

Factors in childhood as predictors of asthma in adult life

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Abstract

Objective—To determine which factors measured in childhood predict asthma in adult life.

Design—Prospective study over 25 years of a birth cohort initially studied at the age of 7.

Setting—Tasmania, Australia.

Subjects—1494 men and women surveyed in 1991-3 when aged 29 to 32 (75% of a random stratified sample from the 1968 Tasmanian asthma survey of children born in 1961 and at school in Tasmania).

Main outcome measures—Self reported asthma or wheezy breathing in the previous 12 months (current asthma).

Results—Of the subjects with asthma or wheezy breathing by the age of 7, as reported by their parents 25.6% (190/741) reported current asthma as an adult compared with 10.8% (81/753) of subjects without parent reported childhood asthma ($P < 0.001$). Factors measured at the age of 7 that independently predicted current asthma as an adult were being female (odds ratio 1.57; 95% confidence interval 1.19 to 2.08); having a history of eczema (1.45; 1.04 to 2.03); having a low mild forced expiratory flow rate (interquartile odds ratio 1.40; 1.15 to 1.71); having a mother or father with a history of asthma (1.74 (1.23 to 2.47) and 1.68 (1.18 to 2.38) respectively); and having childhood asthma (1.59; 1.10 to 2.29) and, if so, having the first attack after the age of 2 (1.66; 1.17 to 2.36) or having had more than 10 attacks (1.70; 1.17 to 2.48).

Conclusion—Children with asthma reported by their parents in 1968 were more likely than not to be free of symptoms as adults. The subjects who had more severe asthma (especially if it developed after the age of 2 and was associated with reduced expiratory flow), were female, or had parents who had asthma were at an increased risk of having asthma as an adult. These findings have implications for the treatment and prognosis of childhood asthma, targeting preventive and educational strategies, and understanding the onset of asthma in adult life.

Introduction

Few population based and truly prospective cohort studies have been published of the natural course of asthma from childhood to adult life.¹ The onset of asthma is often preceded by allergic disease (eczema or hay fever) and a positive result of skin tests with allergens (atopy).^{2,3} Impaired lung function in childhood predicts asthmatic symptoms as a teenager, although this association might be confounded by undiagnosed asthma.⁴

Most studies of the long term prognosis of childhood asthma have been based on selected groups of patients with severe or moderate asthma and provide limited information about the full range of the disease.¹ Asthma is episodic, and, although remission may occur during teenage years, it is uncommon after the age of 30.⁵ Predictors of asthma in adulthood include various markers of initial severity,^{6,8} other atopic conditions,^{4,7,8} and a family history of asthma.⁷

We present findings from a follow up over 25 years of random samples from a population survey of 7 year old Tasmanian schoolchildren, designed to assess the

natural course of asthma.⁹ Measures of respiratory function, history and family history of asthma and allergy, and parental smoking were recorded for all but 1% of the population in 1968. We resurveyed the subjects in 1991-3 to study onset and prognosis and the extent to which childhood factors predict asthma in adult life.

Methods

1968 TASMANIAN ASTHMA SURVEY

In 1968 the parents of all 8683 children born in 1961 and attending school in Tasmania were asked to complete questionnaires on their and their children's history of respiratory symptoms and asthma. The survey aimed to study the natural course of asthma, asking about easily described and recognisable symptoms so as not to rely on diagnoses.⁹ Returns for 99% of the children were received.¹⁰

Questions relevant to the current analysis are given in the appendix. Children for whom the answer to question 1 ("Has he or she at any time in his or her life suffered from attacks of asthma or wheezy breathing?") was "yes" were considered to have had childhood asthma, and parents were asked about the recency, frequency, age at onset, and number of attacks (questions 2 to 5). A history of hay fever was determined by question 6. Subjects were considered to have had a history of eczema if they answered "yes" to question 7 or 8, about infantile and flexural eczema. In parents asthma, hay fever, and smoking status were determined by questions 9 to 11.

Forced expiratory volume in one second, vital capacity, and mid forced expiratory flow were measured with spirometry.

