

Original article

Adulthood asthma after wheezing in infancy: a questionnaire study at 27 years of age

Background: Wheezing in early childhood is a heterogeneous condition, the long-term prognosis varying from total recovery to chronic asthma. Though short-term outcome has been actively studied, there is lack of data on long-term outcome until adulthood. The aim of the study was to evaluate the prevalence and risk factors of asthma at 26–29 years of age after early-life wheezing.

Methods: At the median age of 27.3 years (range 26.3–28.6), a questionnaire was sent to 78 study subjects hospitalized for wheezing at <24 months of age, and 59 (76%) answered. Asthma, allergy and weight status were compared with selected controls followed up from birth and with non-selected population controls recruited for this adulthood study.

Results: Doctor-diagnosed asthma was present in 20% of the former bronchiolitis patients, compared with 5% in the two control groups (OR 2.1, 95% CI 0.3–17.9 *vs* selected controls; OR 5.2, 95% CI 1.7–15.8 *vs* nonselected controls). The respective figures for current self-reported asthma were 41% and 7–10% (OR 11.4, 95% CI 2.3–56.1 *vs* selected controls; OR 12.2, 95% CI 4.4–33.7 *vs* nonselected controls). Current allergic rhinitis and current smoking were significantly associated with asthma, but current overweight or obesity was not. In multivariate analyses, early-life wheezing was an independent risk factor of adulthood asthma.

Conclusion: An increased asthma risk in early-life wheezers continues, even after many symptom-free years at school age, at least until 27 years of age.

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Wheezing in early childhood is a heterogeneous condition, the long-term prognosis varying from total recovery to chronic asthma and reduced lung function continuing until adulthood, as documented in two prospective birth cohort studies (1–3) and in two prospective post-bronchiolitis follow-up studies (4–8). The post-bronchiolitis follow-ups have shown that asthma risk remains as increased despite many symptom-free years during childhood and adolescence.

We have prospectively followed up from 1981–1982 onwards a group of children treated in hospital for bronchiolitis before the age of 24 months. The prevalence of doctor-diagnosed asthma was 15% at the age of 8–10 years (9), 14% at the median age of 14.9 years (10) and 30% at the median age of 19.0 years (4).

In 2008, the former bronchiolitis patients were 26–29 years old, and we carried out a questionnaire study to find out the asthma and allergy status of these subjects, compared with selected controls from nonallergic families with no early-life bronchiolitis followed up from birth and with nonselected population-based controls. In addition, the study design allowed the evaluation of early-life risk factors, measured and registered in infancy, for later asthma within the study group.

Subjects and methods

Design

Eighty-three children were hospitalized for bronchiolitis at the age of 1–23 months during a 12-month study period in 1981–1982 at Kuopio University Hospital (Finland) (11, 12). The diagnosis of bronchiolitis was clinically confirmed in all cases by one of the authors (MK), and all children were recruited to attend a follow-up study. The diagnostic criteria of bronchiolitis were the presence of respiratory infection and wheezing and/or prolonged expiration. Most (72%) of the children were wheezing for the first time. Clinical follow-up visits have been organized at the ages of 2–3 years (12), 4.5–6 years (13), 8–10 years (9) and 18–20 years (4). In addition, a questionnaire study was performed at the median age of 14.9 years (10).

Seventy-two newborns without a family history of atopy were recruited in 1979–1980 as controls with no intervention in a birth cohort study on atopy prevention (14), and have been thereafter prospectively followed-up (4, 15). None of these controls were hospitalized for bronchiolitis or other lower respiratory infection before the age of 2 years. These subjects have been used as controls for the present bronchiolitis cohort in earlier phases of the study (4), as were also used in this study.

This study was carried out in 2008 when the study subjects were 26–29 years old. The questionnaire was sent to 78 study subjects with bronchiolitis in infancy and to 72 control subjects followed-up from infancy with current addresses available, and 59 (76%) and 39 (54%) answered.

For this study, nonselected population-based controls, born like the former bronchiolitis patients in the primary area of Kuopio University Hospital, and matched for gender and birth month, were obtained by 4 : 1 ratio for the 82 cases (55 males and 27 females; one subject has died) from the Population Register Centre (Finland). The questionnaire was sent to 328 controls, and 121 (37%) answered. From these 121 subjects, a control group of 105 subjects (60 females consisting of two controls for each case selected by the closest birth days, and all 61 males who answered, on average 1.65 control for the cases) was constructed.

