage ($p < 0.001$). The proportion of children who reported personal smoking fell between 1974 and 1986 from 34.9% to 25.8%, and there was a significant trend towards lower cigarette consumption within smokers ($p < 0.001$). In multiple logistic regression on the combined dataset, after adjustment for cohort, the occurrence of asthma and/or wheezy bronchitis at age 16 was inversely related to birth weight (χ^2 test for trend $p < 0.01$) and to maternal age (table 4). There was a more complicated association with social class with the highest risk occurring in social class II, and also with maternal cigarette consumption during pregnancy where higher risks were associated with 1-4 and 15+ cigarettes per day than with 5-14 per day. The occurrence of asthma and/or wheezy bronchitis was also related to the child's personal cigarette consumption with an odds ratio of 1.44 (95% CI 1.14 to 1.82) associated with smoking at levels of 40+ cigarette per week. There was no significant relationship between asthma and/or wheezy bronchitis at age 16 and duration of breast feeding, birth order or maternal smoking during pregnancy, expressed as a binary variable. There were no significant cohort and risk factor interactions. The odds ratios for asthma

Table 4 Comparison of the association between potential risk factors and asthma/wheezy bronchitis (A/WB) in the past year at age 16 in 1974 and 1986, with the odds ratios for each risk factor in the combined dataset after adjustment for cohort

	1974		1986		Odds ratios in the combined dataset	χ^2 test (df)	χ^2 test for trend (df=1)
	Total	Percentage with A/WB at age 16	Total	Percentage with A/WB at age 16			
Birth weight (kg)							
<2.0	97	2.1	125	12.0	1.00	8.76*	7.77**
2.0-2.5	500	4.8	414	6.8	0.77	(df=3)	
2.5-3.0	1979	3.9	1623	7.9	0.78		
>3.0	7708	3.7	6389	6.0	0.64		
Maternal age							
<20	572	4.5	764	9.2	1.00		
20-24	3065	4.0	3091	6.1	0.71	14.34*	5.42*
25-29	3530	3.9	2700	6.9	0.76	(df=5)	
30-34	2119	3.0	1267	5.8	0.60		
35-39	1075	4.3	530	5.3	0.71		
40+	254	3.9	160	5.0	0.65		
Duration of breast feeding							
Never breast fed	3055	4.2	4766	6.5	1.00	4.98	0.02
<1 month	2438	3.4	1281	5.2	0.82	(df=2)	
>1 month	4327	3.6	1661	7.5	1.00		
Maternal smoking in pregnancy (cigs/day)							
None	7041	4.0	4942	6.3	1.00		
1-4	699	3.0	566	8.8	1.12	8.08*	0.008
5-14	1778	3.3	1788	5.4	0.84	(df=3)	
15+	365	5.5	1037	7.2	1.19		
Child's smoking at age 16 (cigs/week) (1986 categories)							
None	6026	3.4	3630	6.4	1.00		
1-9 (1-10)	815	2.9	420	5.7	0.87	11.43*	4.88*
10-19 (11-20)	441	4.1	190	6.8	1.14	(df=4)	
20-39 (21-40)	846	3.5	254	4.3	0.90		
40+ (41+)	1134	5.2	396	8.1	1.44		
Birth order							
1 (oldest)	3828	3.7	3321	6.9	1.00		
2	3177	4.1	2849	5.9	0.95		
3	1601	3.6	1320	6.2	0.93	2.40	0.102
4	827	4.1	598	7.9	1.13	(df=4)	
5+	900	4.3	462	6.1	1.01		
Father's social class as birth							
I	431	3.0	424	4.7	1.00		
II	1315	4.8	1008	8.1	1.72	14.61*	0.16
IIINM	1003	3.7	1070	6.1	1.28	(df=5)	
IIIM	5113	3.4	3795	6.0	1.22		
IV	1270	4.4	1195	6.4	1.42		
V	982	4.1	494	6.5	1.40		

* $p < 0.05$; ** $p < 0.01$.

