



clinical investigations

Wheezy Bronchitis in Childhood*

A Distinct Clinical Entity With Lifelong Significance?

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Background: Historically, clinicians have recognized the existence of the clinical syndrome of childhood wheezy bronchitis. In the late 1960s, children with this syndrome were relabeled as having asthma, and the term *wheezy bronchitis* was abandoned. In a 1989 study of a cohort that originally had been studied in 1964, we reported that those who had childhood wheezy bronchitis had as adults attained lung function similar to that of healthy control subjects and had less significant symptoms than did those who had experienced childhood asthma, in whom lung function was reduced. In this study, we reexamined these subjects 12 years later to determine whether the improved outcome of the wheezy bronchitis group had been maintained.

Methods: In 2001, we followed up the 283 participants of the 1989 study, who were now aged 45 to 50 years. In interviews, respiratory symptoms and smoking status were assessed. Spirometry was measured.

Results: One hundred seventy-seven subjects (63%) completed the study. After adjusting for age, height, gender, socioeconomic status, smoking status, and number of pack-years smoked, the current FEV₁ in the childhood asthma group (mean, 2.45 L; 95% confidence interval, 2.29 to 2.62) was significantly lower than the wheezy bronchitis group (2.78 L, 95% confidence interval, 2.64 to 2.91; $p < 0.01$) and the control group (2.96 L; 95% confidence interval, 2.83 to 3.1; $p < 0.01$). The difference between the wheezy bronchitis group and the control subjects was not significant ($p = 0.06$). Between 1989 and 2001, both the childhood wheezy bronchitis group ($p < 0.01$) and the childhood asthma group ($p = 0.01$) had greater declines in FEV₁ than did the control group (asthma group decline, -0.75 L [95% confidence interval, -0.66 to -0.84]; wheezy bronchitis group decline, -0.75 L [95% confidence interval, -0.68 to -0.83]; control group decline, -0.59 L [95% confidence interval, -0.52 to -0.67]). In 2001, the asthma group had more symptoms than did the wheezy bronchitis group ($p < 0.01$), who were more symptomatic than the control group ($p < 0.01$). **Conclusion:** Those with childhood wheezy bronchitis, having achieved normal lung function in earlier adulthood, now show a more rapid decline in lung function than did control subjects. If this rate of decline persists, these subjects may develop obstructive airways disease in later life.

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Key words: asthma; longitudinal study; lung function; respiratory symptoms; wheezy bronchitis

The natural history of childhood wheezing illnesses remains incompletely understood. Historically, clinicians have recognized distinct syndromes

of “wheezy bronchitis” and asthma. In the late 1960s, due to concerns about the undertreatment of asthma, most forms of childhood wheezing, including wheezy bronchitis,¹ were subsumed into the diagnostic category of *asthma*. However, in recent years, it has again been recognized that differing wheezing syndromes occur in children. In infants, workers in both the United Kingdom and the United States have described transient wheezing conditions that do not lead to asthma or allergy in later childhood.^{2,3}

A cross-sectional school survey in Aberdeen, Scotland, in the early 1960s⁴ identified 6% of children, aged 10 to 15 years, whose parents answered “yes” to

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the question "Does (your child's) chest ever sound wheezy or whistling?" They were then classified, after review by a physician, as having "asthma" or "wheeze in the presence of infection," with the latter corresponding to the diagnosis of wheezy bronchitis that was in use at that time.⁵ The main determining factor in ascribing a diagnosis of asthma was a history of wheeze precipitated by factors other than a cold or upper respiratory infection. In a follow-up study of these individuals,⁶ we have previously shown that the children in whom wheezy bronchitis was diagnosed had different outcomes as adults than those in whom asthma was diagnosed. At ages 34 to 40 years, those who had wheezy bronchitis as children had normal lung function and less significant symptoms compared to those who had asthma in whom lung function had been reduced.⁶ In a new cross-sectional study of Aberdeen schoolchildren that was carried out in 1994, Omran and Russell⁷ again found about 6% of schoolchildren who described wheeze but had no diagnosis of asthma. Interestingly, this prevalence figure was unchanged since 1964, whereas the prevalence of doctor-diagnosed asthma had risen from 4.8%⁵ to 19.6%.⁷ If wheezy bronchitis is a distinct clinical entity, the question arises of whether the natural history of this condition will continue to diverge from that of asthma.

