

## ORIGINAL ARTICLE Asthma and Rhinitis

## Environmental risk factors related to the incidence of wheeze and asthma in adolescence

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Experimental  
Allergy

## Summary

**Background** Asthma is common among adolescents, but there are few population-based studies on the risk factors for incident asthma and wheeze at this age group.

**Objective** To study risk factors for incident asthma and wheeze in adolescence.

**Method** Within the Obstructive Lung Disease In Northern Sweden (OLIN) studies, a cohort of 3430 school children (age 7–8 year) was recruited in 1996. In the present study, this cohort was followed from age 12–19 year. At baseline (age 12 year), 3151 participated and skin prick tests (SPT) were performed. The cohort was resurveyed annually, and risk factors for the cumulative incidence of asthma and wheeze from age 12–19 year were analysed using multivariate Cox regression.

**Results** Female sex (wheeze: HR 1.4 95%CI 1.2–1.6; asthma: HR 1.8 95%CI 1.2–2.5) and a positive SPT to cat, dog or horse at baseline (wheeze: HR 1.6 95%CI 1.2–2.1; asthma: HR 2.3 95%CI 1.4–4.0) were significantly associated with the cumulative incidence of wheeze and asthma. Increasing numbers of siblings were inversely related to the incidence of wheeze (HR 0.9 95%CI 0.8–0.97) and asthma (HR 0.8 95%CI 0.7–0.97). Parental asthma was related to the incidence of asthma (HR 1.8 95%CI 1.2–2.6) while ever smoking (HR 2.0 95%CI 1.6–2.4) and house dampness (HR 1.3 95%CI 1.1–1.6) were risk factors for the incidence of wheeze. Maternal ETS exposure increased the risk of incident asthma in non-sensitized subjects (HR 1.9 95%CI 1.0–3.7).

**Conclusion and clinical relevance** Several environmental risk factors related to the incidence of asthma and wheeze in adolescence were identified and may be possible targets for intervention and prevention.

**Keywords** adolescents, asthma, epidemiology, prospective studies, risk factors, wheezing

*Submitted 9 January 2014; revised 4 March 2014; accepted 15 March 2014*

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Cite this as: L. Hedman, M.

Andersson, A. Bjerg, B. Forsberg, B.

Lundbäck, E. Rönmark, *Clinical & Experimental Allergy*, 2015 (45) 184–191.

## Introduction

Asthma is common among adolescents, but there are few population-based studies on the risk factors for incident asthma and wheeze at this age group [1–5]. Adolescence introduces not only physiological changes but also new behaviours such as cigarette smoking. During late adolescence, the boy-to-girl prevalence ratio changes from asthma being more common in boys into being more frequent among girls and women, further underlining the importance of this time period in asthma epidemiology [1, 2, 6, 7].

Allergic sensitization [2] and allergic conditions such as rhinitis [1, 7, 8] and eczema [1, 5] are major determinants for the incidence of asthma and wheeze in

adolescence. A family history of asthma [7], female sex [1, 2, 7], and low birth weight [9–11] also predict asthma onset. Having older siblings and day-care attendance has been identified as protective factors against developing asthma [12]. Of special interest are the potential preventable risk factors for new-onset asthma which include overweight [9, 10], air pollution [13], indoor exposure to moulds and dampness [14] and personal smoking [2, 3, 15]. To our knowledge, no population-based study has analysed all these factors comprehensively.

Within the Obstructive Lung Disease in Northern Sweden (OLIN) studies, a cohort of school children was followed from 1996 to 2007 [16–18]. We have previously reported on risk factors for incident asthma and

wheeze up to 10 years of age [16]. The aim of the present study was to identify risk factors for new-onset asthma and wheeze in adolescence.

## Material and methods

### Study population

The OLIN paediatric study I is a longitudinal study of asthma, allergic conditions and sensitization among school children in three municipalities in Northern Sweden. The aims and methods have been described previously [19]. At recruitment in 1996, the parents of all 3525 children aged 7–8 years (median 8 years) enrolled in the first and second grades of primary school were invited to complete a questionnaire. Informed consent was obtained from the parents who signed the questionnaire and approved of their child's participation in the study. The questionnaire participants formed a cohort ( $n = 3430$ ; 97% of invited) that was resurveyed annually by questionnaires until high school graduation at the age of 19 years in 2006 and 2007, respectively. The study population in the present paper consisted of the 3151 children (51% boys and 92% of the participants from 1996) who participated in 2000 (the baseline survey) at the age of 11–12 years (median 12 years; Fig. 1). The yearly participation rate from 12 to 19 years ranged from 87% to 93%. The study was approved by the Regional Ethical Review Board at Umeå University, Sweden (96–032; 96–121; 99–408).

