

Original article

Time trends in asthma and wheeze in Swedish children
1996–2006: prevalence and risk factors by sex

Background: Recent data suggest that the previously rising trend in childhood wheezing symptoms has plateaued in some regions. We sought to investigate sex-specific trends in wheeze, asthma, allergic conditions, allergic sensitization and risk factors for wheeze.

Methods: We compared two population-based cohorts of 7 to 8-year olds from the same Swedish towns in 1996 and 2006 using parental expanded ISAAC questionnaires. In 1996, 3430 (97%) and in 2006, 2585 (96%) questionnaires were completed. A subset was skin prick tested: in 1996, 2148 (88%) and in 2006, 1700 (90%) children participated.

Results: No significant change in the prevalence of current wheeze ($P = 0.13$), allergic rhinitis ($P = 0.18$) or eczema ($P = 0.22$) was found despite an increase in allergic sensitization (20.6–29.9%, $P < 0.01$). In boys, however, the prevalence of current wheeze (12.9–16.4%, $P < 0.01$), physician-diagnosed asthma (7.1–9.3%, $P = 0.03$) and asthma medication use increased. In girls the prevalence of current symptoms and conditions tended to decrease. The prevalence of all studied risk factors for wheeze and asthma increased in boys relative to girls from 1996 to 2006, thus increasing the boy-to-girl prevalence ratio in risk factors.

Conclusions: The previously reported increase in current wheezing indices has plateaued in Sweden. Due to increased diagnostic activity, physician diagnoses continue to increase. Time trends in wheezing symptoms differed between boys and girls, and current wheeze increased in boys. This was seemingly explained by the observed increases in the prevalence of risk factors for asthma in boys compared with girls. In contrast to the current symptoms of wheeze, rhinitis or eczema, the prevalence of allergic sensitization increased considerably.

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The prevalence of childhood asthma and allergic conditions increased during the second half of the 20th century (1). Recent data suggest that the increase in asthma symptoms has ceased in some, preferably westernized, countries and this prevalence plateau has not been limited to areas with the highest prevalence (2–5). However, diverging prevalence trends in wheeze have been observed in neighbouring countries such as Belgium (prevalence 12.0–8.3%) and Germany (14.2–17.5%) (3) and also within the same country (United Kingdom) (2, 6, 7). Very little is known about the possible determinants for this development (8).

During childhood, asthma is more common in boys. Sex-specific prevalence trends have been observed (9–12), but while some studies report decreased boy-to-girl ratio (9, 11), others report the opposite (10, 12). To date no reliable explanations for these conflicting results have been presented. Trends in childhood allergic rhinitis and eczema have not been studied to the same extent as

wheeze, and the results are even more conflicting (2, 7, 9). Currently, there is no 'gold standard' test for asthma, rhinitis or eczema and epidemiological studies rely mainly on self-reported data. Wheeze during the last 12 months is widely considered an indicator of childhood asthma (3), although studying a broader range of symptoms may better reflect complex prevalence trends. Furthermore, allergic sensitization, which is associated with wheeze and also affects its clinical picture (13, 14) can be measured objectively and integrated with questionnaire data. The few studies available suggest a stabilization in the prevalence of allergic sensitization (4, 5).

In Swedish children, the prevalence of asthma symptoms is comparable with most of Western Europe (15–17). The Obstructive Lung Disease in Northern Sweden (OLIN) first paediatric cohort started in 1996 (16) and has been followed longitudinally (13, 18, 19) to date. Questionnaire and skin prick test data from 1996 allowed us to repeat the study in a new cohort 10 years later

(2006) using identical methods. Our aim was to study the prevalence trends in asthma and its risk factors, allergic conditions and allergic sensitization with special focus on differences by sex.

Material and methods

First OLIN paediatric study

The first OLIN paediatric cohort was established in 1996 and it has been described in detail (13, 16, 18–20). All children in first and second grade classes (age 7–8 years) in three towns (Kiruna, Luleå and Piteå) in Northern Sweden were invited to a questionnaire study. The parental questionnaire included the International Study of Asthma and Allergy in Childhood (ISAAC) core questions (15) and added detailed questions about symptoms, physician diagnoses, medication use and possible determinants of disease (16). A clinical validation of the questionnaire showed >99% specificity and ~70% sensitivity for the question of physician-diagnosed asthma, when compared both to predefined criteria for an asthma diagnosis and to paediatricians' assessments (20). All children in two of the three towns (Kiruna and Luleå) were also invited to skin prick testing (below).