To address this issue, we have reinvestigated those subjects among whom we had previously reported outcome of childhood wheezy bronchitis and asthma in adulthood⁶ to determine whether, 12 years later, the achievement of normal lung function in the childhood wheezy bronchitis group had been maintained.

MATERIALS AND METHODS

Study Population

In 1964, a random community survey of one in five children, who were between the ages of 10 and 15 years (2,511 patients) and attended school in Aberdeen, reported that 288 children had wheeze. After clinical assessment, 121 were classified as having *asthma*, which was clinically defined as "recurrent dyspnea of an obstructive type without other demonstrable cause," and 167 children were classified as having "wheeze only in the presence of upper respiratory tract infection," a condition then recognized as *wheezy bronchitis*. The remaining 2,223 children had no respiratory symptoms.^{4,5} In 1989, a study was carried out to determine the outcome of childhood wheeze in adulthood,⁶ which traced 189 of those patients with childhood asthma and wheezy bronchitis in 1964, and included a random sample of 94 patients from among those who had no respiratory symptoms as children in 1964.

In 2001, we attempted to trace (Data Discoveries Ltd; Edinburgh, Scotland) all 283 subjects who had been interviewed in 1989. For those not found, we checked the Patient Administration System at Aberdeen Royal Infirmary for a current address.

Finally, subjects for whom no address could be found by either method were traced via the Community Health Index at the Grampian Health Board.

Protocol

One researcher (C.A.E.) interviewed all subjects who agreed to participate between August 2000 and July 2001, either at the Chest Clinic in Aberdeen Royal Infirmary or in their own home. The interview included a modified version of the Medical Research Council 1986 Respiratory Symptoms Questionnaire,⁸ and questions on current medication and smoking. At the time of the interview, FEV₁ and FVC were measured using a portable spirometer (Compact II; Vitalograph; Buckingham, UK), which was calibrated daily. The spirometry measurements were performed with subjects in a sitting position without the use of nose clips. Three values were obtained, and the highest FEV₁ and FVC values were used. The highest of three peak flow measurements also was recorded using a peak flowmeter (mini-Wright; Clement Clarke; Harlow, UK). Subjects to whom a bronchodilator was prescribed were requested not to use it in the 6 h before the tests were performed. Thirty-eight subjects had been prescribed bronchodilators, and of these, 9 subjects used the bronchodilator within 6 h of the tests being performed.

Skin-prick tests also were performed at the time of the interview using house dust mite (*Dermatophagoides pteronyssinus*), cat hair, and mixed grass pollens (rye, Timothy, False Oat, Cocks Foot, Meadow fescue, and June). The positive control contained 10 mg/mL histamine in a solution of glycerol and saline solution. The negative control contained a solution of glycerol and saline solution (Alk Abelló; Hungerford, UK). A positive test was defined as a wheal diameter of ≥ 3 mm 10 min after inoculation.^{9,10} Subjects who used antihistamine tablets were requested not to take them 2 days prior to the test. The study was approved by the Grampian Research Ethics Committee.

Statistical Analysis

Statistical analyses were performed using a statistical software package (SPSS, version 10.0 for Windows; SPSS; Chicago, IL). FEV₁ was expressed in liters. Univariate analysis of variance was used to examine the effects of the original childhood group on lung function, adjusted for height, age, gender, socioeconomic status, smoking status, and number of pack-years smoked. Socioeconomic status was measured by postal codes, using the Carstairs deprivation index.^{11,12} This index has been calculated for each postal code sector in Scotland from census data and combines information on household overcrowding, car ownership, male unemployment, and the percentage of households in which the head has a semi-skilled or manual occupation. These values then were classified into seven categories^{13,14} from socioeconomic status 1 (the very affluent) to socioeconomic status 7 (the severely deprived). Following the approach of Ulrik and Lange,¹⁵ no adjustment was made for the FEV₁ value in 1989.