### Questionnaire

The questionnaire included the International Study of Asthma and Allergies in Childhood (ISAAC) core questions [20]. Questions about physician diagnoses and medication as well as on possible environmental, social and behavioural risk factors for asthma and allergic disorders were added [18]. From recruitment to baseline,

from age 8–12 years, the parents completed the questionnaire. From 13 years of age and onward, the teenagers completed the questionnaire at school and questions regarding personal smoking were added. This methodological shift has been validated with good agreement between parental and teenagers responses [21, 22].

### Skin prick tests

All children in two of the municipalities (Luleå and Kiruna) were invited to skin prick tests (SPT) for ten common airborne allergens at baseline in 2000, and 2052 (91%) participated. SPTs were performed according to EAACI standards [23]. The allergen extracts included a Swedish standard panel of birch, timothy, mugwort, dog, cat, horse, two mites (*Dermatophagoides farinae* and *D. pteronyssinus*) and two moulds (*Cladosporium* and *Alternaria*). A positive test was defined as a reaction with a mean wheal diameter of  $\geq 3$  mm to at least one allergen.

### Definitions

**Definitions of the outcome variables** *Physician-diagnosed asthma*: Have you been diagnosed by a physician as having asthma? *Current wheeze*: Have you had wheezing or whistling in the chest in the last 12 months? *Current asthma* was defined as having physician-diagnosed asthma and either current wheeze or use of asthma medication during the last 12 months.

**Potential risk factors at any time from birth until baseline (age 12 years)** *Ever cat*: ever having kept a cat in the home.

*House dampness*: current or previous signs of dampness in the home.

*Respiratory infections*: ever having had pertussis, croup, pneumonia or other severe respiratory infection, for example respiratory syncytial (RS) virus.

**Potential risk factors at baseline (age 12 years)** *Overweight*: Weight and height were measured at a clinical examination, and weight/height<sup>2</sup> (body mass index, BMI) was calculated. Because the definition of overweight based on BMI changes by age and varies by sex among children, we dichotomized BMI based on the age and sex-specific cut-off suggested by Cole et al. [24].

*Allergic sensitization*: a positive reaction to any of the tested allergens.

*Living in an apartment*: compared to living in a house.

*Parental history of asthma*: parental report of asthma by one or both parents.

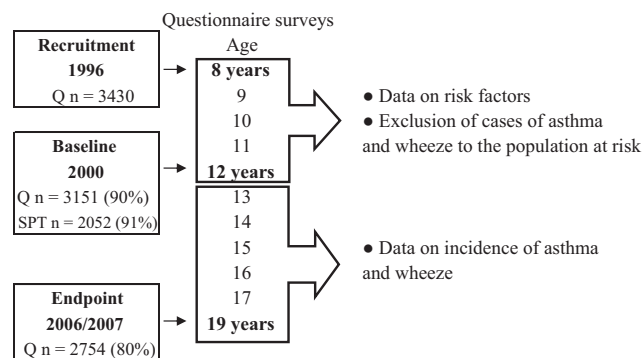


Fig. 1. Flow chart of the study design in the OLIN paediatric study I from age 8–19 years. Q, questionnaire; SPT, skin prick test.

**Self-reported traffic exposure:** living within 200 m from a heavily trafficked road or much used bus stop.

**Number of siblings** was based on the report at recruitment (8 year).

**Maternal ETS (environmental tobacco smoke) exposure:** The mother smoked during pregnancy and the child was continuously exposed from recruitment to baseline (from age 8–12 years).

**Ever smoking** was defined as a report of daily smoking in any of the questionnaire surveys from baseline to endpoint (13–19 years).

### Statistical analyses and data management

Analyses were performed using the IBM SPSS software (Version 20.0; SPSS Inc, Chicago, IL, USA). This study has 80% power ( $\alpha = 0.05$ ) to detect a three percentage point difference in cumulative incidence, assuming a prevalence of exposure of 25% and 9% incidence among the exposed. For assessment of differences in prevalence and mean-values,  $\chi^2$ -tests and *t*-tests were used. Potential risk factors for the cumulative incidence of asthma and wheeze were analysed in bivariate Cox regression models and expressed as unadjusted hazard ratios (HR). Significant risk factors for the cumulative incidence of asthma or wheeze identified in the bivariate analyses were included in multivariate Cox regression models and the results were expressed as adjusted HR. Multivariate risk factor analyses stratified by sex and allergic sensitization, respectively, were also performed. A confidence interval of 95% was applied, and thus a *P*-value <0.05 was considered statistically significant.

