Incidence and prognosis of asthma and wheezing illness from early childhood to age 33 in a national British cohort

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Abstract

***Objective*—To describe the incidence and prognosis of wheezing illness from birth to age 33 and the relation of incidence to perinatal, medical, social, environmental, and lifestyle factors.**

***Design*—Prospective longitudinal study.**

***Setting*—England, Scotland, and Wales.**

***Subjects*—18 559 people born on 3-9 March 1958. 5801 (31%) contributed information at ages 7, 11, 16, 23, and 33 years. Attrition bias was evaluated using information on 14 571 (79%) subjects.**

***Main outcome measure*—History of asthma, wheezy bronchitis, or wheezing obtained from interview with subjects' parents at ages 7, 11, and 16 and reported at interview by subjects at ages 23 and 33.**

***Results*—The cumulative incidence of wheezing illness was 18% by age 7, 24% by age 16, and 43% by age 33. Incidence during childhood was strongly and independently associated with pneumonia, hay fever, and eczema. There were weaker independent associations with male sex, third trimester antepartum haemorrhage, whooping cough, recurrent abdominal pain, and migraine. Incidence from age 17 to 33 was associated strongly with active cigarette smoking and a history of hay fever. There were weaker independent associations with female sex, maternal albuminuria during pregnancy, and histories of eczema and migraine. Maternal smoking during pregnancy was weakly and inconsistently related to childhood wheezing but was a stronger and significant independent predictor of incidence after age 16. Among 880 subjects who developed asthma or wheezy bronchitis from birth to age 7, 50% had attacks in the previous year at age 7; 18% at 11, 10% at 16, 10% at 23, and 27% at 33. Relapse at 33 after prolonged remission of childhood wheezing was more common among current smokers and atopic subjects.**

***Conclusion*—Atopy and active cigarette smoking are major influences on the incidence and recurrence of wheezing during adulthood.**

Introduction

Most epidemiological studies of asthma and other wheezing illnesses have been cross sectional, in which existing (prevalent) cases are compared with healthy subjects. Prevalence is influenced by both incidence and prognosis. Investigation of the causes of disease should ideally focus on new (incident) cases and the healthy population from which they are drawn, whereas factors which influence the persistence of symptoms are of greater relevance to affected people.[1]

In this paper we describe the pattern of incidence and prognosis of wheezing illness in a large, nationally representative sample of young British adults who have been contacted at intervals since birth.[2-4] We also examined the relation of incidence to a range of perinatal, medical, social, environmental, and lifestyle factors.

Subjects and methods

The British national child development study (1958 cohort) is a longitudinal study of all people in England, Scotland, and Wales born during one week, 3-9 March 1958. It started as a study of perinatal morbidity and mortality[5] and subsequently included immigrants with the same birth dates. The cohort was followed up at ages 7, 11, and 16 by parental interview and examination by school medical officers.[6,7] Cohort members were interviewed at ages 23 and 33.[8] At ages 7, 11, 16, and 23 questions were asked relating to a history of asthma or wheezy bronchitis. At age 33 a more inclusive question was asked, referring to a history of wheezing, irrespective of diagnosis, and respondents were asked if they had ever had asthma (see appendix).

The incidence of wheezing illness was assessed over three periods: birth to 7, 8 to 16, and 17 to 33 years. As in previous reports,[2-4] we considered incident cases to be subjects without a history of asthma or wheezy bronchitis at all previous follow ups whose parents reported that they had ever had asthma or wheezy bronchitis at ages 7, 11, and 16; subjects who reported asthma or wheezy bronchitis since their 16th birthday at age 23; or subjects who reported having ever had asthma or wheezing, or both, at age 33. Subjects with a history of asthma or wheezy bronchitis at previous follow ups were excluded from the denominator for the second and third periods.

Persistence of wheezing at each follow up was assessed by responses indicating one or more attacks of asthma or wheezy bronchitis in the previous year at ages 7, 11, 16, and 23 and by a report of wheezing or whistling in the chest in the previous year at age 33. There was no specific inquiry about attacks of asthma in the previous year at age 33.