RESULTS

Tracing Exercise

Details of the tracing and response rates are shown in Table 1. In total, 63% of the subjects completed the study. Neither smoking status nor symptoms (wheeze and cough) of subjects in 1989 were related to participation in the 2001 study. The gender

Table 1—Derivation of the Study Population*

Variables	Childhood			Total
	Asthma	Wheezy Bronchitis	No Childhood Respiratory Symptoms	
Patients in 1989	78	111	94	283
Died	1 (1)	3 (3)	3 (3)	7 (2)
Moved away/unable to trace	1 (1)	5 (4)	4 (4)	10 (4)
Not replied	20 (26)	21 (19)	15 (16)	56 (20)
Refusals	10 (13)	17 (15)	6 (6)	33 (12)
Completed study	46 (59)	65 (59)	66 (69)	177 (63)

*Values given as No. (%).

distribution of those who participated did not differ from those who refused. However, subjects from affluent areas (*ie*, socioeconomic status 1 to 3) were more likely to agree to participate in the 2001 study than were those from less affluent areas (*ie*, socioeconomic status 4 to 7) [72% vs 55%, respectively; $p < 0.01$].

Table 2 shows the characteristics of the 177 participants in the present study. As in the 1964 cohort and the 1989 sample, male subjects were more common in the childhood asthma and wheezy bronchitis groups than in the childhood asymptomatic group. Subject in these groups were more likely to be using respiratory medication ($p < 0.01$). Current cough ($p = 0.44$), smoking habit ($p = 0.51$), number of pack-years smoked ($p = 0.58$), and time smoked (*ie*, number of years; $p = 0.69$) did not differ

significantly among the three study groups. A higher proportion of subjects in the childhood asthma group reported having ever had hay fever or eczema, although this was not significant. Atopy on skin-prick testing differed among the three childhood groups ($p < 0.01$), with the childhood asthma group having the greatest proportion of atopy.

Change in Respiratory Symptoms

In 1989, the childhood asthma group had a greater proportion of wheeze than did the childhood wheezy bronchitis group, who in turn had more wheeze than the childhood no respiratory symptom group (*ie*, the control group). In 2001, this pattern continued. Table 3 shows the proportion of subjects with current wheeze among the childhood no-respiratory-symptom group increased from 9% in 1989 to 21% in 2001. This appears to be a greater change in incidence than that occurring in the childhood asthma and childhood wheezy bronchitis groups. However, after adjusting for age, height, gender, socioeconomic status, smoking status, and number of pack-years smoked, logistic regression showed no statistical difference between the change in current wheeze among the groups.

Between 1989 and 2001, the incidence of cough increased across all childhood groups, but most dramatically in the childhood no-respiratory-symptom group, which saw a threefold increase. However, like wheeze, the change in the incidence of cough

Table 2—Characteristics of the Study Population*

Characteristics	Total	Childhood Asthma (n = 46)	Childhood Wheezy Bronchitis (n = 65)	No Childhood Respiratory Symptoms (n = 66)
Gender				
Male	96 (54)	29 (63)	39 (60)	28 (42)
Female	81 (46)	17 (37)	26 (40)	38 (58)
Age	47.8	47.9 (± 1.4)	47.9 (± 1.6)	47.7 (± 1.4)
Socioeconomic score ⁹				
1–3	110 (62)	26 (56)	40 (62)	44 (67)
4–7	67 (38)	20 (44)	25 (38)	22 (33)
Use bronchodilators	38 (22)	22 (48)	12 (19)	4 (6)
Atopic	91 (51)	36 (78)	32 (49)	23 (35)
Ever had eczema	56 (32)	19 (41)	18 (28)	19 (29)
Ever had hay fever	63 (36)	21 (46)	21 (32)	21 (32)
Used steroids in last 12 mo	11 (6)	7 (15)	3 (5)	1 (1)
Smoking status				
Never smoked	88 (50)	23 (50)	34 (52)	31 (47)
Ex-smoker	44 (25)	8 (17)	18 (28)	18 (27)
Current smoker	45 (25)	15 (33)	13 (20)	17 (26)
Unadjusted mean 2001 FEV ₁ , † L	2.76	2.51 (± 0.90)	2.86 (± 0.73)	2.84 (± 0.74)
Unadjusted absolute decline FEV ₁ 1989–2001, L	0.69	0.76 (± 0.41)	0.75 (± 0.28)	0.59 (± 0.28)

*Values given as No. (%) or mean $\pm$ SD.