**The cumulative incidence of asthma and wheeze, respectively, was defined as:** Number of new cases/Population at risk. The incident cases had reported having asthma or wheeze, respectively, in any of the annual questionnaire surveys between 13 and 19 years of age. Those excluded from the population at risk for asthma had reported having asthma in any of the questionnaire surveys from 8 to 12 years of age or were classified as having asthma in a previously published validation study [25]. The population at risk for wheeze excluded those who had reported current wheeze in any of the questionnaire surveys from 8 to 12 years of age. At baseline, the population at risk for asthma consisted of 2747 individuals (49.5% boys), and the population at risk for wheeze included 2578 individuals (49.6% boys).

### Results

From baseline at age 12 years to end-point at age 19 years (mean follow-up time 6.5 years), the cumulative incidence of physician-diagnosed asthma was 7.2%

(*n* = 197), of current asthma 6.3% (*n* = 172), and current wheeze 22.0% (*n* = 567), which has been presented in a previous publication [7]. The incidence was significantly higher among girls (Fig. 2a) and among sensitized (Fig. 2b).

### Risk factors for incident asthma and wheeze

The prevalence of risk factors in the population at risk for wheeze was almost identical to the prevalence of risk factors in the population at risk for asthma given in Table 1. The prevalence of most risk factors in the population at risk for asthma and wheeze, respectively, was similar among boys and girls. However, the prevalence of ever smoking and ever having a cat was significantly higher among the girls, while having a positive SPT was more common in boys.

Bivariate analyses of risk factors for asthma and wheeze are presented in Table 1. Female sex (HR 1.6 95%CI 1.2–2.1 and HR 1.4 95%CI 1.2–1.7, respectively), a positive skin prick test (both to any of the tested allergens, to animals and to pollen, HRs 1.6–2.5) and a parental history of asthma (HR 1.8 95%CI 1.3–2.4 and HR 1.3 95%CI 1.1–1.6) were significant risk factors for asthma and wheeze. The number of siblings was inversely associated with the incidence of both asthma (HR

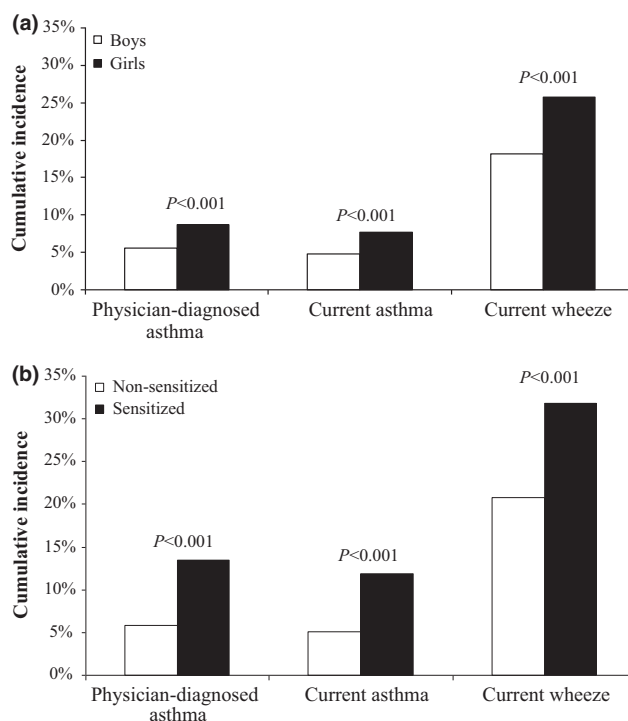


Fig. 2. (a) The cumulative incidence (%) of asthma and wheeze from 12 to 19 years of age, by sex. (b) The cumulative incidence (%) of asthma and wheeze from 12 to 19 years of age, by allergic sensitization at the age of 12 year.