The association of incidence with a wide range of perinatal, medical, social, environmental, and lifestyle variables was assessed by cross tabulation and multiple logistic regression using SAS.[9]

Results

Originally, 17 414 births were included in the 1958 perinatal mortality survey, and a further 1145 subjects were included subsequently. At age 7, 14 571 (79% of 18 559) contributed information on asthma and bronchitis with wheezing. A history of wheezing illness at ages 7, 11, 16, 23, and 33 was available for 5801 subjects (31% of 18 559), including 1046 with a history of asthma or wheezy bronchitis by the age of 7. Information on the occurrence of wheezing attacks in the previous year was complete at each follow up for 880 of these subjects (84% of 1046).

Table 1 shows the incidence and prognosis of wheezing illness in the group with complete linked data and the corresponding values calculated using all available information.[2] The estimates differ only slightly, suggesting minimal bias due to sample attrition.

INCIDENCE

We examined the relation between incidence of asthma or wheezing in each of the follow up periods, and a range of perinatal, medical, social, environmental, and lifestyle variables summarised in the box. A full set of tabulations, based on the linked dataset, is available from us on request. Perinatal, medical, social, and lifestyle variables that were significantly related (at the 5% level) to incidence in one or more periods were included in multiple logistic regression models, as shown in table 2. Housing tenure was excluded because of its close association with father's social class.

Incidence during childhood was strongly and independently associated with pneumonia, hay fever, and eczema. There were weaker independent associations ($P<0.05$) with male sex, third trimester antenatal haemorrhage,

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Table 1—*Incidence and prognosis of asthma and wheezing illness in subjects with complete and incomplete data and using all available information. Values are percentages (proportions)*

	All available information	Fully linked data set	Incomplete information
Incidence by period			
Birth to age 7	18.3 (2665/14 571)	18.0 (1046/5801)	18.5 (1619/8770)
Age 8 to age 16	7.9 (568/7198)	7.8 (371/4755)	8.1 (197/2443)
Age 17 to age 33	24.4 (1071/4384)	24.4 (1071/4384)	
Cumulative incidence to age 33			
Prospective*	42.9 (2488/5801)	42.9 (2488/5801)	
Retrospective†	29.1 (3307/11 345)	28.0 (1627/5801)	30.3 (1680/5544)
Prognosis of asthma or wheezy bronchitis reported at age 7			
Wheeze in past year at age:			
7	49.4 (1181/2393)	50.2 (442/880)	48.8 (739/1513)
11	19.4 (421/2174)	18.2 (160/880)	20.2 (261/1294)
16	11.7 (206/1764)	10.2 (90/880)	13.1 (116/884)
23	9.7 (189/1957)	9.7 (85/880)	9.7 (104/1077)
33	26.5 (464/1752)	27.4 (241/880)	25.6 (223/872)

*Cumulative incidence derived from successive follow ups. This does not equal the sum of incidences for each period because different denominators are used for each period.
†Proportion recalling asthma or wheezing at any age when interviewed at age 33.

whooping cough, recurrent abdominal pain, and migraine (table 2). Maternal smoking was significantly related to childhood wheezing only in the few mothers (4%) who smoked during pregnancy but not when the child was aged 16 (table 2), perhaps reflecting cessation of smoking by mothers of wheezy children. The adjusted odds ratio comparing all children of mothers who smoked during pregnancy with the remainder were 1.02 (95% confidence interval 0.82 to 1.26) for wheezing at ages 0-7 and 1.04 (0.74 to 1.46) at ages 8-16.

Active smoking was strongly associated with adult onset wheezing. There was evidence of a dose-response relation, both with duration of smoking (table 2) and with amount smoked (table 3). Smoking as an adult was weakly associated with wheezing in childhood (table 3), suggesting little selective uptake or avoidance of smoking by previously wheezy children. Incidence from age 17 to 33 was also strongly associated with a history of hay fever. There were weaker independent associations ($P<0.05$) with female sex, maternal albuminuria during pregnancy, maternal smoking, and a history of migraine or eczema (table 2). Variation in incidence in adult onset wheezing with social class was highly confounded by smoking and disappeared after mutual adjustment. The independent associations of asthma incidence with birth order, gestational age, periodic vomiting, and paternal smoking were not significant at the 5% level (table 2).

MODIFICATION OF EFFECT BY ATOPY

Interactions were examined between atopic history (defined as a report of hay fever, allergic rhinitis, or eczema at one or more follow ups) and all variables with one or more significant associations shown in table 2. Few interactions were significant at the 5% level, and these are shown in table 3.