†Eight subjects from childhood asthma group and one subject from childhood wheezy bronchitis group used a bronchodilator within 6 h of 2001 spirometry tests. Mean FEV₁ was lower for this group (mean difference, -0.63 ; 95% confidence interval, -1.28 to 0.01 ; $p = 0.06$).

Table 3—Change in Respiratory Symptoms from 1989 to 2001*

Variables	Total	Childhood Asthma (n = 46)	Childhood Wheezy Bronchitis (n = 65)	No Childhood Respiratory Symptoms (n = 66)
Wheeze in 1989†	55 (31)	28 (61)	21 (32)	6 (9)
Wheeze in 2001‡	67 (38)	30 (65)	23 (35)	14 (21)
Cough in 1989†	41 (23)	15 (33)	20 (31)	6 (9)
Cough in 2001‡	64 (36)	19 (41)	25 (39)	20 (30)

*Values given as No. (%).

†In 1989, each group was significantly different in incidence of cough and wheeze ($p < 0.01$).

‡In 2001, each group was significantly different in incidence of wheeze ($p < 0.01$) but not cough ($p = 0.28$). Logistic regression showed no statistical difference between the groups in the change in incidence of current wheeze ($p = 0.70$) or current cough ($p = 0.23$) from 1989 to 2001.

since 1989, after adjusting for the same variables, showed no significant differences among the groups.

The reported severity of symptoms differed among the three groups. The proportions of subjects producing phlegm on most days for 3 months were 28% (childhood asthma group), 15% (childhood wheezy bronchitis group), and 12% (control group) [$p = 0.07$]. Wheeze interfering with activities in the past week was reported by 24% (childhood asthma group), 2% (childhood wheezy bronchitis group), and 3% (control group) [$p < 0.01$], and admissions to hospital for chest problems in the past 10 years by 30% (childhood asthma group), 9% (childhood wheezy bronchitis group), and 3% (control group) [$p < 0.01$].

Lung Function in 2001

After adjusting for height, age, gender, socioeconomic status, smoking status, and number of pack-years smoked, the childhood asthma group had a significantly lower adjusted FEV₁ than did both the childhood wheezy bronchitis group ($p < 0.01$) and the control group ($p < 0.01$) [Table 4]. The difference between the childhood wheezy bronchitis group and the control group in current FEV₁ was of borderline significance ($p = 0.06$).

Decline in Lung Function Since 1989

After adjusting for height, age, gender, socioeconomic status, smoking status, and number of pack-years smoked, the absolute decline in FEV₁ values over the 12-year period between 1989 and 2001 was significantly greater in the childhood asthma group and childhood wheezy bronchitis group than in the control group (Table 5). Calculated as an annual rate over the 12-year period (1989 to 2001), the adjusted

Table 4—Mean Adjusted FEV₁ Values and Differences Among Groups*

Groups	Mean Adjusted FEV ₁ , L	Adjusted FEV ₁ Difference, L	95% CI for Difference
Childhood no respiratory symptoms	2.96		
Childhood wheezy bronchitis	2.78	− 0.18	− 0.38 to − 0.01
Childhood asthma†	2.45	− 0.51	− 0.73 to − 0.30‡

*CI = confidence interval.

†The childhood asthma group had a significantly lower adjusted FEV₁ than the childhood wheezy bronchitis group (difference, − 0.33; 95% CI, − 0.54 to − 0.11; $p < 0.01$).

‡Because the confidence interval does not include zero, then this group of subjects is statistically different from the childhood no respiratory symptoms group at the 5% level.

mean FEV₁ decline was 65 mL per year in both the childhood asthma group and the childhood wheezy bronchitis group, and the decline was 50 mL per year in the control group.