**Table 1.** Factors related to the incidence of asthma and wheeze, respectively, from 12 to 19 years of age (bivariate analysis), expressed as unadjusted hazard ratios with 95% confidence interval

|                                | Prevalence of risk factors among the population at risk for asthma ( <i>n</i> = 2747)<br>% | Incidence of physician-diagnosed asthma |           | Incidence of current asthma |           | Incidence of current wheeze |           |
|--------------------------------|--------------------------------------------------------------------------------------------|-----------------------------------------|-----------|-----------------------------|-----------|-----------------------------|-----------|
|                                |                                                                                            | HR                                      | 95% CI    | HR                          | 95% CI    | HR                          | 95% CI    |
| Female sex                     | 50.5                                                                                       | 1.57                                    | 1.18–2.09 | 1.62                        | 1.16–2.25 | 1.45                        | 1.23–1.71 |
| Positive skin prick test (SPT) | 25.8                                                                                       | 2.38                                    | 1.70–3.33 | 2.39                        | 1.62–3.51 | 1.64                        | 1.33–2.03 |
| Positive SPT to furred animal  | 18.2                                                                                       | 2.52                                    | 1.77–3.57 | 2.52                        | 1.68–3.78 | 1.79                        | 1.43–2.25 |
| Positive SPT to pollen         | 19.0                                                                                       | 1.90                                    | 1.32–2.73 | 1.78                        | 1.16–2.72 | 1.59                        | 1.26–2.01 |
| Parental history of asthma     | 17.7                                                                                       | 1.76                                    | 1.29–2.41 | 1.80                        | 1.26–2.58 | 1.31                        | 1.07–1.60 |
| Ever smoking                   | 16.2                                                                                       | 1.38                                    | 0.96–1.97 | 1.52                        | 1.02–2.27 | 2.01                        | 1.66–2.43 |
| Number of siblings (Mean)*     | 1.8                                                                                        | 0.82                                    | 0.71–0.95 | 0.81                        | 0.68–0.96 | 0.91                        | 0.84–0.98 |
| Ever cat                       | 39.8                                                                                       | 0.67                                    | 0.49–0.90 | 0.66                        | 0.46–0.93 | 0.88                        | 0.74–1.05 |
| House dampness                 | 24.1                                                                                       | 0.83                                    | 0.59–1.17 | 0.75                        | 0.50–1.13 | 1.28                        | 1.06–1.54 |
| Self-reported traffic exposure | 34.7                                                                                       | 1.24                                    | 0.93–1.65 | 1.22                        | 0.88–1.70 | 1.25                        | 1.05–1.48 |
| Maternal ETS exposure          | 12.3                                                                                       | 1.22                                    | 0.78–1.92 | 1.03                        | 0.60–1.78 | 1.40                        | 1.09–1.80 |
| Respiratory infections         | 58.3                                                                                       | 1.07                                    | 0.81–1.42 | 1.10                        | 0.80–1.53 | 1.15                        | 0.97–1.36 |
| Overweight                     | 25.2                                                                                       | 1.31                                    | 0.91–1.87 | 1.26                        | 0.83–1.90 | 1.20                        | 0.96–1.51 |
| Urban living                   | 57.0                                                                                       | 1.14                                    | 0.85–1.53 | 1.09                        | 0.77–1.52 | 1.09                        | 0.92–1.29 |
| Living in an apartment         | 21.9                                                                                       | 0.85                                    | 0.59–1.23 | 0.85                        | 0.56–1.28 | 1.03                        | 0.85–1.27 |

\*Continuous variable.

0.8 95%CI 0.7–0.95) and wheeze (HR 0.9 95%CI 0.8–0.98). Other risk factors related to the incidence of current wheeze were ever smoking (HR 2.0 95%CI 1.7–2.4), house dampness (HR 1.3 95%CI 1.1–1.5), self-reported traffic exposure (HR 1.3 95%CI 1.1–1.5), and maternal ETS exposure (HR 1.4 95%CI 1.1–1.8). Ever having had a cat at home was inversely related to the incidence of asthma (HR 0.7 95%CI 0.5–0.9).