Second OLIN paediatric study

In 2006, a new cohort of children was recruited similarly; all school children in first and second grade (same ages as in 1996) in the same towns were invited. The same questionnaire was used at the same time of the year (February–April) to adjust for seasonal allergies and infections. In 1996, 3430 (97% of invited) children participated in the questionnaire and 2148 (88%) participated in the skin prick tests. In 2006, the corresponding numbers were 2585 (96%) and 1700 (90%) respectively, due to 20% lower birth rates in 1997–1998 compared with 1987–1988 (21). From 1995 to 2005, the total population of the study area changed by less than 2%, and migration was low (21). Consistently, half of the participants were girls (Table 1). The prevalence of current wheeze or physician-diagnosed asthma was not significantly different in 1996 ($P = 0.415, 0.220$) or 2006 ($P = 0.196, 0.693$) between the children invited to skin prick testing and the children in Piteå.

Skin prick tests

Skin prick testing for allergic sensitization followed the European Academy of Allergology and Clinical Immunology (EAACI)

recommendations (22). The standard panel of 10 inhalant allergens included: birch, timothy, mugwort, cat, dog, horse, *Dermatophagoides pteronyssinus*, *D. farinae*, *Cladosporium* and *Alternaria* (Soluprick, ALK, Hørsholm, Denmark). Allergic sensitization was defined as at least one wheal ≥ 3 mm in diameter. Both studies used the same allergen potency and identical methods. A validation of the skin prick tests by specific IgE in subsets of children has been described in detail (18). In 1996 the correlation between ≥ 3 mm wheal size and specific IgE >0.35 IU/ml by CAP was excellent (18) and in 2006, among the children with a positive skin prick test to any allergen, specific IgE could be detected in 88%.

Data analysis and definitions

Prevalence comparisons used the two-sided chi-squared test and $P < 0.05$ was considered statistically significant. Analyses were also performed separately for boys and girls, and sex-specific prevalence trends were tested (interaction term sex $\times$ study year). Difference by sex in the prevalence of each risk factor and effect modification by sex (interaction term sex $\times$ risk factor) were tested. Statistically significant risk factors for current wheeze in either sex and study year by univariate analysis were included in a multiple logistic regression model, which was thus limited to the skin prick tested children. Risks were approximated by odds ratios with 95% confidence intervals. Data were analysed using the Statistical Package for Social Science (SPSS) software version 11.5 (SPSS Inc., Chicago, IL, USA).

The majority of definitions have been described previously (13, 15, 16, 20). Only definitions with special relevance to this text are explained below.

'Current' condition – symptom/condition present during the last 12 months.

'Lifetime' condition – symptom/condition at present or previously.

'Wheeze before age 7–8 years' – a report of ever wheeze but not current wheeze.

'Physician-diagnosed asthma (allergic rhinitis, eczema)' – 'has the child been diagnosed by a physician as having asthma (allergic rhinitis and eczema)?'

Results

Prevalence trends

From 1996 to 2006, there was no significant increase in the prevalence of current wheeze (11.7–13.0%, $P = 0.128$) when measured in all children (Table 2).

Table 1. Study population: number of invited and participating children by area in 1996 and 2006 respectively

	1996				2006			
	Kiruna	Luleå	Piteå	Total	Kiruna	Luleå	Piteå	Total
Questionnaire								
Invited, <i>n</i>	680	1774	1071	3525	513	1382	809	2704
Participated, <i>n</i>	670	1757	1003	3430	509	1350	726	2585
% of invited	98.5	99.0	93.8	97.3	99.2	97.7	81.6	95.6
% girls	49.6	49.2	48.4		49.7	46.1	48.9	
Skin prick test								
Invited, <i>n</i>	680	1774	–	2454	513	1382	–	1895
Participated, <i>n</i>	617	1531	–	2148	476	1224	–	1700
% of invited	90.7	86.3	–	87.5	92.8	88.6	–	87.5
% girls	49.8	49.4	–		48.9	49.8	–	

Table 2. Prevalence (%) of asthma, airway and allergic symptoms, allergic conditions and allergic sensitization in 1996 and 2006