DISCUSSION

The purpose of this study was to examine whether the difference in adult outcome between childhood wheezy bronchitis and childhood asthma, which was noted in 1989, persisted as subjects moved through middle age. The results indicate that the subjects who had childhood wheezy bronchitis, despite having achieved normal lung function when studied in 1989, were showing in 2001 a more rapid decline in lung function than that of the control group. The rate of decline of FEV₁ in the wheezy bronchitis group is

Table 5—Absolute Decline in Adjusted FEV₁ Over the 12-Year Period 1989 to 2001*

Groups	Mean Adjusted FEV ₁ Decline, L	Adjusted FEV ₁ Decline Difference, L	95% CI for Difference
Childhood no respiratory symptoms	0.59		
Childhood wheezy bronchitis	0.75	0.15	0.04–0.28†
Childhood asthma	0.75	0.15	0.05–0.27‡

*See Table 4 for abbreviation not used in the text. Adjusting for initial (1989) FEV₁ values did not affect the results even though it increased the amount of decline in FEV₁ in the childhood asthma group by 0.04 L and decreased the amount of decline in the childhood no respiratory symptom group by 0.01 L.

†Because the confidence interval does not include zero, then this group of subjects is statistically different from the childhood no respiratory symptoms group at the 5% level.

similar to that in the asthma group. As in 1989, both groups continue to report more wheeze than the control subjects, with the childhood asthma group continuing to show the highest rates of respiratory symptoms. We did not ask about current precipitants of wheeze in this study, although it is evident that subjects in the childhood asthma group experience more interference with activities due to their respiratory symptoms than those in the wheezy bronchitis group, who do not differ from control subjects in this respect. However, the more rapid decline in FEV₁ in the wheezy bronchitis group raises the possibility that this, like the earlier wheezing syndromes in infants, may be a precursor of obstructive lung disease in later life.¹⁶

Could methodologic issues have influenced our results? We have considered several issues. The response rate to the study on this occasion was 63%, raising the question of response bias. However, gender, smoking status, and symptoms were unrelated to participation, although subjects from affluent areas were overrepresented in this study. We therefore consider it unlikely that the results were a consequence of response bias.

Despite advice to the contrary, eight subjects from the childhood asthma group and one subject from the childhood wheezy bronchitis group used a bronchodilator within 6 h of the spirometry measurement. These subjects were among those with the lowest FEV₁ values, and their mean FEV₁ was lower than that of subjects who had not used their bronchodilator. The use of a bronchodilator at the time of this study is, therefore, unlikely to have produced a spuriously high value for the rate of decline in FEV₁ values. Could smoking have influenced the findings? The effect of being classified in the initial group (*ie*, asthma, wheezy bronchitis, or control) is independent of current smoking, which was adjusted for along with the number of pack-years smoked.

In this study, we have not adjusted current FEV₁ values or rates of decline for the value in 1989, rather we have followed the method of Ulrik and Lange¹⁵ and Vollmer.¹⁷ Adjustment for 1989 values would tend to exaggerate rates of decline in those subjects with low initial FEV₁, would attenuate the decline among those with high initial values, and would have the potential to obscure a biologically significant trend.

Previous studies on the rate of decline of lung function and its relationship to wheezing illnesses have drawn conflicting conclusions. A longitudinal study by Strachan et al¹⁸ of the long-term outcome of childhood wheeze found that adults in whom wheezing had been diagnosed as children but who had reported no symptoms in early adult life did not differ from healthy control subjects in pulmonary

function at age 35 years. Similarly, Kelly et al¹⁹ showed that lung function at 28 years was normal in a group of childhood asthmatic patients who had stopped wheezing, although it was increasingly abnormal in those who continued to wheeze. Interestingly, however, in the study by Strachan et al¹⁸ a subset of asymptomatic adults who had experienced transient wheezing before age 7 years had reduced FEV₁ values compared to control subjects. Peat et al²⁰ found that subjects between the ages of 22 years and 69 years who had asthma had a greater rate of decline in FEV₁ than did nonasthmatic subjects, although not all subjects with asthma had steep rates of decline. In contrast, Ulrik and Lange¹⁵ showed that lung function decline in subjects who were 20 to 90 years of age who had chronic asthma did not differ from that of nonasthmatic subjects. These conflicting results might be due to differences among the groups in terms of their age at adult follow-up. The timing of repeated measurements may be critical due to the nonlinear decline in lung function in adulthood.²¹ Alternatively, they might reflect differing outcomes for childhood wheeze, depending on whether the wheeze was infection-related (*ie*, wheezy bronchitis) or asthma-related.