Questionnaire data

The questionnaire comprised questions on the presence of wheezing symptoms, prolonged (>4 weeks) cough apart from infection, repeated night cough and doctor-diagnosed asthma, the use of maintenance medication (inhaled corticosteroids or leukotriene antagonists) and on-demand bronchodilator medication for asthma, the presence of nasal symptoms apart from infection, and the presence of skin symptoms suggestive for atopic dermatitis. Doctor-diagnosed asthma was recorded separately for the mother, father, siblings and the children of the subjects. The attendants were asked to estimate how many cigarettes they smoke daily, and the daily consumption of one or more cigarettes during the preceding 12 months was defined as current smoking. In addition, the weights and heights were asked for the calculation of body mass index (BMI; weight/the square of height). In the case of doctor-diagnosed asthma, the time of asthma diagnosis was recorded: during the preceding 12 months, during the preceding 24 months or ever in life. The presence of symptoms and use of asthma medication were recorded only for the preceding 12 months.

Early-life data on allergy

Data on parental atopy, parental asthma, atopic dermatitis, respiratory syncytial virus (RSV) and non-RSV etiology of bronchiolitis, blood eosinophils apart from infection, total serum immunoglobulin E (IgE), allergen-specific IgE to 8 inhaled outdoor or indoor allergens and the recurrence of wheezing were collected during the first 24 months of life (11). Respiratory syncytial virus etiology of bronchiolitis was studied by both serology and antigen detection in nasopharyngeal samples, and was found in 32 (40%) cases (11). Atopic dermatitis in early life was confirmed by an experienced dermatologist. Blood eosinophil counts $>0.45 \times 10^9/\text{l}$ and total serum IgE concentrations $>60 \text{ IU/l}$ were regarded as elevated (16, 17). In allergen-specific IgE, all cases over the detection limit ($>0.35 \text{ IU/l}$) were considered as positive (18). If either atopic dermatitis, positive total IgE or positive allergen-specific IgE was present, the subject was defined to have early-life atopy.

Definition of asthma and allergy

Bronchial asthma was defined by two different ways reflecting the degree of certainty of the diagnosis. (1) Current doctor-diagnosed asthma: either asthma diagnosed by a doctor during the preceding 24 months, or the use of maintenance medication for asthma during the preceding 12 months. (2) Current self-reported asthma: either a weekly use of on-demand bronchodilating drugs, or asthma diagnosed by a doctor previously and the presence of wheezing symptoms, prolonged cough or repeated night cough during the preceding 12 months (current doctor-diagnosed asthma included by both criteria).

The months when runny or stuffy nose occurred were recorded for the preceding 12 months. The calendar year was divided into

four periods (spring from March to May, summer from June to August, autumn from September to November and winter from December to February). Allergic rhinitis was defined to be present if nasal symptoms, respectively, occurred during the spring or summer time. Atopic dermatitis was regarded if the subjects reported itching eczema in typical areas.

Statistics

The data were analyzed using the SPSS 14.0 statistical package (SPSS Inc., Chicago, IL, USA). When the former bronchiolitis group was compared with selected controls from nonatopic families, chi-square test, Fisher's exact test and logistic regression analysis were applied. When the former bronchiolitis group was compared with nonselected, population-based controls, logistic regression analysis, adjusted first for age and gender and further also for current smoking and allergic rhinitis, was applied. The chi square and Fisher's exact tests were not used, as the subjects were age- and gender-matched. When the subjects with current self-reported asthma or current doctor-diagnosed asthma were compared with the controls, chi-square test and logistic regression were applied. Within the bronchiolitis group, the significance of early-life risk factors as predictors of asthma was assessed by the chi-square test, Fisher's exact test and logistic regression analysis.

Ethics

This follow-up study was approved by the Ethics Committee of Kuopio University and Kuopio University Hospital. The attendants accepted the use of the collected data by undersigning a specific permission form, posted with the study questionnaire.

Results

The median age was 27.3 years (range 26.3–28.6) in the former bronchiolitis group, compared with 28.5 (28.2–28.7) in the controls with no bronchiolitis ($P < 0.01$) and 27.5 (26.2–28.6) in age- and gender-matched population controls. The proportion of males was 63%, 54% and 58% in the three groups, respectively.