	1996 <i>n</i> = 3430 % (<i>n</i>)	2006 <i>n</i> = 2585 % (<i>n</i>)	1996 vs 2006 <i>P</i> -value
Current (last 12 months) prevalence (%)			
Current wheeze	11.7 (400)	13.0 (335)	0.128
1–3 episodes last 12 months	6.2 (213)	6.8 (175)	0.382
≥4 episodes last 12 months	3.8 (131)	4.1 (105)	0.631
Sleep-disturbing wheeze	5.1 (176)	5.9 (153)	0.184
Asthma medications	7.1 (242)	8.7 (226)	0.016
Medications or wheeze	12.8 (438)	14.6 (378)	0.038
Rhinitis symptoms	14.0 (479)	15.2 (393)	0.177
Eczema symptoms	27.2 (934)	25.8 (667)	0.215
Lifetime prevalence (%)			
Ever wheeze	21.3 (729)	24.1 (623)	0.009
Wheeze before age 7–8	10.5 (359)	12.3 (318)	0.026
Physician-diagnosed asthma	5.7 (197)	7.4 (191)	0.010
Rhinitis diagnosis	6.5 (223)	7.8 (202)	0.049
Eczema diagnosis	13.4 (461)	15.2 (394)	0.048
Skin prick test (%)			
Allergic sensitization	<i>n</i> = 2148 20.6 (443)	<i>n</i> = 1700 29.9 (508)	<0.001

The prevalence of current wheeze by number of wheezing episodes in the last 12 months was similar in 1996 and 2006 (Fig. 1). The prevalence of current symptoms of allergic rhinitis and eczema was likewise stable.

In contrast to current symptoms of asthma, rhinitis and eczema, physicians' diagnoses of these conditions increased: For asthma from 5.7% to 7.4% ($P = 0.010$), rhinitis ($P = 0.049$) and eczema ($P = 0.048$). Current use of asthma medications increased from 7.1% to 8.7%, $P = 0.016$. There were also statistically significant increases in the lifetime prevalence of ever wheeze (21.3–24.1%, $P = 0.009$) and wheeze before age 7–8, and the prevalence of allergic sensitization increased considerably from 20.6% to 29.9%, $P < 0.001$.

Prevalence trends by sex

Stratification by sex (Table 3) revealed statistically significant increases among boys of current wheeze (12.9–16.4%, $P = 0.007$) and sleep-disturbing wheeze (6.2–8.0%, $P = 0.046$). In girls, these wheezing indices tended to decrease, although not statistically significantly. The increase in current wheeze among boys was confined to 1–3 episodes (6.3–9.1%, $P = 0.004$) whereas in girls, this decreased (6.1–4.3%, $P = 0.036$). These trends in current wheeze and 1–3 episodes of wheeze in the last 12 months were statistically significantly sex dependent, $P = 0.017$ and 0.001 respectively.

Lifetime prevalence, however, did not show this sex-specific pattern (Table 3). Ever wheeze and physician-diagnosed asthma increased in both sexes, although not statistically significant in girls. Wheeze before age 7–8, however, increased by 38% in girls and 4% in boys (interaction term sex $\times$ study year $P = 0.057$). The prevalence of allergic sensitization increased by 45%

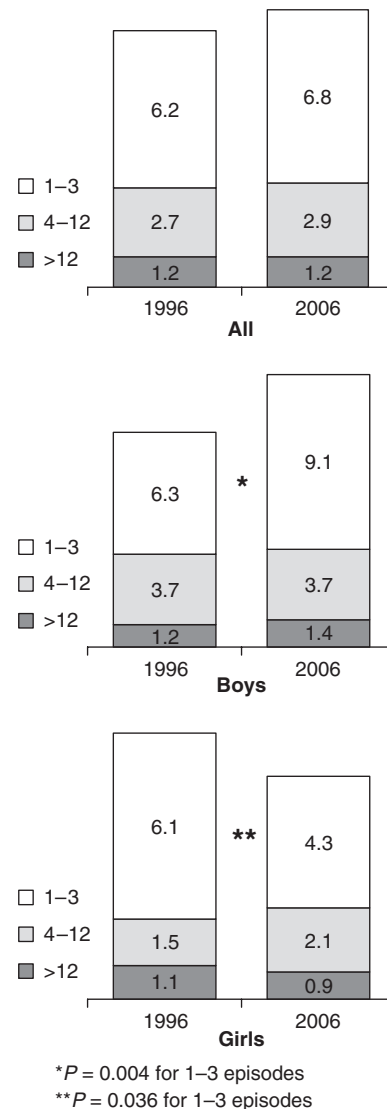


Figure 1. Prevalence of current wheeze by number of wheezing episodes (1–3, 4–12, >12) during the last 12 months in 1996 and 2006.