1991-3 TASMANIAN LONG TERM HEALTH SURVEY

During 1991-3, 2000 subjects in the birth cohort of the Tasmanian asthma survey were selected at random with a pseudorandom number generator (SAS)—1000 from the 1349 subjects who had had childhood asthma and 1000 from the 6993 who did not have childhood asthma; in 341 subjects asthma status in childhood has not been recorded. A questionnaire was sent between July 1991 and February 1993 to the 1723 subjects for whom addresses were available. As well as addressing general health issues the questionnaire included items based on those in the 1968 Tasmanian asthma survey. "Current asthma" was defined as the occurrence of an attack of asthma within the previous 12 months; "current atopic asthma" as current asthma with current hay fever or eczema; and "frequent asthma" as the occurrence of more than 10 attacks in the previous 12 months. Subjects were not informed of the responses their parents had given in 1968.

STATISTICAL METHODS

Multiple logistic regression with GLIM¹¹ was used to study asthma as an adult as a function of factors measured at the age of 7. Estimates of odds ratios, standard errors, and confidence intervals were based on asymptotic likelihood theory, and parsimonious models were derived with procedures outlined by Hosmer and Lemeshow.¹² Analyses were performed separately on subjects with and without childhood

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asthma as reported by their parents (parent reported childhood asthma) and on the pooled data, with a factor for childhood asthma to account for the stratified sampling.

Each measurement of lung function was standardised for height separately for both sexes, expressed as a percentage of the predicted value, and modelled as a continuous measurement. From a fitted logistic regression line the predicted risk for a subject on the 75th centile of lung function (r_u) and for a subject on the 25th centile (r_l) was calculated. The interquartile odds ratio was defined as $r_l(1-r_u)/(r_u(1-r_l))$. Other factors were treated as binary variables. Missing values for conditions were coded as being unaffected.

The prevalence in 1991-3 of a condition in the entire birth cohort studied in 1968 was estimated by weighting the prevalence in the two samples by 0.162 and 0.838 for subjects with and without parent reported childhood asthma respectively, with approximate standard errors derived by the delta method.¹³

Results

Questionnaires were returned by 1494 subjects (86.7% response rate) representing 74.7% of the total sample (74.1% of those with childhood asthma and 75.3% of those without; 73.7% of men and 76.0% of women). The respondents' ages ranged from 29 to 32 (mean 31.0); their current place of residence was Tasmania (1121 (75%)), Victoria (134 (9%)), New South Wales (90 (6%)), elsewhere in Australia (134 (9%)), and outside Australia (15 (1%)).

Table I shows that, of the 741 subjects with parent reported childhood asthma, 254 (34.3%) reported onset of asthma by age 7 and 155 (20.9%) reported onset after age 7. Almost half of the subjects, therefore, gave responses that contradicted those of their parents in 1968. Of the 753 subjects without parent reported childhood asthma, 24 (3.2%) gave responses that contradicted those of their parents and 127 (16.9%) reported that they had had asthma at some point in

their life. The estimated 1991-3 prevalences in adults of current, frequent, and atopic asthma were significantly higher in women than in men ($P < 0.05$).

Current asthma was reported by 25.6% (190/741) of the subjects with parent reported childhood asthma compared with 10% (81/753) of the subjects without (odds ratio=2.86; 95% confidence interval 2.15 to 3.79). The proportions for current atopic asthma were 21.1% (156/741) and 8.2% (62/753) respectively (2.95; 2.15 to 4.04) and for current frequent asthma 5.4% (40/741) and 2.1% (16/753) respectively (2.63; 1.46 to 4.74).