### Multivariate analyses

In multivariate analyses, significant risk factors related to the incidence of both asthma and wheeze were female sex (HR 1.7 95%CI 1.3–2.3 and HR 1.4 95%CI 1.2–1.6, respectively) and positive skin prick test (HR 2.3 95%CI 1.6–3.3 and HR 1.6 95%CI 1.3–2.0, data not given in table). Sensitization to any animal was related to the incidence of both asthma and wheeze (HR 2.2 95%CI 1.4–3.5 and HR 1.6 95%CI 1.2–2.1, respectively) while sensitization to any pollen was related neither to the incidence of asthma nor wheeze. A higher number of siblings was inversely associated with the incidence of both asthma and wheeze (HR 0.8 95%CI 0.7–0.97 and HR 0.9 95%CI 0.8–0.97). Ever smoking (HR 2.05 95%CI 1.6–2.4) and house dampness (HR 1.3 95%CI 1.1–1.6) were significant risk factors for the incidence of current wheeze. A parental history of asthma was significantly related to the incidence of asthma (HR 1.7 95%CI 1.2–2.4; Table 2).

Among non-sensitized, female sex (HR 2.0 95%CI 1.2–3.3 and HR 1.4 95%CI 1.0–1.7, respectively) and number of siblings (HR 0.7 95%CI 0.5–0.9 and HR 0.8 95%CI

0.7–0.9) were related to the incidence of both asthma and wheeze. Ever smoking (HR 2.1 95%CI 1.6–2.8), and house dampness (HR 1.3 95%CI 1.0–1.7) were related to the incidence of wheeze while maternal ETS exposure was related to physician-diagnosed asthma (HR 1.9 95%CI 1.0–3.7). Among sensitized children, no statistically significant risk factors were found, although the associations between ever smoking and asthma or wheeze, respectively, were borderline significant (Table 3).

Boys and girls had similar risk factor patterns. However, ever smoking was a significant risk factor for the incidence of current asthma only among girls (HR 1.7 95%CI 1.0–2.7). Parental history of asthma and ever cat were significant risk factors only among the boys, HR 2.4 95%CI 1.3–4.5 and HR 0.4 95%CI 0.2–0.8, respectively (Table 4).

### Discussion

This prospective and population-based study described several factors related to the incidence of asthma and wheeze during adolescence. These included female sex, a parental history of asthma, a positive skin prick test and an inverse association with number of siblings. The preventable factors, smoking and house dampness, were also identified as increasing the risk of current wheeze. Self-reported exposure to vehicle traffic was a borderline significant risk factor for current wheeze and maternal ETS exposure was a risk factor for asthma among the non-sensitized.

From 12 to 19 years of age, the cumulative incidence of asthma was 6–7% and 22% for wheeze. The annual

**Table 2.** Factors related to the incidence of asthma and wheeze, respectively, from 12 to 19 years, in a multivariate Cox regression analysis, expressed as hazard ratios with 95% confidence intervals. All independent variables were included in the models

|                                        | Incidence of physician-diagnosed asthma |           | Incidence of current asthma |           | Incidence of current wheeze |           |
|----------------------------------------|-----------------------------------------|-----------|-----------------------------|-----------|-----------------------------|-----------|
|                                        | HR                                      | 95% CI    | HR                          | 95% CI    | HR                          | 95% CI    |
| Female sex                             | 1.70                                    | 1.25–2.30 | 1.76                        | 1.23–2.51 | 1.37                        | 1.15–1.63 |
| Positive skin prick test to any animal | 2.19                                    | 1.38–3.50 | 2.33                        | 1.36–4.00 | 1.60                        | 1.20–2.13 |
| Positive skin prick test to any pollen | 1.16                                    | 0.72–1.88 | 1.03                        | 0.58–1.81 | 1.22                        | 0.91–1.63 |
| Parental history of asthma             | 1.68                                    | 1.20–2.35 | 1.75                        | 1.19–2.57 | 1.17                        | 0.95–1.45 |
| Ever smoking                           | 1.33                                    | 0.92–1.92 | 1.49                        | 0.98–2.26 | 1.95                        | 1.60–2.38 |
| Number of siblings*                    | 0.84                                    | 0.72–0.97 | 0.82                        | 0.69–0.97 | 0.89                        | 0.83–0.97 |
| Ever cat                               | 0.76                                    | 0.55–1.05 | 0.78                        | 0.54–1.14 | 0.92                        | 0.77–1.11 |
| House dampness                         | 0.80                                    | 0.56–1.14 | 0.76                        | 0.50–1.16 | 1.29                        | 1.07–1.56 |
| Self-reported traffic exposure         | 1.10                                    | 0.81–1.50 | 1.07                        | 0.75–1.53 | 1.18                        | 0.99–1.40 |
| Maternal ETS exposure                  | 1.21                                    | 0.77–1.93 | 1.04                        | 0.60–1.81 | 1.21                        | 0.94–1.57 |

\*Entered as a continuous variable.