When examining the relationship between childhood lung problems and adult outcome, the timing of the adult measurements may be important. For example, Strachan and Gerritsen²² reviewed three longitudinal studies with a cohort of subjects aged between 29 and 35 years. They concluded that adults who have outgrown their childhood wheezing tendency have ventilatory function similar to that of healthy control subjects, and they suggested that the abnormalities of neonatal airway function that precede transient wheezing in early childhood do not predict adult obstructive lung disease. These results would be compatible with our 1989 results from the subjects in the wheezy bronchitis group who had normal function at age 34 to 40 years. However, Tager et al²³ have suggested that FEV₁ decline in asymptomatic, nonsmoking men does not start until after 35 years of age, and this study suggests that the effect of childhood wheezy bronchitis is not seen until later middle age.

The absolute rates of decline reported in our study are comparable to those reported by others. Lange et al²⁴ described an unadjusted FEV₁ decline of 58 mL per year over > 15 years in male smokers aged 40 to 59 years with asthma, compared to nonsmokers in whom FEV₁ declined by 33 mL per year. FEV₁ in nonasthmatic male smokers declined by 40 mL per year, compared to a decline of 24 mL per year in nonasthmatic nonsmokers. Pelkonen et al²⁵ recently reported that the FEV₁ decline in male nonsmokers aged 55 to 74 years over a 15-year

period, extrapolated from measurements of forced expiratory volume in 0.75 s, was 50 mL per year. Rates of lung function decline may be nonlinear as Kerstjens et al²¹ have highlighted. In the present study, where FEV₁ measurements were made at two time points only, it is not possible to confirm whether the decline in FEV₁ is, or is not, linear between the ages of 37 and 48 years.

There is evidence from other studies that childhood wheezing illness may be associated with reduced adult lung function.²⁶ For example, among 239 subjects with a mean age of 57, asthma or wheeze at ≥ 2 years of age was associated with a reduction in FEV₁ as adults.²⁷ In the 1958 British birth cohort study,¹⁸ adults aged 35 years who had a history of asthma or wheezy bronchitis by 7 years had statistically lower FEV₁ values compared to adults in the control group. These studies did not specifically differentiate between a childhood diagnosis of asthma or wheezy bronchitis when classifying the groups for analysis. In an epidemiologic study such as this, we cannot identify the mechanisms of wheeze and therefore cannot exclude the possibility that the wheezy bronchitis syndrome may represent another asthma phenotype. However, additional evidence that the distinction may be important comes from our previous observations in 1997, on the children of a sample of the probands from our 1989 study. We found that the male children of subjects from the wheezy bronchitis group had lower FEV₁ and FVC values than did children of those in the asthmatic or control groups.²⁸ This raises the possibility that there may be a heritable or shared environmental component to the wheezy bronchitis syndrome.

CONCLUSION

This study together with previous studies of the same cohort demonstrate that the natural history of childhood asthma and childhood wheezy bronchitis differ after adjusting for potential confounders. Subjects who have childhood asthma have persistent respiratory symptoms, reduced lung function in early adulthood, and a more rapid decline in lung function through middle age. Those who have childhood wheezy bronchitis have lesser symptoms than those in the asthma group, achieve normal lung function in early adulthood, but then demonstrate an accelerated decline in lung function through middle age, which is similar to those who had childhood asthma. It is conceivable that these subjects may progress to COPD. This study highlights the importance of differentiating these two childhood wheezing diagnoses in longitudinal studies.