The proportion of subjects with parent reported childhood asthma who reported current asthma increased with (a) age at first attack (23% (104/456) for < 2 , 30% (67/227) for 2 to 5, 33% (19/58) for > 5 ; $P < 0.05$); (b) frequency of attacks (21% (73/346) for ≤ 1 a year, 30% (117/395) for > 1 a year, 32% (43/134) for ≥ 1 a month, 41% (14/34) for ≥ 1 a fortnight; $P < 0.001$); and (c) total number of attacks (22% (119/535) for ≤ 10 , 29% (32/112) for 11 to 20, 41% (39/94) for > 20 ; $P < 0.01$) and decreased with time since last attack (36% (36/100) for within the past month, 30% (143/481) within the past year, 18% (47/260) > 1 year ago; $P < 0.001$).

Table II shows that childhood lung function was in general lower, although not always significantly so, in the subjects with current asthma, irrespective of whether they had had parent reported childhood asthma. Table III shows the proportion of subjects with current asthma according to the presence or absence of each risk factor. Odds ratio estimates of risks for current asthma (except those of parental smoking) were ≥ 1 and did not differ between the subjects who had had parent reported childhood asthma and those who had not, and the lower limit of the 95% confidence interval was close to or greater than 1 in at least one of these two groups of subjects.

In the subjects with parent reported childhood asthma the independent risk factors were being female (odds ratio 1.43; 1.01 to 2.02), first attack after the age of 2 (1.71; 1.20 to 2.43), more than 10 attacks (1.77; 1.22 to 2.57), mid forced expiratory flow (interquartile odds ratio 1.60; 1.25 to 2.06), maternal asthma (1.90; 1.28 to 2.82), and paternal asthma (1.61; 1.08 to 2.40). After these factors were allowed for, the time since the last attack (1.48; 0.99 to 2.24), hay fever (1.41; 0.98 to 2.03), vital capacity (interquartile odds ratio 1.20; 0.97 to 1.47), and paternal hay fever (1.45; 0.97 to 2.17) were of marginal significance.

In the subjects without parent reported childhood asthma the independent risk factors were being female (1.75; 1.08 to 2.84), maternal hay fever (1.80; 1.07 to 3.03), and forced expiratory volume in one second (interquartile odds ratio 1.42; 1.00 to 2.03), while paternal asthma (2.02; 0.97 to 4.21) was of marginal significance.

Table IV shows a parsimonious model fitted to the combined data. The strengths of association were independent of whether the subjects had had parent reported childhood asthma. After the risk factors shown in table IV were allowed for, the time since the last attack (1.48; 0.99 to 2.24) was of marginal significance, but the other lung function measures

TABLE I—Adults reporting asthma in 1991-3 by presence or absence of parent reported asthma up to age of 7 and adjusted for sampling. Values are numbers (percentages) unless stated otherwise

Self reported asthma (1991-3)	Parent reported childhood asthma (n=741)	No parent reported childhood asthma (n=753)	Overall* % (SE)
Ever had asthma:			
Men	252 (56.1)	54 (14.8)	21.5 (1.6)
Women	162 (55.5)	73 (18.8)	24.8 (1.7)
Total	414 (55.9)	127 (16.9)	23.2 (1.2)
Age at first attack (years):			
<7	254 (34.3)	24 (3.2)	8.2 (0.6)
7-14	58 (7.8)	29 (3.9)	4.5 (0.6)
15-21	35 (4.7)	15 (2.0)	2.4 (0.5)
>21	62 (8.4)	58 (7.7)	7.8 (0.8)
Current asthma:			
Men	103 (22.9)	29 (8.0)	10.4 (1.2)
Women	87 (29.8)	52 (13.4)	16.1 (1.5)
Total	190 (25.6)	81 (10.8)	13.2 (1.0)
Frequent current asthma:			
Men	29 (6.5)	3 (0.8)	1.7 (0.4)
Women	11 (3.8)	13 (3.4)	3.5 (0.8)
Total	40 (5.4)	16 (2.1)	2.6 (0.5)
Atopic current asthma:			
Men	82 (18.3)	21 (5.8)	7.8 (1.1)
Women	74 (25.3)	41 (10.6)	13.0 (1.4)
Total	156 (21.1)	62 (8.2)	10.3 (0.9)

*Adjusted for sampling (see statistical methods).