Sex differences in incidence during childhood were more obvious in the atopic group ($P=0.001$ in test for interaction), whereas the associations of abdominal pain with childhood wheezing ($P<0.02$) and migraine with wheezing of later onset ($P<0.001$) were largely restricted to the non-atopic group. Maternal smoking during pregnancy was associated with an increased risk of childhood wheezing among non-atopic subjects but a slightly decreased risk among atopic subjects ($P<0.01$ in test for interaction). Active smoking increased the risk of adult onset wheezing in both atopic and non-atopic subjects, but both the relative and excess risk were greater in the non-atopic group ($P<0.002$).

PROGNOSIS

Figure 1 shows the prognosis for children who developed asthma or wheezy bronchitis before the 7 year follow up. Each symbol represents 1% of this linked dataset of 880 subjects, and the natural course for each 1% subsample can be followed vertically on the diagram. One half of these children with a history of early wheezing illness were still affected in the previous year at age 7, but more than two thirds of them experienced no attacks at age 11. On the other hand, some children who had apparently outgrown their wheezing tendency at age 7 later developed further wheezing episodes. Over half (57% (138/241)) of the subjects who wheezed before the age of 7 years and reported wheezing in the previous year at the age of 33 had been free of attacks for seven years from the age of 16 to 23.

When interviewed at age 23, 1303 subjects with a history of wheezing illness from birth to age 16 denied attacks of asthma or wheezy bronchitis since their 16th birthday. To assess whether this group reported an excess of wheezing at age 33, they were compared with 3928 subjects with no history of asthma or wheezy bronchitis at any follow up to the age of 23 inclusive (table 4). In both groups, the prevalence of wheezing in the previous year at the age of 33 was strongly related to both atopy and cigarette smoking, but smoking was a more important risk factor for adult wheezing among non-atopic subjects ($P<0.001$ in test for interaction). Independent of these factors, the group who seemed to have outgrown their childhood wheezing tendency by

Variables analysed in relation to incidence of wheezing illness* at ages 0-7, 8-16, 17-33, and 0-33 years†

Perinatal factors
Sex
Maternal age (at birth of child)
Birth order
Gestational age
Birth weight
Birth weight for gestational age
Maternal albuminuria in pregnancy
Maternal blood pressure in pregnancy
Maternal haemoglobin in pregnancy
Antepartum haemorrhage
Induction of labour
Duration of membrane rupture
Mode of delivery
Neonatal resuscitation
Breast feeding

Place of birth
Longitude
Latitude
Degree of urbanisation
Smoke pollution (winter 1962-3)
Sulphur dioxide pollution (winter 1962-3)

Other diseases
Pneumonia
Whooping cough
Tonsillectomy
Hay fever or allergic rhinitis
Eczema or eczematous rashes
Recurrent abdominal pain
Periodic vomiting
Recurrent headache or migraine

Socioeconomic factors
Father's social class (at age 11)
Housing tenure (at age 7)
Household amenities shared (at age 11)
Ever been in care (by age 11)
Number of siblings (at age 11)

Smoking
Maternal smoking during pregnancy
Maternal smoking at age 16
Paternal smoking at age 16
Own smoking at ages 16, 23, and 33

*Asthma or wheezy bronchitis at ages 0-23, asthma or wheezing by age 33.
†Full tabulations available on request from the authors or on the Internet (home page http://www.bmj.com/bmj/).

Table 2—*Associations of perinatal, medical, social, and lifestyle factors with incidence of wheezing illness at ages 0-7, 8-16, and 17-33, adjusted for all other factors shown*