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REFERENCES

- Williams H, McNicol KN. Prevalence, natural history, and relationship of wheezy bronchitis and asthma in children: an epidemiological study. *BMJ* 1969; 4:321–325
- Sporik R, Holgate ST, Cogswell JJ. Natural history of asthma in childhood: a birth cohort study. *Arch Dis Child* 1991; 66:1050–1053
- Martinez FD, Wright AL, Taussig LM, et al. Asthma and wheezing in the first six years of life: The Group Health Medical Associates. *N Engl J Med* 1995; 332:133–138
- Illsley R, Wilson F. The Aberdeen child development survey. In: Mednick SA, ed. Prospective longitudinal research: an empirical basis for the primary prevention of psychological disorders. Oxford, UK: Oxford Medical Publications, 1981; 66–68
- Dawson B, Illsley R, Horobin G, et al. A survey of childhood asthma in Aberdeen. *Lancet* 1969; 1:827–830
- Godden DJ, Ross S, Abdalla M, et al. Outcome of wheeze in childhood: symptoms and pulmonary function 25 years later. *Am J Respir Crit Care Med* 1994; 149:106–112
- Omran M, Russell G. Continuing increase in respiratory symptoms and atopy in Aberdeen schoolchildren. *BMJ* 1996; 312:34
- National Occupational Health and Safety Commission. A questionnaire on respiratory symptoms. Available at: <http://www.nohsc.gov.au/OHSInformation/NOHSCPublications>. Accessed August 24, 2001
- Bodner CH, Ross S, Little J, et al. Risk factors for adult onset wheeze: a case control study. *Am J Respir Crit Care Med* 1998; 157:35–42
- Rusznak C, Davies RJ. ABC of allergies: diagnosing allergy [erratum published in *BMJ* 1998; 316:1078] *BMJ* 1998; 316:686–689
- Carstairs V. Deprivation indices: their interpretation and use in relation to health. *J Epidemiol Community Health* 1995; 49(suppl):S3–S8
- Morris R, Carstairs V. Which deprivation? A comparison of selected deprivation indexes. *J Public Health Med* 1991; 13:318–326
- McLoone P, Boddy FA. Deprivation and mortality in Scotland, 1981 and 1991. *BMJ* 1994; 309:1465–1470
- McLoone P. Targeting deprived areas within small areas in Scotland: population study. *BMJ* 2001; 323:374–375
- Ulrik CS, Lange P. Decline of lung function in adults with bronchial asthma. *Am J Respir Crit Care Med* 1994; 150:629–634
- Silverman M. Out of the mouths of babes and sucklings: lessons from early childhood asthma. *Thorax* 1993; 48: 1200–1204
- Vollmer WM. Comparing change in longitudinal studies: adjusting for initial value. *J Clin Epidemiol* 1988; 41:651–657
- Strachan DP, Griffiths JM, Johnston ID, et al. Ventilatory function in British adults after asthma or wheezing illness at ages 0–35. *Am J Respir Crit Care Med* 1996; 154:1629–1635
- Kelly WJ, Hudson I, Raven J, et al. Childhood asthma and adult lung function. *Am Rev Respir Dis* 1988; 138:26–30
- Peat JK, Woolcock AJ, Cullen K. Rate of decline of lung function in subjects with asthma. *Eur J Respir Dis* 1987; 70:171–179
- Kerstjens HA, Rijcken B, Schouten JP, et al. Decline of FEV₁

- by age and smoking status: facts, figures, and fallacies. *Thorax* 1997; 52:820–827
- 22 Strachan D, Gerritsen J. Long-term outcome of early childhood wheezing: population data. *Eur Respir J Suppl* 1996; 21:42s–47s.
 - 23 Tager IB, Segal MR, Speizer FE, et al. The natural history of forced expiratory volumes: effect of cigarette smoking and respiratory symptoms. *Am Rev Respir Dis* 1988; 138:837–849
 - 24 Lange P, Parner J, Vestbo J, et al. A 15-year follow-up study of ventilatory function in adults with asthma. *N Engl J Med* 1998; 339:1194–1200
 - 25 Pelkonen M, Notkola IL, Tukiainen H, et al. Smoking cessation, decline in pulmonary function and total mortality: a 30 year follow up study among the Finnish cohorts of the Seven Countries Study. *Thorax* 2001; 56:703–707
 - 26 Britton J, Martinez FD. The relationship of childhood respiratory infection to growth and decline in lung function. *Am J Respir Crit Care Med* 1996; 154(suppl):S240–S245
 - 27 Shaheen SO, Sterne JA, Tucker JS, et al. Birth weight, childhood lower respiratory tract infection, and adult lung function. *Thorax* 1998; 53:549–553
 - 28 Christie GL, Helms PJ, Ross SJ, et al. Outcome of children of parents with atopic asthma and transient childhood wheezy bronchitis. *Thorax* 1997; 52:953–957

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