TABLE II—Mean (SE) percentage predicted childhood lung function in 1968 for subjects with or without current asthma by presence or absence of parent reported childhood asthma in 1968

Lung function measure	Parent reported childhood asthma			No parent reported childhood asthma		
	Current asthma	No current asthma	Difference	Current asthma	No current asthma	Difference
Forced expiratory volume in one second	96.9 (1.2)	98.6 (0.7)	1.7 (1.4)	98.0 (1.5)	100.8 (0.5)	2.8* (1.6)
Mid forced expiratory flow	88.2 (1.8)	96.1 (1.1)	7.9** (2.0)	99.4 (2.8)	101.8 (0.9)	2.4 (3.0)
Vital capacity	100.2 (1.1)	99.9 (0.6)	-0.3 (1.2)	97.6 (1.6)	100.3 (0.5)	2.7* (1.6)

* $P < 0.10$, ** $P < 0.001$.

TABLE III—Number (percentage) of subjects with current asthma according to presence or absence of each childhood risk factor, and odds ratios (95% confidence interval) of univariate associations between current asthma and childhood risk factors

Childhood risk factor	Parent reported asthma as child			No parent reported asthma as child		
	Current asthma		Odds ratio (95% confidence interval)	Current asthma		Odds ratio (95% confidence interval)
	With factor	Without factor		With factor	Without factor	
Being female	87/292 (29.8)	103/449 (22.9)	1.43 (1.02 to 1.99)	52/388 (13.4)	29/365 (8.0)	1.79 (1.12 to 2.88)
First attack after age of 2	86/285 (30.2)	104/456 (22.8)	1.46 (1.05 to 2.04)			
More than 10 attacks	71/206 (34.5)	119/535 (22.2)	1.84 (1.29 to 2.61)			
More than one year since last attack	143/481 (29.7)	47/260 (18.1)	1.92 (1.32 to 2.78)			
More than one attack in past two years	117/395 (29.6)	73/346 (21.1)	1.57 (1.13 to 2.20)			
Hay fever	81/245 (33.1)	109/496 (22.0)	1.75 (1.25 to 2.46)	8/63 (12.7)	73/690 (10.6)	1.23 (0.53 to 2.67)
Eczema	63/202 (31.2)	127/539 (23.6)	1.47 (1.03 to 2.10)	12/69 (17.4)	69/684 (10.1)	1.88 (0.96 to 3.67)
Forced expiratory volume in one second	49/177 (27.7)	37/145 (25.5)	1.22 (0.99 to 1.50)*	21/137 (15.3)	13/151 (8.6)	1.40 (0.99 to 1.98)
Mid forced expiratory flow	71/220 (32.3)	14/107 (13.1)	1.58 (1.25 to 2.00)*	19/158 (12.0)	16/184 (8.7)	1.15 (0.84 to 1.59)
Vital capacity	52/180 (28.9)	50/185 (27.0)	1.00 (0.83 to 1.20)*	31/180 (17.2)	15/181 (8.3)	1.34 (0.98 to 1.82)
Maternal asthma	56/158 (35.4)	134/583 (23.0)	1.84 (1.26 to 2.69)	8/60 (13.3)	73/693 (10.5)	1.31 (0.60 to 2.84)
Paternal asthma	52/152 (34.2)	130/563 (23.1)	1.70 (1.16 to 2.50)	10/56 (17.9)	71/697 (10.2)	1.92 (0.93 to 3.96)
Maternal hay fever	65/238 (27.3)	124/503 (24.9)	1.14 (0.80 to 1.61)	24/152 (15.8)	57/601 (9.5)	1.79 (1.07 to 2.99)
Paternal hay fever	60/178 (33.7)	130/563 (23.1)	1.69 (1.17 to 2.44)	14/98 (14.3)	67/655 (10.2)	1.46 (0.79 to 2.70)
Maternal smoking	78/286 (27.3)	112/455 (24.6)	1.15 (0.82 to 1.61)	21/247 (8.5)	60/506 (11.9)	0.69 (0.41 to 1.16)
Paternal smoking	105/432 (24.3)	85/309 (27.5)	0.85 (0.61 to 1.18)	40/426 (9.4)	41/327 (12.5)	0.72 (0.46 to 1.14)

*Interquartile odds ratio (see statistical methods).