Table 5 Odds ratios for asthma prevalence at 16 (1970 cohort versus 1958 cohort), both unadjusted and adjusted for single potential risk factors

Potential risk factor	Levels of factor after recategorisation	Odds ratio unadjusted	Odds ratio adjusted
Birth weight (kg)	4	1.77	1.77
Maternal age	6	1.75	1.71
Duration of breast feeding	3	1.80	1.78
Birth order	5	1.72	1.72
Maternal smoking in pregnancy	4	1.72	1.70
Child's smoking at age 16	5	1.79	1.82
Father's social class	6	1.71	1.71
Sex	2	1.76	1.77

The unadjusted odds ratio is the odds ratio for asthma prevalence at 16 (1970 versus 1958 cohort) including only those children on whom information is also available for the relevant risk factor, and these differ between risk factors due to the differing numbers of children included. The adjusted odds ratio is the odds ratio for asthma prevalence at 16 (1970 versus 1958 cohort) after adjustment for the effect of the relevant risk factor.

and/or wheezy bronchitis at age 16 adjusted for any one of the potential risk factors were, however, little changed from the unadjusted value (table 5) and attributable risks for most of the risk factors examined were small, the largest being 4.7% for maternal age. In the dataset of children with complete data for all risk factors ($n=10\ 835$) the unadjusted odds ratio for asthma and/or wheezy bronchitis in the past year at 16 for 1986 compared with 1974 was 1.75 (95% CI 1.46 to 2.09). After adjustment for sex, birth weight, maternal age, breast feeding, birth order, smoking during pregnancy (expressed as a binary variable), father's social class at birth, and child's smoking at 16 (expressed as a binary variable), the odds ratio was virtually unchanged at 1.77 (95% CI 1.46 to 2.15). Thus, after allowing for the change in disease prevalence which may be attributed to changes in any of these factors, there was an unexplained increase of approximately 77% in the prevalence of asthma and/or wheezy bronchitis in the past year. If child's smoking at 16 was excluded, the number of children with complete data increased to 15 524 and the equivalent unadjusted and adjusted odds ratios were 1.72 (95% CI 1.49 to 2.00) and 1.67 (95% CI 1.42 to 1.95), respectively.

Only one significant association was apparent with the occurrence of frequent wheeze – namely, a significant trend towards greater occurrence of frequent wheeze with increasing levels of maternal cigarette consumption during pregnancy (odds ratio (OR) for 15+ cigarettes/day 1.89, 95% CI 1.16 to 3.06). The attributable risk of frequent wheeze in relation to the increase in maternal smoking was 13%. However, the odds ratio for frequent wheeze in 1986 compared with 1974 after adjustment for all risk factors was 2.25 (95% CI 1.35 to 3.78) and little changed from the unadjusted value of 2.17 (95% CI 1.35 to 3.50). Absence from school due to asthma or wheeziness was significantly related only to maternal cigarette consumption in pregnancy (OR for 15+ cigarettes/day = 1.63, 95% CI 1.12 to 2.37) and child's smoking at age 16 (OR = 1.73 for 40+ cigarettes/day, 95% CI 1.18 to 2.54), but there was no significant increase in school absence due to asthma or wheeziness either before (unadjusted OR for 1986 compared with 1974 = 1.07, 95% CI 0.76 to 1.50) or after adjustment for all risk factors (adjusted OR = 1.16, 95% CI 0.80 to 1.67).

Discussion

There is considerable evidence that wheezing in pre-teenage and teenage children has increased in prevalence over recent decades in a number of countries. In this study we have used data from two nationally representative British birth cohorts to establish whether the prevalence of wheezing illness in teenagers at age 16 increased between 1974 and 1986 in the UK, and to investigate for the first time the role of several potential aetiological factors in the increase. The prevalence of wheezing illness at age 16 increased by approximately 70%, and there was a significant increase in the proportion of children with more frequent occurrence of symptoms. The increase in prevalence was most marked in those children with other expressions of atopy, but was largely unexplained by changing distributions of risk factors including maternal age, birth order, and smoking during pregnancy.

The 1958 and 1970 British birth cohorts provide a unique opportunity to study aetiological effects prospectively, since the samples studied are nationally representative and used very similar data collection methods. Both cohorts suffered inevitable loss to follow up at age 16, and in the 1970 cohort this is particularly so in males and those in lower social class groups. Since the observed increase in prevalence was more marked in females, the overall prevalence rate in 1986 may have overestimated the true value. However, we found that there was no evidence that responders at age 16 in either cohort were more likely to have a previous history of wheezing, either within the population or within the under-represented groups, and that adjustment for differential response by sex and social class made little difference to the prevalence ratio between cohorts, so that no marked bias was, in fact, introduced.