($P < 0.001$) in both sexes. This increase was not different ($P = 0.819$) between wheezers (40–54%, $P = 0.002$) and nonwheezers (18–26%, $P < 0.001$).

Risk factors for current wheeze

The prevalence and strength of association (Table 4) of several risk factors for current wheeze were studied. In general, the prevalence of having any of the studied risk factors was lower in boys than in girls in 1996 (Table 4, Fig. 2) whereas the opposite was observed in 2006. Figure 2 displays the ratio (boys to girls) in prevalence of each risk factor, in 1996 and 2006. A ratio above one means higher prevalence in boys and vice versa. For every studied risk factor, this ratio increased from 1996 to 2006, meaning that the risk factor prevalence increased in boys

Table 3. Prevalence (%) of asthma, airway symptoms and allergic sensitization by sex in 1996 and 2006, including change (%) and *P*-value 1996 vs 2006

	Boys			Girls		
	1996 <i>n</i> = 1749 % (<i>n</i>)	2006 <i>n</i> = 1333 % (<i>n</i>)	1996 vs 2006 <i>P</i> -value	1996 <i>n</i> = 1681 % (<i>n</i>)	2006 <i>n</i> = 1252 % (<i>n</i>)	1996 vs 2006 <i>P</i> -value
Current (last 12 months) prevalence (%)						
Current wheeze*	12.9 (226)	16.4 (218)	0.007	10.4 (174)	9.3 (117)	0.367
1–3 episodes last 12 months†	6.3 (111)	9.1 (121)	0.004	6.1 (102)	4.3 (54)	0.036
≥4 episodes last 12 months	4.9 (86)	5.1 (68)	0.816	2.7 (45)	3.0 (37)	0.651
Sleep-disturbing wheeze	6.2 (108)	8.0 (107)	0.046	4.0 (68)	3.7 (46)	0.607
Asthma medications	8.1 (141)	10.8 (144)	0.009	6.0 (101)	6.5 (82)	0.549
Medications or wheeze	14.2 (249)	17.9 (238)	0.006	11.2 (189)	11.2 (140)	0.959
Lifetime prevalence (%)						
Ever wheeze	24.2 (423)	28.0 (373)	0.017	18.2 (306)	20.0 (250)	0.228
Wheeze before age 7–8	12.3 (216)	12.8 (171)	0.691	8.5 (143)	11.7 (147)	0.004
Physician-diagnosed asthma	7.1 (124)	9.3 (124)	0.025	4.3 (73)	5.4 (67)	0.205
Skin prick test (%)						
Allergic sensitization	<i>n</i> = 1073 22.3 (239)	<i>n</i> = 858 32.6 (280)	<0.001	<i>n</i> = 1075 19.0 (204)	<i>n</i> = 842 27.1 (228)	<0.001

*Interaction term sex × study year *P* = 0.017.†Interaction term sex × study year *P* = 0.001.

Table 4. Risk factors for current wheeze by sex in 1996 and 2006 respectively; strength of association and risk factor prevalence