		Incidence of asthma or wheezing illness					
		Ages 0-7 (n=3147)		Ages 8-16 (n=2606)		Ages 17-33 (n=2051)	
Risk factor	Categories (or units) compared	Odds ratio (95% confidence interval)	χ^2	Odds ratio (95% confidence interval)	χ^2	Odds ratio (95% confidence interval)	χ^2
Sex	Male *v* female	1.26 (1.03 to 1.53)	5.19, df=1*	1.50 (1.10 to 2.05)	6.64, df=1**	0.80 (0.64 to 1.00)	3.86, df=1*
Maternal age	Per year	0.98 (0.96 to 1.00)	2.23, df=1	0.97 (0.94 to 1.00)	3.10, df=1	1.01 (0.99 to 1.04)	1.21, df=1
Birth order	Per position	1.02 (0.94 to 1.11)	0.28, df=1	0.99 (0.86 to 1.14)	0.02, df=1	1.06 (0.97 to 1.16)	1.65, df=1
Gestation	<37 *v* ≥37 weeks	1.12 (0.67 to 1.87)	0.18, df=1	0.66 (0.26 to 1.69)	0.83, df=1	1.03 (0.56 to 1.88)	0.01, df=1
Albuminuria	Any *v* none	1.20 (0.86 to 1.67)	1.16, df=1	0.86 (0.48 to 1.54)	0.26, df=1	1.63 (1.14 to 2.34)	6.74, df=1**
Bleeding in pregnancy	At <28 weeks *v* none	0.40 (0.19 to 0.85)	7.77, df=2*	0.59 (0.22 to 1.58)	7.08, df=2*	1.16 (0.64 to 2.12)	0.63, df=2
	At ≥28 weeks *v* none	1.33 (0.71 to 2.50)		2.98 (1.33 to 6.66)		0.78 (0.35 to 1.76)	
Pneumonia by age 7	Age 0-1 *v* none	2.00 (1.10 to 3.65)	32.87, df=2***	2.28 (0.89 to 5.84)	10.56, df=2**	0.45 (0.16 to 1.27)	3.52, df=2
	Age 2-7 *v* none	4.24 (2.57 to 7.01)		3.90 (1.72 to 8.87)		1.54 (0.64 to 3.71)	
Whooping cough by age 11	Age 0-7 *v* none	1.24 (0.95 to 1.61)	3.27, df=2	1.92 (1.31 to 2.83)	10.31, df=2**	0.95 (0.68 to 1.31)	0.23, df=2
	Age 8-11 *v* none	1.25 (0.84 to 1.87)		1.29 (0.67 to 2.49)		0.91 (0.56 to 1.47)	
Tonsillectomy by age 16	Age 0-7 *v* none	1.20 (0.93 to 1.54)	5.65, df=2	1.22 (0.82 to 1.81)	1.77, df=2	1.19 (0.89 to 1.58)	2.38, df=2
	Age 8-16 *v* none	1.43 (1.03 to 1.99)		1.34 (0.79 to 2.25)		1.26 (0.85 to 1.88)	
Hay fever	Per follow up reported	1.34 (1.22 to 1.47)	34.72, df=1***	1.44 (1.24 to 1.66)	20.92, df=1***	1.54 (1.36 to 1.74)	47.4, df=1***
Eczema	Per follow up reported	1.33 (1.17 to 1.52)	17.04, df=1***	1.25 (1.01 to 1.53)	4.00, df=1*	1.23 (1.02 to 1.48)	4.74, df=1*
Abdominal pain	Per follow up reported	1.26 (1.07 to 1.49)	7.36, df=1**	1.16 (0.89 to 1.52)	1.14, df=1	1.20 (0.99 to 1.47)	3.29, df=1
Vomiting	Per follow up reported	1.12 (0.91 to 1.37)	1.17, df=1	0.98 (0.69 to 1.38)	0.02, df=1	1.23 (0.96 to 1.58)	2.73, df=1
Migraine	Per follow up reported	1.14 (1.01 to 1.28)	4.48, df =1*	0.99 (0.80 to 1.23)	0.01, df=1	1.16 (1.01 to 1.34)	4.26, df=1*
Father's social class at age 11†	II	0.91 (0.58 to 1.43)	1.79, df=5	1.32 (0.62 to 2.85)	2.02, df=5	0.95 (0.57 to 1.58)	7.24, df=5
	IIINM	1.02 (0.62 to 1.67)		1.60 (0.71 to 3.62)		1.43 (0.83 to 2.49)	
	IIIM	1.05 (0.69 to 1.60)		1.21 (0.58 to 2.55)		0.88 (0.54 to 1.43)	
	IV	1.06 (0.66 to 1.69)		1.14 (0.50 to 2.58)		1.02 (0.60 to 1.75)	
	V	0.84 (0.44 to 1.61)		1.34 (0.49 to 3.66)		0.89 (0.44 to 1.77)	
Paternal smoking at age 16	Yes *v* no	1.08 (0.89 to 1.33)	0.63, df=1	1.15 (0.83 to 1.59)	0.71, df=1	0.92 (0.73 to 1.15)	0.54, df=1
Maternal smoking	In pregnancy only *v* never	1.72 (1.11 to 2.67)	6.75, df=3	0.94 (0.39 to 2.25)	0.66, df=3	1.71 (0.97 to 3.00)	8.59, df=3*
	At 16 only *v* never	1.11 (0.83 to 1.48)		1.18 (0.75 to 1.85)		1.19 (0.86 to 1.65)	
	Pregnancy and at 16 *v* never	0.94 (0.74 to 1.20)		1.10 (0.76 to 1.60)		1.40 (1.08 to 1.82)	
Cohort member's smoking	At 16, 23, or 33; *v* never	ND		ND		2.25 (1.75 to 2.89)	109.5, df=2***
	At 16, 23, and 33; *v* never	ND		ND		4.42 (3.31 to 5.92)	