(forced expiratory volume in one second and vital capacity) had negligible effect (1.01 (0.81 to 1.28) and 1.03 (0.86 to 1.22) respectively).

We predicted from the parsimonious model that a child with none of the risk factors shown in table IV had a 7% chance of having current asthma as an adult. Each risk factor was associated with about a 50% increase in risk. For a child with one risk factor the chance was 11%, with two 16%, with three 24%, with four 34%, and so on. This predicted chance was greater than 50% in only 0.5% of all the children and in 5% of the children with parent reported asthma.

TABLE IV—Odds ratios (95% confidence intervals) for associations between risk factor reported during childhood and current asthma for parsimonious multivariate models. All risk factors are binary, and lung function measures are for subjects on 25th centile versus those on 75th centile

Childhood risk factor	Odds ratio for parsimonious model
History of asthma (up to age of 7)	1.59 (1.10 to 2.29)
Being female	1.57 (1.19 to 2.08)
First attack after age of 2	1.66 (1.17 to 2.36)
More than 10 attacks	1.70 (1.17 to 2.48)
Eczema	1.45 (1.04 to 2.03)
Mid forced expiratory flow*	1.40 (1.15 to 1.70)
Maternal asthma	1.74 (1.23 to 2.47)
Paternal asthma	1.68 (1.18 to 2.38)

*Interquartile odds ratio (see statistical methods).

Current atopic asthma had the same independent risk factors as those for current asthma (table IV), plus hay fever (1.66; 1.17 to 2.35). Frequent current asthma was predicted by onset of asthma after the age of 2, more than 10 attacks of asthma up to the age of 7, and hay fever or eczema as a child.

Discussion

This study shows that for children who were 7 years old in 1968 the independent predictors for having symptoms of asthma as an adult were being female and having atopy, reduced lung function, parents with a history of asthma, and a history of asthmatic symptoms in childhood themselves, especially if their symptoms were severe and began after the age of 2.

The most common risk factor was being female. Although boys were more likely than girls to have had asthma by the age of 7 (19.0% v 13.2%; $P < 0.001$),¹⁰ women were more likely than men to have current, frequent, and atopic asthma. Similar reversals in sex ratios between childhood and adulthood were observed in a study of hospital admissions¹⁴ and in health census

data.¹⁵ That differences between the sexes might be due to pubertal hormonal changes has been discussed¹⁴ with reference to animal studies and a report of high hormone concentrations in women with asthma.¹⁶ We found that childhood atopy predicts frequent and atopic asthma as an adult, which confirms the findings of a 16 year follow up of 7 year olds living in Britain.²

The Tasmanian asthma surveys have shown that childhood lung function can predict asthma as an adult. Earlier follow ups showed that 7 year old children without asthma were more likely to develop asthmatic symptoms over the next six years if their mid forced expiratory flow was low rather than normal.⁴ We extended this to show that low mid forced expiratory flow at the age of 7 also predicted asthma in adult life up to 25 years later. Reduced flow indicates narrowing of the small airways and is considered to be a measure of the severity of airflow limitation in people with asthma.¹⁷

We studied familial aggregation of self reported asthma as an adult in parent-offspring pairs measured at about the same age. The increased risk associated with a parental history (odds ratio about 1.7) is aetiologically important; theoretical considerations suggest that underlying susceptibility factors must exist which have associated risks at least an order of magnitude greater.^{18,19} If familial aggregation is due to many genetic loci (a polygenic factor) then the risk is about 20 times greater for people in the upper quarter of genetic susceptibility than for those in the lower quarter.²⁰ Some of this association could be due to continuing familial associations in environmental factors. Although few children still lived with their parents, over 90% still lived in Tasmania or the other southern states of Australia.