	1996				2006			
	OR (95% CI)		Prevalence (%)		OR (95% CI)		Prevalence (%)	
	Boys (<i>n</i> = 932)	Girls (<i>n</i> = 964)	Boys	Girls	Boys (<i>n</i> = 759)	Girls (<i>n</i> = 748)	Boys	Girls
Parental asthma	2.0 (1.3–3.1)	2.5 (1.6–3.9)	16.9	17.5	2.2 (1.4–3.4)	2.1 (1.1–3.6)	25.6	23.1
Birth weight <2500 g	1.9 (0.8–4.4)	2.5 (1.1–5.7)	3.8	4.6	0.5 (0.1–2.1)	1.3 (0.3–4.7)	3.6	3.9
Respiratory infections	2.7 (1.7–4.3)	4.2 (2.4–7.2)	60.0	59.9	4.6 (3.0–7.1)	3.4 (2.2–6.9)	31.0**	26.1
Maternal smoking	1.5 (0.98–2.3)	1.3 (0.9–2.1)	29.8**	33.2	0.9 (0.5–1.6)	1.8 (0.9–3.8)	16.3	15.3
Damp home	1.7 (1.1–2.7)	2.0 (1.2–3.1)	16.5	18.6	1.2 (0.7–2.1)	2.0 (0.97–4.3)	12.3	12.3
Ever cat at home	0.7 (0.4–1.2)	0.6 (0.4–1.1)	28.7**	32.9	1.0 (0.6–1.7)†	0.2 (0.1–0.6)	28.1	29.7
Allergic sensitization	2.9 (1.9–4.5)	3.6 (2.3–5.7)	22.3*	19.0	2.9 (1.9–4.4)	4.3 (2.4–7.5)	32.6**	27.1

All listed factors were included in one multivariate model. Odds ratios (OR) including 95% confidence intervals (CI) are presented (significant associations in bold). The prevalence in boys and girls of each risk factor is presented and prevalence differences by sex were tested.

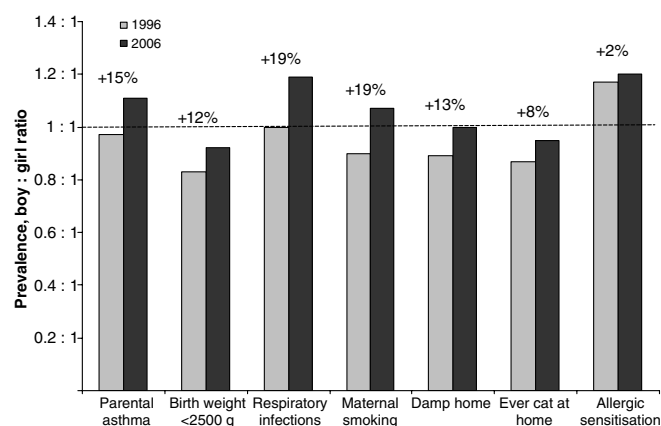
P* < 0.10, *P* < 0.05.†Significant risk interaction by sex, *P* = 0.016.

Figure 2. Boy-to-girl prevalence ratio of risk factors 1996 and 2006, respectively. The prevalence in boys of each risk factor divided by the prevalence in girls is displayed as a ratio, and values above 1 : 1 thus indicate higher prevalence in boys, and vice versa.

compared with girls. The highest ratio increases were seen for respiratory infections and maternal smoking (+19% each), parental asthma (+15%) and living in a damp home (+13%) (Fig. 2).

Respiratory infections was equally prevalent in both sexes in 1996 but significantly more prevalent among boys in 2006, *P* = 0.008 (Table 4). Maternal smoking was more prevalent in girls in 1996 (*P* = 0.034) but not in 2006. Between 1996 and 2006 the nonsignificant inverse association between ever having had a cat in the home and current wheeze disappeared in boys but was strengthened in girls (interaction term sex × ever cat *P* = 0.016).

Discussion

We measured trends in several asthma and allergy indices at age 7–8 from 1996 to 2006. The prevalence of wheezing

indices increased statistically significantly in boys but tended to decrease in girls, resulting in level prevalence trends when measured in all children. Concurrently, the prevalence of risk factors for wheeze increased in boys compared with girls, thus increasing the boy-to-girl ratio in risk factor prevalence. In contrast to the level prevalence of current wheeze, rhinitis and eczema, the prevalence of allergic sensitization increased considerably.

The validity of our results is supported by applying identical methods to two large population-based cohorts with very high participation. The geographical, age and sex distribution was identical in the both cohorts and the study areas were demographically stable including low migration rates (21). Symptoms, physician diagnoses and medication use were studied using a comprehensible and internationally renowned questionnaire, which has been validated clinically in our 1996 cohort (20). Likewise, the skin prick tests have been validated in 1996 (18) and in 2006.