Twenty-eight (48%) of the former bronchiolitis patients still, as young adults, suffered from wheezing, prolonged cough or night cough, but compared with controls, the difference was significant only for wheezing (Table 1). Instead, previous asthma was significantly more common (54%) in the former bronchiolitis group than in either of the two control groups (9–10%, ORs 10.8–16.6). Only 5% of the cases and 0–3% of the controls used bronchodilators weekly. There were no significant differences in allergic rhinitis or atopic dermatitis between the cases and either of the two control groups (Table 1). A family history of asthma in parents or siblings was present in a third of the former bronchiolitis patients; the difference vs the two control groups was significant for asthma in siblings but not for asthma in parents (Table 1). More than half of the study subjects were overweight (BMI >25) and nearly 15% obese (BMI >30), with no significant differences between cases and controls. As many as 41% of the former

Table 1. Questionnaire data in 59 young adults, hospitalized for bronchiolitis in infancy, compared with 39 selected controls not having bronchiolitis in infancy and with 105 nonselected population-based controls

Questionnaire data	Bronchiolitis group (<i>n</i> = 59)	Control group 1* (<i>n</i> = 39)	OR (95% CI) [†]	Control group 2 [‡] (<i>n</i> = 105)	OR (95% CI) [§]
Asthma in parents	17 (29)	7/38 (17.9)	1.79 (0.66–4.85)	21/103 (20)	1.67 (0.78–3.53)
Asthma in siblings	19/58 (32)	3/38 (7.7)	5.68 (1.55–20.86)	15/103 (14.3)	2.84 (1.30–6.18)
Body mass index >25 (kg/m ²)	32 (54)	16/38 (41)	1.69 (0.74–3.87)	42 (40)	1.93 (1.00–3.74)
Body mass index >30 (kg/m ²)	8 (13.6)	6/38 (15)	0.85 (0.27–2.69)	17 (16.2)	0.86 (0.34–2.14)
Current smoking	24 (40.7)	11 (28.2)	1.75 (0.73–4.17)	18 (17.1)	3.26 (1.53–6.92)
Wheezing symptoms	25 (42.4)	11 (28.2)	1.87 (0.79–4.46)	22 (21)	2.93 (1.44–5.97)
Prolonged cough (smokers/non-smokers)	5/1 (8.5/1.7)	3/2 (7.7/5.1)	0.77 (0.22–2.72)	3/3 (2.8/2.8)	1.66 (0.50–5.58)
Night cough	5 (8.5)	7 (17.9)	0.42 (0.12–1.45)	6 (5.7)	1.44 (0.41–5.03)
Allergic rhinitis	28 (47.5)	14/38 (35.9)	1.55 (0.67–3.57)	45/104 (42.9)	1.23 (0.64–2.35)
Atopic dermatitis	12 (20.3)	5 (12.8)	1.74 (0.56–5.39)	18 (17.1)	1.37 (0.60–3.15)

Values are denoted as *n* (%).

For the definitions of current smoking, prolonged cough and night cough, see the text.

OR, odds ratio; CI, confidence interval.

*Control group 1 = controls from nonatopic families followed-up from birth.

[†]Logistic regression with no adjustments.

[‡]Control group 2 = nonselected population-based controls matched for age and sex.

[§]Logistic regression adjusted for sex and age.

Table 2. Asthma by two definitions in 59 adults, hospitalized for bronchiolitis in infancy, compared with 39 selected controls not having bronchiolitis in infancy (control group 1)

Definition of asthma	Bronchiolitis group (<i>n</i> = 59)	<i>P</i>	Control group 1 (<i>n</i> = 39)
Current doctor-diagnosed asthma	12/58 (20.3%)	0.048 [§]	2 (5.1%)
OR (95% CI)*	2.88 (0.36–22.99)		1.00
OR (95% CI) [†]	2.84 (0.35–22.94)		1.00
OR (95% CI) [‡]	2.12 (0.25–17.89)		1.00
Current self-reported asthma	24 (40.7%)	0.002 [§]	4 (10.3%)
OR (95% CI)*	13.52 (2.90–63.03)		1.00
OR (95% CI) [†]	13.35 (2.85–62.51)		1.00
OR (95% CI) [‡]	11.39 (2.31–56.11)		1.00

For the definitions of current doctor-diagnosed and self-reported asthma, see the text.

OR, odds ratio; CI, confidence interval.

*Logistic regression adjusted for sex and age.

[†]Logistic regression adjusted for sex, age, smoking (yes, no).

[‡]Logistic regression adjusted for sex, age, allergic rhinitis (yes, no).