The differential nesting of the asthma/wheezy bronchitis question in 1974 and 1986 and, in particular, the prior reference to "wheeze" in the latter cohort, is likely to have introduced some differential bias in response. Of the 601 who responded positively to the question on occurrence of asthma/wheezy bronchitis in 1986, 485 (81%) specifically stated in response to the prior question that the cause of the child's wheeze was either "asthma" or "wheezy bronchitis"; if the number of children with asthma or wheezy bronchitis in 1986 is restricted to those with one of these two responses to the prior question, the prevalence ratio for 1986 compared with 1974 is reduced but remains significant at 1.38 (95% CI 1.22 to 1.57). Furthermore, the 1974 question on asthma/wheezy bronchitis was nested within a previous question asking when the most recent attack of asthma or wheezy bronchitis had occurred. If the number of children with asthma or wheezy bronchitis in 1986 is calculated as those who specify the cause of wheeze to be asthma or wheezy bronchitis and whose most recent attack of wheeze is reported to have been in the past 12 months, the prevalence ratio for asthma or wheezy bronchitis in 1986 compared with 1974 is reduced at 1.14 (95% CI 1.00 to 1.31, $p=0.05$). It is therefore possible, though

unlikely, that the differential nesting of the questions in 1974 and 1986 wholly explains the observed increase.

The increase in asthma we observed for teenagers was rather greater in magnitude than estimates of the increase in younger children from other studies in the UK.^{4,9} It seems likely that part of the explanation for these increases in wheezing illness and frequency of symptoms, and for the small increase we have seen in time lost from school, is attributable to the increase in parental and teacher recognition and awareness of both symptoms and severity of asthma. It is recognised that the use of asthma as a diagnostic label has increased in recent years^{20,21} but, in the present study, combining asthma and wheezy bronchitis will have reduced the effect of differential diagnosis of asthma or of diagnostic transfer from wheezy bronchitis to asthma. The consistency of the increase across all levels of social class and the substantial increase in reported frequency of symptoms provide more persuasive evidence for a real increase in wheezing illness. The small effect upon time lost from school may relate to the concurrent improvement in management of asthma over this time span.^{2,22}

The apparent increase in teenage wheeze may be related to an increased tendency for the development of atopy,⁹ or to an increased susceptibility to wheeze as an expression of atopy.¹¹ The expression of atopy measured in terms of allergen skin sensitivity or IgE levels increases during childhood to reach a peak in the early twenties,²³ and recent evidence that wheezing that occurs at age 16 is aetiologically distinct from early childhood wheezing suggests that wheeze in this age group may be more likely to be a manifestation of atopy than of effects attributable to passive smoke exposure or airway size.²⁴ Since skin test and IgE serum levels are not available for the 1970 cohort, we are unable to determine whether the increase in prevalence of wheeze was due to an increase in occurrence of atopy, but we have addressed this question by analysing parental reporting of eczema and hayfever – two atopic conditions which may be more easily recognised by parents than symptoms of asthma – as a marker of childhood atopy. We found a twofold increase in the period prevalence at age 16 of both conditions, suggesting that a general rise in the occurrence of allergic disease in teenagers occurred between 1974 and 1986. We also found that, although not significantly so, the increase in asthma or wheezy bronchitis was more marked in those children with other atopic disease. Thus, it appears that the large increase we have observed in teenage wheezing is a manifestation of a general increase in expression of atopic disease, and to an increased tendency to the development of wheeze within atopic children. Our findings are consistent with evidence from Australia of an increase in the occurrence of airways hyperreactivity in atopic children which suggests that wheeze may be becoming a more common expression of atopy.¹¹

Changes in genetic susceptibility to atopy, or to wheezing as a response to atopy, are

unlikely to have occurred over the 12 year period between 1974 and 1986, and a more probable explanation is that the increase is due to a change in exposure to environmental determinants of asthma, or to environmental factors which promote allergy or wheezing as an expression of allergy in a susceptible child. The onset of most childhood wheezing occurs in infancy,^{25,26} and it has been suggested that in utero and early life exposures are important in both the development of symptoms in early life, the persistence of wheeze into adolescence, and the occurrence of reduced lung function and chronic obstructive airways disease in later life,²⁷ since wheezing in early childhood is strongly associated independently with maternal smoking, particularly during pregnancy,^{28,29} and low birth weight.^{12,24} Low maternal age has been shown to be related to asthma in adolescence³⁰ and the number of older siblings in the house may be inversely related to development of atopy and allergic disease,^{31,32} though these two effects are correlated. There is also conflicting evidence that breast feeding may protect against respiratory infection in infancy and subsequent development of atopic disease.³³