Trends in wheeze and physician-diagnosed asthma

There are little data on prevalence trends in childhood asthma and wheezing from Sweden and other Northern European countries. Aberg et al. demonstrated a doubling in childhood asthma prevalence in Sweden 1979–1991 (17). The global ISAAC phase I–III study is better suited for worldwide comparisons of trends in wheeze, than for in-detail regional studies. The Swedish ISAAC centre did not detect any significant change in current wheeze 1995–2002, but reported only one wheezing outcome, did not stratify by sex and had a 64% response rate (3). We studied several asthma and allergy indices in two large cohorts with high participation rate over 10 years. Our study concludes that no substantial increase in current asthma symptoms occurred 1996–2006 in Swedish 7 to 8-year olds, and this promising finding is in line with the notion that the 'asthma epidemic' has plateaued in parts of the westernized world (23).

In our study the prevalence of physician-diagnosed asthma, allergic rhinitis and eczema increased in contrast to the prevalence of current symptoms of these conditions. The use of asthma medications also increased. This may indicate increased diagnostic activity (12), as previously seen in adults (24). In our study, the ratio of current wheeze to physician-diagnosed asthma was 1.8 in boys both years but decreased in girls (2.4–1.7). Under-diagnosis of asthma in girls has been demonstrated (25), but thus seems to have improved in Northern Sweden. In wheezers only before age 7–8, the proportion with physician-diagnosed asthma increased (14–25%, $P = 0.006$). Hence, increased occurrence and/or awareness of transient preschool-age symptoms contributed to the increase in physician-diagnosed asthma. The increase in wheeze before age 7–8 occurred predominantly in girls ($P = 0.057$) which explains why lifetime wheeze increased in both sexes, with higher symptom persistence in boys.

Sex-specific prevalence trends

The observed level prevalence of current wheeze was attributable to the increased prevalence in boys and a downward trend in girls, a statistically significant difference by sex. Sex-specific trends have been reported previously (9–12). These could in turn contribute to conflicting results in studies within the same region (2, 6, 7), if the sex distributions vary between studies or between the populations in a repeated study. Without our stratification by sex, the increase in prevalence among boys would have been averaged across all children and the findings misinterpreted.

The increased awareness and diagnostic activity may bias prevalence, particularly of mild symptoms and physician diagnoses (6, 26), upwards. In this study, however, several findings support that a real prevalence increase occurred in boys in contrast to girls. The majority of current asthma indices, from mild (1–3 wheezing episodes in the last 12 months) to more severe symptoms (sleep-disturbing wheeze) and asthma medication use, increased in boys. The sex-specific trends in our study increased the boy-to-girl ratio in current wheeze from 1.2 to 1.8, similar to recent observations in Norway and Estonia (10, 27). However, studies in similar age groups conducted during the 1990s in the United Kingdom (9, 11) and Germany (28) oppose these findings. The geographical variations in sex-specific prevalence trends suggest underlying environmental or lifestyle differences between boys and girls. However, until more studies report on sex-specific trends in risk factors similar to this study, this must remain a hypothesis.

Risk factors for current wheeze

Our 10-year perspective points to environmental or lifestyle changes accounting for the prevalence increase in boys. We tested the possibilities of different environmental factors in boys and girls and of sex-specific effects of shared risk factors (29). We studied current wheeze to avoid bias from diagnostic changes (15). In both sexes, the prevalence of maternal smoking and respiratory infections decreased by half, while allergic sensitization and parental asthma increased in prevalence. Importantly, for all studied risk factors, the prevalence decreases were greater in girls and prevalence increases were greater in boys. Although the boy-to-girl ratio change for each risk factor was moderate, the combined effect of all risk factors changing in the same direction should be substantially larger.

Even provided the cross-sectional nature of our study, we believe that the increased boy-to-girl ratio in current wheeze was largely attributable to the increased boy-to-girl ratio in risk factor prevalence. The included risk factors have consistently been shown to associate with wheeze and asthma previously, also in longitudinal studies (14, 19, 30). Male sex is in itself a

predictor of childhood wheeze and seemingly, in 1996 this effect was reduced by relatively lower risk factor prevalence in boys. Ten years later, the boy-to-girl ratio in risk factor prevalence had shifted, increasing the risk in boys, and the prevalence of wheeze had changed accordingly.

Risk factor trends could thus help explaining the diverging sex-specific trends in wheeze observed internationally, however, there are few studies available. A Swiss study found no significant impact of observed trends in potential risk factors (31). However, the prevalence of current wheeze remained constant and the results were not stratified by sex. In Italy, a modest increase in current wheeze could not be explained by the observed risk factor trends (32). However, respiratory infections, allergic sensitization and pet keeping were not studied. We thus encourage other groups to study risk factors in relationship to sex-specific prevalence trends, to elucidate whether these correlate or if essentially new risk factors are introduced.