**Table 3.** Factors related to the incidence of asthma and wheeze, respectively, from 12 to 19 years of age, among non-sensitized and sensitized teenagers, in a Cox regression analysis, expressed as hazard ratios with 95% confidence intervals. All independent variables were included in the models

|                                | Among non-sensitized<br><i>n</i> = 1302 |           |                             |           |                             |            | Among sensitized<br><i>n</i> = 452      |           |                             |           |                             |           |
|--------------------------------|-----------------------------------------|-----------|-----------------------------|-----------|-----------------------------|------------|-----------------------------------------|-----------|-----------------------------|-----------|-----------------------------|-----------|
|                                | Incidence of physician-diagnosed asthma |           | Incidence of current asthma |           | Incidence of current wheeze |            | Incidence of physician-diagnosed asthma |           | Incidence of current asthma |           | Incidence of current wheeze |           |
|                                | HR                                      | 95% CI    | HR                          | 95% CI    | HR                          | 95% CI     | HR                                      | 95% CI    | HR                          | 95% CI    | HR                          | 95% CI    |
| Female sex                     | 1.96                                    | 1.18–3.25 | 2.08                        | 1.15–3.74 | 1.35                        | 1.04–1.74  | 1.04                                    | 0.60–1.78 | 1.19                        | 0.63–2.25 | 1.29                        | 0.89–1.85 |
| Parental history of asthma     | 1.26                                    | 0.61–2.07 | 0.86                        | 0.40–1.83 | 1.08                        | 0.78–1.49  | 1.49                                    | 0.81–2.76 | 1.56                        | 0.76–3.23 | 1.16                        | 0.76–1.78 |
| Ever smoking                   | 1.23                                    | 0.67–2.25 | 1.36                        | 0.70–2.65 | 2.11                        | 1.58–2.82  | 1.78                                    | 0.94–3.38 | 1.96                        | 0.93–4.11 | 1.41                        | 0.90–2.22 |
| Number of siblings*            | 0.68                                    | 0.52–0.89 | 0.67                        | 0.49–0.91 | 0.83                        | 0.73–0.94  | 0.90                                    | 0.71–1.15 | 0.89                        | 0.67–1.18 | 0.95                        | 0.82–1.10 |
| Ever cat                       | 1.09                                    | 0.68–1.77 | 1.20                        | 0.70–2.09 | 0.91                        | 0.70–1.18  | 0.66                                    | 0.33–1.32 | 0.74                        | 0.34–1.61 | 0.93                        | 0.62–1.40 |
| House dampness                 | 0.59                                    | 0.32–1.09 | 0.70                        | 0.36–1.37 | 1.32                        | 1.01–1.74  | 0.86                                    | 0.46–1.61 | 0.91                        | 0.44–1.88 | 1.27                        | 0.86–1.88 |
| Self-reported traffic exposure | 0.99                                    | 0.61–1.62 | 1.07                        | 0.62–1.88 | 1.29                        | 0.997–1.67 | 1.29                                    | 0.74–2.23 | 1.52                        | 0.80–2.88 | 1.27                        | 0.87–1.84 |
| Maternal ETS exposure          | 1.94                                    | 1.01–3.72 | 1.86                        | 0.88–3.96 | 1.05                        | 0.70–1.57  | 0.87                                    | 0.36–2.09 | 0.70                        | 0.24–2.04 | 1.16                        | 0.67–2.01 |

\*Entered as a continuous variable.

incidence rates from 12 to 18 years varied between 1.0–1.5/100 per year among girls and 0.5–1.2/100 per year among boys, and have been presented in detail in a previous report [7]. Similarly, between the ages 8–10 years the incidence rate of asthma was 1/100 per year in the present cohort [16]. Thus, the incidence of asthma and wheeze was still high during adolescence, in line with two other Swedish studies [2, 15]. As the incident cases in the present study were identified based on all annual resurveys, we limit recall bias [7].