[§]Logistic regression with no adjustments.

bronchiolitis patients smoked, compared with 17% of the population-based controls (OR 3.3, 95% CI 1.5–6.0).

Current doctor-diagnosed asthma was present in 20% (seven males and five females; nine were on regular inhaled corticosteroids) of the former bronchiolitis patients, compared with 5% in the two control groups. The respective figures for current self-reported asthma were 41% (16 males and eight females) and 7–10%. The risk of doctor-diagnosed asthma in adulthood after bronchiolitis was 2.8-fold compared with controls with no bronchiolitis and 5.0-fold compared with population-based controls, and the respective figures for self-reported asthma were 13.5- and 11.0-fold (Tables 2

Table 3. Asthma by two definitions in 59 young adults, hospitalized for bronchiolitis in infancy, and in 105 nonselected population-based controls (control group 2)

Definition of asthma	Bronchiolitis group (<i>n</i> = 59)	<i>P</i>	Control group 2 (<i>n</i> = 105)
Current doctor-diagnosed asthma	12/58 (20.3%)	0.003*	5/104 (4.8%)
OR (95% CI)*	5.31 (1.75–16.11)		1.00
OR (95% CI) [†]	5.07 (1.63–15.78)		1.00
OR (95% CI) [‡]	5.16 (1.68–15.83)		1.00
Current self-reported asthma	24 (40.7%)	<0.001*	7/104 (6.7%)
OR (95% CI)*	11.03 (4.19–29.07)		1.00
OR (95% CI) [†]	10.45 (3.87–28.22)		1.00
OR (95% CI) [‡]	12.22 (4.43–33.70)		1.00

For the definitions of current doctor-diagnosed and self-reported asthma, see the text.

OR, odds ratio; CI, confidence interval.

*Logistic regression adjusted for sex and age.

[†]Logistic regression adjusted for sex, age, smoking (yes, no).

[‡]Logistic regression adjusted for sex, age, allergic rhinitis (yes, no).

and 3). The results were robust to adjustments for age, gender, current smoking and current allergic rhinitis, with the exception of doctor-diagnosed asthma in the former bronchiolitis group *vs* controls with no bronchiolitis.

When a subgroup of 24 children with self-reported asthma (doctor-diagnosed asthma included) were compared with the two control groups, there were significant differences in the presence of current wheezing symptoms, current allergic rhinitis and previous asthma, as well as in the presence of asthma in siblings and in current smoking (Table 4). When an identical comparison was performed for the subgroup of 12 subjects with current doctor-diagnosed asthma, the differences were significant only for current wheezing symptoms, previous

Table 4. Questionnaire data in 24 adults with current self-reported asthma (doctor-diagnosed included) hospitalized for bronchiolitis in infancy, compared with selected controls with no early life wheezing (control group 1) and with nonselected population based controls (control group 2)

Questionnaire data	Current self-reported asthma (n = 24)	OR (95% CI)* vs control group 1	OR (95% CI)* vs control group 2
Asthma in parents	9 (37.5)	2.66 (0.83–8.51)	2.58 (0.97–6.87)
Asthma in siblings	13 (54.2)	13.79 (3.31–57.42)	7.47 (2.76–20.20)
Body mass index >25 (kg/m ²)	11 (45.8)	1.16 (0.42–3.26)	1.25 (0.50–3.11)
Body mass index >30 (kg/m ²)	5 (20.8)	1.40 (0.38–5.23)	1.39 (0.46–4.27)
Current smoking	11 (45.8)	2.15 (0.74–6.24)	4.00 (1.52–10.47)
Wheezing symptoms	22 (91.7)	28.00 (5.62–139.63)	42.20 (9.15–194.56)
Prolonged cough	4 (16.7)	1.36 (0.33–5.66)	3.01 (0.75–12.11)
Night cough	4 (16.7)	0.91 (0.24–3.53)	3.10 (0.79–12.20)
Previous asthma	24 (100)	NC [†]	NC [†]
Allergic rhinitis	16 (66.7)	3.43 (1.17–10.04)	2.66 (1.04–6.77)
Atopic dermatitis	6 (25.0)	2.27 (0.61–8.46)	1.66 (0.57–4.87)

Values are denoted as n (%).

For definition, see the text. For controls, the figures are presented in Table 1 (previous asthma in Tables 2 and 3)

OR, odds ratio; CI, confidence interval.

*Logistic regression with no adjustments.