ND = Variable not included in model.
*P<0.05, **P<0.01, ***P<0.001.
†Compared with social class I.

the age of 23 were more likely to report wheezing 10 years later than were those with no history of asthma or wheezy bronchitis in childhood. The prevalence ratio, adjusted for atopic history and current smoking, was 1.47 (1.28 to 1.68, P<0.001).

Discussion

INCIDENCE

To our knowledge, there have been no truly prospective studies of asthma incidence throughout childhood into early adult life. In most studies parents have been interviewed at one point in time and asked to recall past episodes of wheezing in their children. Validation of this technique against previous interviews or general practitioner records suggests that it underestimates the cumulative incidence of wheezing episodes by as much as a third.[4 10] Our estimates of incidence, particularly in early childhood, are likely to be conservative. At least two thirds of children who develop wheezing by the age of 16 first do so before they are 5 years old,[11] and many experience their first attack in infancy.[12] Abnormalities in lung function are detectable before the onset of asthmatic symptoms.[12-15] Some causal agents must therefore act very early in life, possibly before birth.

We were particularly interested in the relation of asthma incidence to perinatal risk factors for wheezing or allergy—namely, maternal age,[11 16] parity,[11 17] birth weight,[16 18] premature delivery,[19-21] birth weight for gestation,[19 20] and breast feeding.[22] None emerged as significant independent risk factors, but unexpected associations were found with antenatal haemorrhage and maternal albuminuria. These deserve further investigation: antenatal haemorrhage has been associated with maternal smoking.[23]

Our results confirm the strong association of asthma incidence with hay fever and eczema,[4] but they also

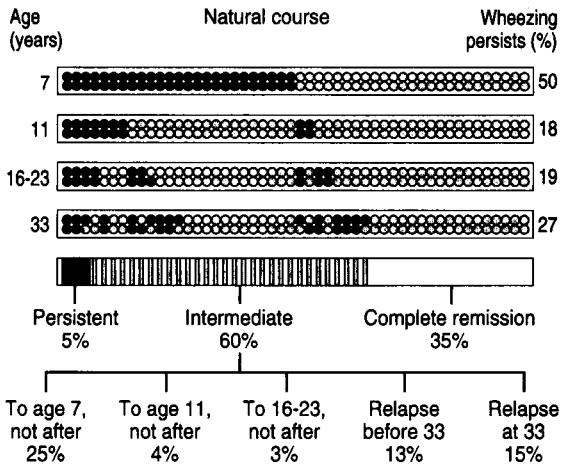

Fig 1—*Prognosis for children who developed asthma or wheezy bronchitis by age 7. Each symbol represents 1% of such children, and the natural course of each 1% subsample can be traced vertically. Filled circles represent subjects reporting asthma or wheezy bronchitis in the previous year at ages 7 and 11, those reporting asthma or wheezy bronchitis since their 16th birthday at age 23, and those reporting wheezing in the previous year at age 33*

Table 3—*Incidence of asthma or wheezing illness* and its association with selected risk factors among atopic and non-atopic subjects. Values are percentages (numbers)*