As expected, the major determinants of the incidence of asthma and wheeze were non-preventable, including allergic sensitization, female sex and parental asthma, in line with previous studies [1, 2]. We note that in our cohort the impact of parental asthma was lower in teenage compared with during childhood. To some extent, this could reflect that the subjects with the strongest hereditary component had already developed symptoms before teenage and were thus excluded from the population at risk in the present study. The continuing high

**Table 4.** Factors related to the incidence of asthma and wheeze, respectively, from 12 to 19 years of age, by sex, in a Cox regression analysis, expressed as hazard ratios with 95% confidence intervals. All independent variables were included in the models

|                                | Girls<br><i>n</i> = 1386   |           |                |           |                |           | Boys<br><i>n</i> = 1361    |           |                |           |                |           |
|--------------------------------|----------------------------|-----------|----------------|-----------|----------------|-----------|----------------------------|-----------|----------------|-----------|----------------|-----------|
|                                | Physician-diagnosed asthma |           | Current asthma |           | Current wheeze |           | Physician-diagnosed asthma |           | Current asthma |           | Current wheeze |           |
|                                | HR                         | 95% CI    | HR             | 95% CI    | HR             | 95% CI    | HR                         | 95% CI    | HR             | 95% CI    | HR             | 95% CI    |
| Positive skin prick test       | 1.82                       | 1.12–2.94 | 1.87           | 1.08–3.24 | 1.58           | 1.17–2.12 | 3.04                       | 1.74–5.33 | 2.88           | 1.48–5.61 | 1.65           | 1.18–2.29 |
| Parental history of asthma     | 1.65                       | 1.08–2.51 | 1.43           | 0.86–2.36 | 1.28           | 0.97–1.67 | 1.76                       | 1.01–3.06 | 2.44           | 1.32–4.49 | 1.06           | 0.75–1.49 |
| Ever smoking                   | 1.31                       | 0.84–2.04 | 1.68           | 1.03–2.73 | 2.09           | 1.64–2.68 | 1.32                       | 0.67–2.61 | 1.05           | 0.44–2.49 | 1.69           | 1.19–2.40 |
| Number of siblings*            | 0.87                       | 0.73–1.03 | 0.84           | 0.68–1.03 | 0.90           | 0.81–0.99 | 0.79                       | 0.61–1.02 | 0.78           | 0.57–1.06 | 0.89           | 0.78–1.02 |
| Ever cat                       | 0.97                       | 0.66–1.44 | 0.96           | 0.61–1.50 | 0.94           | 0.75–1.19 | 0.43                       | 0.23–0.82 | 0.51           | 0.25–1.04 | 0.89           | 0.66–1.18 |
| House dampness                 | 0.65                       | 0.40–1.05 | 0.67           | 0.39–1.16 | 1.25           | 0.98–1.60 | 1.04                       | 0.60–1.81 | 0.95           | 0.49–1.84 | 1.34           | 1.00–1.80 |
| Self-reported traffic exposure | 1.25                       | 0.86–1.83 | 1.16           | 0.74–1.80 | 1.20           | 0.96–1.51 | 0.90                       | 0.53–1.53 | 0.94           | 0.51–1.73 | 1.17           | 0.89–1.55 |
| Maternal ETS exposure          | 1.38                       | 0.80–2.36 | 1.17           | 0.62–2.22 | 1.21           | 0.87–1.70 | 0.88                       | 0.35–2.33 | 0.74           | 0.23–2.43 | 1.21           | 0.80–1.83 |

\*Entered as a continuous variable.

incidence between age 12 and 19, however, points to the importance of other risk factors.

Although available medications (mainly inhaled corticosteroids and  $\beta_2$ -agonists) are effective in treating asthma symptoms, to date there is no cure for asthma. Identification of preventable risk factors thus seems to be a promising public health strategy. However, the risk factor pattern for asthma changes with increasing age, and many studies have been cross-sectional, especially of adolescent populations. In the OLIN paediatric cohort, male sex, respiratory infections and low birth weight were important determinants of asthma during childhood [16, 17, 19] in line with previous studies [1, 6, 11], but were not associated with incident asthma after age 12. It seems reasonable that smaller children with less developed lungs may be more susceptible to adverse effects of respiratory infections while during adolescence and early adulthood other environmental exposures will be introduced and become more important determinants of asthma onset, including preventable factors such as personal smoking.

The risk factor pattern for the incidence of asthma and wheeze differed between those sensitized and non-sensitized at age 12 years. The inverse association between number of siblings and the incidence of asthma and wheeze among non-sensitized is a particularly interesting finding. Children having a higher number of siblings, having older siblings, or attending day care at an early age are more exposed to microbes and infections. According to the hygiene hypothesis, this exposure could decrease the likelihood of developing allergic sensitization and allergic conditions. This has been previously

confirmed, mainly for allergic rhinitis and eczema [26], while some studies have found associations with asthma as well [27, 28]. We have demonstrated that in non-sensitized, the number of siblings was inversely related to the incidence of asthma in adolescence. It should, however, be noted that these children might have become sensitized after the age of 12 years but before the asthma onset and that exposure to sibling-related risk factors could have affected sensitized children already at an earlier age.