Of the risk factors we investigated, the only significant determinant of asthma or wheezy bronchitis in either cohort which changed sufficiently in distribution between 1974 and 1986 to explain more than a negligible proportion of the observed increase was low maternal age. The proportions of teenage mothers in 1974 and 1986 were 5.4% and 9.0%, respectively, consistent with Office of Population Census and Surveys (OPCS) published figures for the proportion of teenage mothers in the UK in 1958 and 1970 of 5.9% and 10.3%, respectively, and suggesting an increase of 67%. However, the effect of maternal age is small and, as a consequence, whether modelled as a categorical or continuous variable, the changing pattern of maternal age was responsible for no more than an estimated 5% of the increase in teenage wheezing illness.

Although OPCS published figures indicate that the prevalence of smoking has fallen in recent years in many sectors of the population, both OPCS and cohort data demonstrate that smoking in younger women was still increasing during this period, from 32.9% to 41.9%.³⁴ There is considerable evidence that maternal smoking – particularly during pregnancy and in the early life of the child – is associated with wheezing in early childhood,^{28,29} and that exposure to cigarette smoke very early in life may increase a child's susceptibility to the development of atopic disease and to more severe expression of atopy in the child.³⁵ However, our findings suggest a weaker relationship between wheezing in adolescence and maternal passive smoking which was not dose-related, and the increase in teenage wheezing illness which could be attributed to maternal smoking in pregnancy was only 2.5%. High levels of maternal cigarette consumption during pregnancy were associated with an increased risk of frequent asthma symptoms, and while the effect

of maternal smoking may be more likely to occur in relation to current passive smoke exposure at age 16, 13% of the considerable increase in frequent symptoms may be attributable to the increase in maternal smoking. However, in both the 1958 and 1970 cohorts maternal smoking in pregnancy was a much stronger predictor of wheezing in early childhood. We were unable to compare the prevalence of wheeze between the cohorts in earlier years due to incomparability of respiratory questions, but it remains important to assess whether the changes we have observed in maternal smoking have contributed to the reported concurrent increase in early childhood wheezing illness.

Our finding that fewer teenagers were smoking, and smoking heavily, in 1986 than in 1974 is consistent with OPCS national data which suggest that, between 1974 and 1986, teenage smoking reduced from 40% to 30%. There was a much reduced response rate to the smoking question in 1986, particularly in males (response rate for males and females of 31.8% and 46.0%, respectively, of those who responded at age 5), which is likely to cause a systematic underestimate of the effect of personal smoking and, in the combined cohort, an increase in wheeze outcomes was associated with high levels of smoking only. Smoking in adolescence may be associated with the onset of a range of respiratory symptoms³⁶ and the reduction in prevalence and intensity of cigarette smoking among teenagers may have been one factor limiting the increase in prevalence between cohorts.

Thus, the present study has suggested a substantial increase in the prevalence of wheezing illness in teenagers in the UK, and has established that several factors previously implicated were not major contributors to the observed increase. Future studies are required to investigate the contribution of changes over time in other potential aetiological factors including levels of outdoor and indoor pollutant exposure, allergen exposure, and diet.

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Appendix

Comparison of the cohort respiratory questions in 1974 and 1986

1974	1986
Has the study child ever had an attack of asthma or wheezy bronchitis?	Has the study child ever had an attack of wheezing or whistling in the chest? What were these thought to be due to? Asthma Wheezy bronchitis Other cause
Did the most recent attack occur: In the past 12 months?	When did the most recent attacks occur: In the past 12 months?
If the child has had asthma or wheezy bronchitis in the past 12 months did this occur: At least once a week Usually less than once a week Less than once a month Frequency unknown	If the teenager has had asthma or wheezy bronchitis in the past 12 months, did this occur: At least once a week Usually less than once a week Less than once a month Frequency unknown

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