[†]NC = not possible to calculate; *P* < 0.001 (Chi-Square test).

[‡]Logistic regression adjusted for sex and age.

Table 5. Early-life risk factors for adulthood asthma after bronchiolitis in infancy

Risk factors	Doctor-diagnosed asthma (n = 12)		Self-reported asthma (n = 24)		No asthma (n = 35)	
	n	%	n	%	n	%
Parental asthma*	3	25	4	16.7	3/33	8.6
Atopic dermatitis*	4	33.3	10	41.7	11/33	31.4
Non-RSV bronchiolitis [†]	9	75	15	62.5	16	45.7
Eosinophils >0.45 × 10 ⁹ /l	6/11	50	11/19	45.8	9/18	25.7
Total IgE >60 IU/l	6/10	50	12/19	50	11/21	31.4
Specific IgE positive	5/11	41.7	7/20	29.2	4/27	11.4
Repeated wheezing at <24 months	12	100	2	100	34	97.1
Atopic dermatitis or total IgE positive or specific IgE positive	9	75	19/22	79.2	17/24	48.6

Early-life risk factors mean those presenting at <24 months of age. For other definitions, see the text.

Statistical significance: significant differences neither between subjects with doctor diagnosed asthma and no asthma nor between subjects self-reported asthma and no asthma.

*Diagnosed by physician; [†]RSV bronchiolitis in 28/59 (47%) cases.

asthma and asthma in siblings (data not shown). The results were similar in univariate analyses and in multivariate analyses adjusted for age and gender (data not shown).

Early-life risk factors were analyzed within the bronchiolitis group (Table 5). None of the early-life factors with adequate data available were significant as risk factors for doctor-diagnosed or self-reported asthma in young adulthood.

Discussion

There are two main positive and two main negative results in the present prospective, controlled, questionnaire study on the adulthood outcome after wheezing in infancy. Firstly, the increased risk for bronchial asthma after bronchiolitis at <24 months of age continued until 27 years of age, when compared with selected controls with no early-life wheezing followed from infancy, as well as with nonselected population-based controls enrolled to this adulthood study. In logistic regression, bronchiolitis in infancy was a significant risk factor for asthma independently from current smoking and allergic rhinitis. Secondly, asthma was strongly associated with current atopy, but not anymore with atopy or other early-life markers at enrolment >25 years ago. Though over half of the study subjects were overweight (and 14% were obese), we failed to find any association between asthma and overweight or obesity. Likewise, the link from non-RSV bronchiolitis in infancy to asthma, observed in the earlier phases of the present cohort (4, 19), as well as in our later post-bronchiolitis cohort (20, 21), was not to be seen anymore at 27 years of age.

Depending on the definition, 20–41% of the subjects with bronchiolitis in infancy had asthma at 27 years of age. The figures are rather constant compared with those of 30–41% observed in the same cohort 8 years earlier (4). Our results are rather similar to the findings of a previous study from Canada (1). In that study, asthma was diagnosed clinically at the age of 17–35 years, but the study subjects were identified and the data on early-life wheezing were collected retrospectively from the patient records of two hospitals. The prevalence of asthma was 38% after hospitalization for bronchiolitis before the age of 18 months, being significantly higher than in controls with no such history. By contrast, wheezing in infancy was not associated with asthma in adulthood in a birth cohort from the UK (22, 23). In that cohort, data on wheezing were collected prospectively, but the number of infants with wheezing was too small to allow any proper risk estimation.

In the birth cohort study from Tucson, AZ, USA, follow-up has now continued until 22 years of age (2, 3). In that cohort, 60% of the children had wheezed during their first 3 years of life, and 30% of them had asthma at 13 years, 20% at 16 years (24) and 30% at 22 years of age (3). In addition, lung function was impaired after early-childhood wheezing independently from asthma or asthma-like symptoms in adulthood (2). Wheezing infants with atopy were at a particular risk to have permanent or chronic asthma later (3, 25). In the post-bronchiolitis study from Gothenburg, Sweden, 30% of the children had asthma at age 10 years (26) and 43% at age 17–18 years (6), and the presence of asthma was linked with atopy and tobacco smoke exposure both in early life in disagreement with our results, and in adulthood in agreement with our results (6, 7).