In the present study, personal smoking was related to the incidence of wheeze, similar to findings in other studies [3, 29]. Personal smoking was a borderline significant risk factor for the incidence of asthma, in line with other studies as well [3, 15]. Thus, respiratory health is affected already after a few years of smoke exposure. In a previous cross-sectional publication based on the present cohort, we demonstrated significant associations between both personal smoking and ETS exposure and the prevalence of asthma and wheeze at age 16–17 years [30]. In the present longitudinal study, ETS exposure was, however, not related to the incidence of asthma or wheeze during the teen ages. ETS exposure has consistently been described as strongly related to asthma among young children [31] and among teenagers; however, the association is weaker [3]. It is likely that ETS exposure decrease in adolescence as teenagers spend less time with their parents compared with younger children or that ETS exposure at a younger age has a greater impact on respiratory health than exposure in adolescence.

Although house dampness was related to the incidence of wheeze in our study, it was not related to the incidence

of asthma. Damp housing is often considered an established risk factor for asthma in children [32]. However, house dampness is not consistently associated with asthma in adults [32], and our finding might be explained by a decreasing susceptibility by age. Also, in damp buildings non-specific airway symptoms may be prevalent among both asthmatic and non-asthmatic individuals [32], which may partly explain damp buildings as a risk factor for wheeze. As damp housing is related to several symptoms beside asthma, and as reported wheezing is used as an indicator of asthma in many studies, damp buildings are indeed a target for intervention also in adolescence.

We found that self-reported traffic exposure was a borderline significant risk factor for the incidence of wheeze among non-sensitized. Previously, a borderline significant association has been found between self-reported traffic exposure and the prevalence of wheeze among children aged 7–8 years in the same study area as the present cohort. In that study, when using objective exposure assessment, the association became stronger and statistically significant, also restricted to non-sensitized children [33]. Thus, our finding indicates an effect of traffic air pollution also on the incidence of asthma and in adolescence.

Personal smoking, ETS exposure, house dampness and probably also traffic exposure were the environmental risk factors related to the incidence of wheeze in our study area. It has previously been shown that reduction of exposure to indoor moulds [34] and ETS, respectively [35], improved morbidity among children with asthma. According to our findings, reduced exposure by smoking prevention, traffic planning and improved housing can probably also decrease the incidence of wheeze and possibly also asthma in disease-free subjects.

The strengths of this study include the prospective design with high participation rates and few lost to follow up. The internationally used ISAAC protocol also strengthens the validity of the data. The limitations include that we have not validated the self-reported asthma diagnosis in adolescence nor the environmental

exposures. However, previous studies of this cohort have shown very high specificity of physician-diagnosed asthma at 7–8 years as reported by parents [25] and high agreement between parents and teenagers in the question about physician diagnosis of asthma [22]. In a similar cohort recruited in 2006, the impact of self-reported and objective vehicle traffic exposure in the study area was described [33]. Others have used objective measures to validate self-reported smoking [36] and house dampness [37] and found good agreement as well.

In conclusion, female sex, asthma heredity and sensitization are major risk factors for incident asthma and wheeze among adolescents. Increasing number of siblings was inversely associated with both incident asthma and wheeze. Maternal smoking was significantly associated with incident asthma among non-sensitized subjects. Ever having smoked and house dampness were identified as environmental risk factors for wheeze and are important, as they may be possible targets for intervention and prevention.

## Acknowledgements

Sigrid Sundberg, Aina Jonsson, Kerstin Kemi Björnström and Lena Gustafsson are acknowledged for data collection, and Ola Bernhoff and Helena Backman for database management. The Swedish Heart-Lung Foundation, The Swedish Foundation for Health Care Science and Allergy Research (Vårdal), The Swedish Asthma and Allergy Association's Research Foundation, Visare Norr, Umeå University, Västerbotten County Council, Norrbotten County Council and the Swedish Research Council are acknowledged for financial support. Additional funding was provided by GlaxoSmithKline World Wide Epidemiology, ALK and ThermoFisher.

## Conflict of interest

The authors declare no conflict of interest.

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