Severe childhood asthma predicted asthma as an adult, which suggests that minimising the severity and especially the number of attacks (by drug treatment and avoidance of factors that trigger attacks) might prevent symptoms in later life. A study of the long term effects of the use of corticosteroids showed that symptoms in people with severe asthma were reduced if attacks of asthma were prevented.²¹

Onset of parent reported asthma or wheezing before the age of 2 did not predict asthma as an adult. Infants with wheeze do not exhibit bronchial hyperresponsiveness to histamine²² and therefore may not have asthma. Their wheeze may be due to small airways disease or obstructive lesions of the trachea or major bronchi.²³

Two thirds of the subjects with parent reported childhood asthma reported that they had not had

Clinical implications

- Asthmatic symptoms in childhood may abate during teenage years, although asthma may occur for the first time after childhood
- Asthma in children and young adults is often preceded by an allergy, and impaired lung function as a child predicts asthmatic symptoms as a teenager
- This study shows that three quarters of all subjects aged 29-32 who had had asthma in childhood had had no asthmatic symptoms as adults
- Childhood risk factors for having asthmatic symptoms at age 29-30 were being female and having eczema, a parent with asthma, poor lung function, and asthma, especially if it was frequent
- High risk groups can be used as targets for preventive strategies

asthma by the age of 7 (see table I), which indicated that they did not know, had forgotten, or refused to disclose whether they had had it. This finding confirms the unreliability of prevalence surveys for ascertaining the proportion of subjects with a history of wheeze² and supports our choice of asthma in the past 12 months as the most relevant outcome measure.

Of the subjects without parent reported childhood asthma, 16% (95% confidence interval 14% to 20%) reported that they had had asthma at some point in their life. If these symptoms had developed over the intervening 25 years the average annual incidence would have been 0.6% (0.5% to 0.7%) a year, which would be with incidences found in other cohort studies.¹

Three in every four subjects with parent reported asthma were free of asthmatic symptoms in adult life; one in every nine subjects without parent reported asthma, however, had developed symptoms during the intervening 25 years. Given that in the 1968 Tasmanian asthma survey there were five times fewer children with parent reported asthma than children without,¹⁰ only one third of 30 year old subjects with asthma had had asthma before the age of 7. If childhood asthma was underreported by parents in 1968, however, this estimate would be too low.

CONCLUSION

In conclusion, we have identified substantial risk factors from a 25 year prospective study designed to assess the natural course of asthma and based on a population based birth cohort with a good, unbiased response rate. The probability of children with asthma suffering asthma as adults might be reduced by maintaining lung function and limiting the severity and number of attacks during childhood. High risk groups, such as girls with asthma with poor lung function and a family history of asthma, can be identified from table IV and used as targets for preventive strategies. In most cases, childhood asthma did not seem to persist, which may be comforting for children with asthma and their parents, and most asthma in these adults in the early 1990s seems to have developed after the age of 7. These findings have implications for the treatment and prognosis of childhood asthma, for understanding the onset of asthma in adults, and for focusing health education about asthma.

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Appendix

Questionnaire for child

- 1 Has he or she at any time in his or her life suffered from attacks of asthma or of wheezy breathing? (Note: Please regard "asthma" and "wheezy breathing" as being much the same thing for this survey; we do not ask you to try to tell the difference.)
- 2 How long is it since the last attack?
- 3 On average (as near as you can say), how often do these attacks tend to occur (over the last 2 years or so)?
- 4 At what age did these attacks begin?
- 5 Since the attacks began, approximately how many has he or she had altogether?
- 6 Does he or she get attacks of "hay fever" (that is, sneezing, running or blocked nose, sometimes with itchy eyes or nose)?
- 7 Did he or she have infantile (baby) eczema?
- 8 Has he or she ever had eczema in the creases (bends) of elbows, wrists, or knees?

Questionnaire for parents

- 9 Have you ever had asthma or attacks of wheezing like asthma?
- 10 Have you ever suffered from "hay fever"?
- 11 Do you smoke every day (or six days out of seven)?

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