Risk factor	Atopic subjects‡				Non-atopic subjects			
	No of subjects†	0-16	17-33	0-33	No of subjects†	0-16	17-33	0-33
Sex:								
Male	870	39.2 (341)	30.1 (159)	57.5 (500)	1917	21.6 (414)	19.0 (285)	36.5 (699)
Female	985	27.1 (267)	35.1 (252)	52.7 (519)	2029	19.5 (395)	22.9 (375)	37.9 (770)
Recurrent abdominal pain:								
No follow ups	1250	32.4 (405)	31.8 (269)	53.9 (674)	2763	19.1 (527)	19.7 (441)	35.0 (968)
1 Follow up	405	33.8 (137)	34.7 (93)	56.8 (230)	786	22.9 (180)	23.8 (144)	41.2 (324)
> 1 Follow up	129	34.1 (44)	40.0 (34)	60.5 (78)	194	31.4 (61)	31.6 (42)	53.1 (103)
Recurrent headache/migraine:								
No follow ups	1158	30.6 (354)	33.0 (265)	53.5 (619)	2590	18.6 (483)	18.3 (386)	33.6 (869)
1 Follow up	183	28.4 (52)	38.2 (50)	55.7 (102)	387	21.7 (84)	28.1 (85)	43.7 (169)
> 1 Follow up	144	39.6 (57)	31.0 (27)	58.3 (84)	249	24.5 (61)	35.6 (67)	51.4 (128)
Smoking during pregnancy:								
No	1273	33.5 (426)	30.6 (259)	53.8 (685)	2585	18.9 (489)	19.5 (409)	34.7 (898)
Yes	521	32.2 (168)	39.9 (141)	59.3 (309)	1230	24.5 (301)	24.4 (227)	42.9 (528)
Cohort member's smoking:								
Never	858	33.1 (284)	26.7 (153)	50.9 (437)	1646	19.0 (312)	11.1 (148)	27.9 (460)
At 16, 23, or 33	463	32.6 (151)	38.8 (121)	58.7 (272)	1046	20.5 (214)	25.5 (212)	40.7 (426)
At 16, 23, and 33	268	33.6 (90)	45.5 (81)	63.8 (171)	633	22.4 (142)	38.3 (188)	52.1 (330)
Amount smoked daily at age 23:								
Not current smoker	1200	32.6 (391)	28.3 (229)	51.7 (620)	2366	19.3 (457)	12.9 (247)	29.8 (704)
< 10 cigarettes	158	34.8 (55)	31.1 (32)	55.1 (87)	332	22.9 (76)	27.0 (69)	43.7 (145)
10-19 cigarettes	243	31.7 (77)	41.0 (68)	59.7 (145)	569	22.3 (127)	32.6 (144)	47.6 (271)
≥ 20 cigarettes	253	33.2 (84)	48.5 (82)	65.6 (166)	677	22.0 (149)	37.9 (200)	51.6 (349)

*Asthma or wheezy bronchitis at ages 0-23, asthma or wheezing by age 33.
†Cohort members with complete information on asthma or wheezy bronchitis by 7, by 11, by 16, by 23 and on asthma or wheezing by 33.
‡Report of hay fever, allergic rhinitis, or eczema at one or more follow ups.

show important differences between the risk factors for wheezing illness and other allergic conditions. Hay fever and eczema in this cohort were associated with small sibships,[17] higher socioeconomic status,[24] and lower latitude,[25] factors that were not related to asthma and wheezing (table 2). In an attempt to resolve this paradox, we investigated whether the risk factors for wheezing differed between atopic and non-atopic subjects. Few variables showed substantial differences, but smoking (both active and passive) seemed to be more important as a risk factor for non-atopic wheezing (table 3). Stronger associations among the non-atopic group also emerged for a history of recurrent abdominal pain or migraine,[26] which may reflect a functional abnormality of smooth muscle of relevance to the pathogenesis of asthma.

The influence of maternal smoking on the incidence of wheezing during early childhood was weak and inconsistent, in contrast to the findings of several other studies,[11 27 28] but smoking during pregnancy was an independent predictor of adult onset wheeze (tables 2 and 3). This last effect may be due to residual confounding by active smoking after 16 years of age, which was the dominant risk factor for wheezing of later onset. Cigarette smoking is a powerful risk factor for the development of chronic mucus hypersecretion and progressive airflow obstruction in middle and old age[29] but, remarkably, has not been reported in several studies of asthma incidence.[14 30-32] The four year incidence of doctor diagnosed asthma among people aged 10-39 years in Tucson, Arizona, was three times greater among smokers than among non-smokers at the start of the observation period.[33]

Table 4—*Prevalence of wheezing in past year at age 33 among subjects with no attacks of asthma or wheezy bronchitis at ages 16-23, by history of asthma or wheezy bronchitis in childhood, atopic history,* and smoking at age 33. Values are percentages (proportions) unless stated otherwise*