In this study at 27 years of age, the prevalence of doctor-diagnosed asthma was 20% after wheezing in infancy, 5% in selected controls with no early wheezing and no family risk of asthma, and in nonselected population controls collected for this study. The figures for self-reported asthma were 41%, 10% and 7%, respectively. The prevalence of asthma in Finnish young adults was 3% at 16 and 5% at 32 years of age in a recent population-based study (27). Thus, both the selected and nonselected controls of this study reflected well the situation in the age-specific population.

We failed to confirm the association between overweight and asthma or asthma-like symptoms, though numerous reports have suggested this association. Three earlier epidemiological studies found an association between asthma symptoms and obesity in children (28–30), and three prospective follow-up studies failed to confirm the presence of this association (31–33). However, when the results were combined in a meta-analysis, an association between the development of overweight during childhood and later onset of asthma was documented (34). Only cross-sectional data were analyzed in this study. In the most recent population-based, long-term follow-up study from Finland, overweight was associated with asthma, but not earlier than at 24–39 years of age (35). Thus, the association, though present later, may not be demonstrable in early adulthood at 27 years of age.

We failed to confirm the link between non-RSV bronchiolitis in infancy and later asthma, though observed in the earlier phases of the present cohort (4, 19), as well as in our later postbronchiolitis cohort (20, 21). During long-term follow-ups started from infancy, the study subjects are faced to numerous later risk factors and disease modifying factors which weaken the effect of early-life risk factors. Another explanation may be that finally only 12–24 subjects, depending on definition, suffered from adulthood asthma, and the figures are too small to multivariate analyses separating the effects of early-life and later risk factors.

The main shortcoming of this study is the small number of study subjects with asthma and asthma-like symptoms. The confidence intervals for both current doctor-diagnosed and self-reported asthma were rather large, and the results should be interpreted with caution. In particular, this needs for caution concerns the results of the subgroups analyses. Certain subgroup analyses, e.g. for the severity or etiology of bronchiolitis, were not possible. The proportion of drop-outs, calculated from the 83 bronchiolitis patients recruited in infancy, was nearly 30%. In addition, the data were collected by posted questionnaires only. The data obtained from interview and clinical studies are more reliable, but especially in clinical studies, the numbers of drop-outs are usually greater, and the numbers of controls must be limited.

When assessing the outcome after bronchiolitis, or after other infections in infancy, the results are highly

dependent on the numbers of controls and on how the controls have been selected. An important question is whether we should use, when studying the outcome after early-life infection, healthy controls, healthy population-based controls, nonselected population-based controls, controls with the same clinical presentation (but different etiology), controls with the same etiology (but different presentation), or available population data from the epidemiological surveys. In this study, we used two different controls, highly selected controls from non-atopic families with no infantile bronchiolitis prospectively followed-up from birth (with a 54% drop-out ratio), and nonselected, age- and gender-matched controls from the same area with no prospective follow-up data available (with a 37% answering ratio). The questionnaires were sent by using a 1 : 4 patient-control ratio, and in the analyses, appropriate controls were included for women by 1 : 2 and for men by 1 : 1.65 patient-control ratio. Though the number of the controls followed prospectively from birth was clearly under-powered to many analyses, the analyses gave surprisingly similar results by both controls.

The main strength of this study is the long prospective follow-up from infancy to the median age of 27 years. In fact, this study is the longest prospective follow-up thus far published after bronchiolitis in infancy. In infancy, the basic data were registered prospectively and carefully during hospitalization and at two control visits, including at that time advanced viral antigen determinations. On the other hand, corresponding data were not available for the two control groups. The definitions of asthma were rather strict, being based on current medication, current symptoms and doctor-made asthma diagnoses either within recent 24 months (doctor-diagnosed asthma) or earlier (self-reported asthma). Thus, the diagnosis was never based on respiratory symptoms alone which are known to be nonspecific, especially in smokers. Atopic constitution and passive and active smoking are factors significantly predisposing to both early-life wheezing and later asthma (36, 37), as was seen also in this study for current allergic rhinitis and current smoking. Therefore, current smoking and current allergic rhinitis were included as covariates in the logistic regression model, and early childhood wheezing proved to be, independently from allergy and smoking, a significant risk factor for asthma in early adulthood.

In conclusion, this prospective, controlled, long-term follow-up study showed that an increased asthma risk in early-life wheezers continues, even after symptom-free years at school age, at least until 27 years of age. Adulthood asthma was strongly associated with current atopy, but not anymore with atopic or other early-life markers at enrolment >25 years ago. Adjusted analyses confirmed that bronchiolitis in infancy was a significant risk factor for asthma independently from current smoking and current allergy.

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