	Asthma or wheezy bronchitis by age 16		
	Yes	No	Prevalence ratio (95% confidence interval)
Non-atopic non-smoker	8.7 (40/459)	6.1 (117/1917)	1.43 (1.01 to 2.01)
Atopic non-smoker	20.9 (93/446)	13.2 (108/820)	1.58 (1.23 to 2.04)
Non-atopic smoker	31.9 (74/232)	23.0 (203/881)	1.38 (1.11 to 1.73)
Atopic smoker	37.3 (62/166)	25.5 (79/310)	1.47 (1.11 to 1.93)
All subjects†	20.6 (269/1303)	12.9 (507/3928)	1.60 (1.40 to 1.83)

*One or more reports of hay fever, allergic rhinitis, or eczema.
†Cohort members interviewed at age 23 who denied attacks of asthma or wheezy bronchitis since their 16th birthday and for whom there was complete information on atopic history, smoking at age 33, and history of wheezing illness in childhood.

PROGNOSIS

A quarter of children with a history of asthma or wheezy bronchitis by the age of 7 reported wheeze in the previous year at the age of 33. This is consistent with the findings of studies in Tasmania[14] and Melbourne,[34] which have followed up population based samples of 7 year olds with a history of asthma or wheezing illness into their 30s.

Simple two point estimates of prognosis (table 1) conceal the complex pattern of remissions and relapses experienced by individual subjects (fig 1). In Melbourne, as in this British cohort, there was a tendency for symptoms to recur in adulthood after a period of remission during late teenage years.[35] We believe that our study is unique in showing that, even after a disease free interval of seven years or more, subjects with a history of wheezing illness in childhood retained a risk of later wheezing above that of their healthy peers (table 4). This may reflect greater awareness of asthmatic symptoms when they recur or a degree of continuity between environment or lifestyle in childhood and adult life. However, the increased risk was not explained by atopy and smoking, the two dominant influences on long term prognosis. Persistent abnormalities of airway function, which have been shown in three studies of asthmatic children in remission,[36-38] may predispose to the development of symptoms on exposure to new environmental agents in adulthood, particularly cigarette smoking.

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Key messages

- About half of British people born in 1958 experienced one or more episodes of wheezing illness by 33 years of age. Less than two thirds of these recalled wheezing when interviewed at age 33.
- Incidence of wheezing illness at all ages was strongly and consistently related to a history of hay fever or eczema (atopy). Associations with maternal smoking during pregnancy, abdominal pain, and migraine were largely confined to those without atopy
- Active smoking was a powerful and potentially avoidable risk factor for wheeze starting in adult life among both atopic and non-atopic subjects
- A quarter of the children with a history of asthma or wheezy bronchitis by age 7 reported wheeze in the past year at age 33
- Recurrence of wheezing after prolonged remission during late adolescence was strongly associated with atopy and cigarette smoking.

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Appendix

QUESTIONS USED TO DEFINE THE OCCURRENCE OF WHEEZING ILLNESS

At age 7

Has your child ever had attacks of asthma? If yes, how many attacks in the past year?

Has your child ever had attacks of bronchitis with wheezing? If yes, how many attacks in the past year?

At age 11

Has your child ever had attacks of asthma or wheezing bronchitis? If yes, how frequently do these attacks occur? (Answer chosen from: at least once a week; usually less than once a week but can expect one attack a month; at least one attack in the past year but less frequently than once a month; had attacks in the past year but don't know how frequently; no attacks in the past year.)

At age 16

Has your child ever had attacks of asthma or wheezy bronchitis? If yes, how frequently do these attacks occur? (Answer chosen from same options as given at age 11.)

At age 23

Have you had an attack of asthma or wheezy bronchitis since your 16th birthday? If yes, have you had an attack of asthma or wheezy bronchitis in the past 12 months?

At age 33

Some people feel that their chest is sometimes wheezy or whistling. Have you ever had wheezing or whistling in your chest at any time in the past? If yes, have you ever had any wheezing or whistling in your chest at any time in the past 12 months? If yes, how many times have you had any wheezing or whistling in your chest in the past 12 months? (Answers chosen from none; 1-4 times; 5 or more times; don't know.)

All subjects at the age of 33 were asked whether they had ever been told that they had asthma.

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