Symptoms and allergic sensitization

Considering the large increase in sensitization prevalence in both sexes, one would have expected a corresponding increase in wheeze, rhinitis and eczema symptoms. However, the proportion of wheeze attributable to sensitization has a wide geographical variation (33). There are two major implications of the rise in sensitization: First, as persistence (13, 14) and severity of symptoms, lung function and bronchial hyper-responsiveness (34), are all related to allergic sensitization, the clinical picture in wheezers will likely change in our study area. Second, as it seems that the environment of the latter cohort increased the proportion of sensitized children but was less likely to evoke allergy symptoms in those, future study of the 2006 cohort should assess whether those children will develop future symptoms.

Our observations contrast with the findings from Germany and Switzerland where the prevalence of

allergic sensitization was stable 1992–2000 (5, 31), and from Australia where it decreased slightly despite a moderate increase in the prevalence of rhinitis (4). Although differences in sensitization profiles between the studies may have contributed, the increase in sensitization in our study was not limited to a single allergen but rather uniform across the allergen panel, and this was validated by specific IgE (18). The risk factors studied were only weakly associated with sensitization in 1996 (16), but the presence of fewer siblings in our second cohort may have contributed to the increase in sensitization.

In conclusion, symptoms of asthma, allergic rhinitis and eczema did not increase despite an increase in allergic sensitization by 45%. Improved diagnostic activity led to higher prevalence of physician-diagnosed conditions in 2006. Stratification by sex revealed an increase in wheeze among boys and an opposite trend in girls. The prevalence ratio (boys vs girls) of all studied risk factors for wheeze increased, thus providing a plausible explanation for the sex-specific trends in wheeze.

Ethical approval

The ethical committee at the University Hospital of Northern Sweden in Umeå approved the study.

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References

1. Sears M, Beaglehole R. Asthma morbidity and mortality: New Zealand. *J Allergy Clin Immunol* 1987;**80** (3 Pt 2):383–388.
2. Anderson HR, Ruggles R, Strachan DP, Austin JB, Burr M, Jeffs D et al. Trends in prevalence of symptoms of asthma, hay fever, and eczema in 12–14 year olds in the British Isles, 1995–2002: questionnaire survey. *BMJ* 2004;**328**:1052–1053.
3. Asher MI, Montefort S, Björkstén B, Lai CKW, Strachan DP, Weiland SK et al. Worldwide time trends in the prevalence of symptoms of asthma, allergic rhinoconjunctivitis, and eczema in childhood: ISAAC Phases One and Three repeat multicountry cross-sectional surveys. *Lancet* 2006;**368**: 733–743.
4. Toelle BG, Ng Man Kwong G, Belousova E, Salome CM, Peat JK, Marks GB. Prevalence of asthma and allergy in schoolchildren in Belmont, Australia: three cross sectional surveys over 20 years. *BMJ* 2004;**328**:386–387.
5. Zöllner IK, Weiland SK, Piechotowski I, Gabrio T, von Mutius E, Link B et al. No increase in the prevalence of asthma, allergies, and atopic sensitisation among children in Germany: 1992–2001. *Thorax* 2005;**60**:545–548.

6. Ng Man Kwong G, Proctor A, Billings C, Duggan R, Das C, Whyte MK et al. Increasing prevalence of asthma diagnosis and symptoms in children is confined to mild symptoms. *Thorax* 2001; **56**:312–314.
7. Shamssain M. Trends in the prevalence and severity of asthma, rhinitis and atopic eczema in 6- to 7- and 13- to 14-yr-old children from the north-east of England. *Pediatr Allergy Immunol* 2007; **18**:149–153.
8. Grize L, Gassner M, Wuthrich B, Bringolf-Isler B, Takken-Sahli K, Sennhauser FH et al. Trends in prevalence of asthma, allergic rhinitis and atopic dermatitis in 5-7-year old Swiss children from 1992 to 2001. *Allergy* 2006; **61**:556–562.
9. Devenny A, Wassall H, Ninan T, Omran M, Khan SD, Russell G. Respiratory symptoms and atopy in children in Aberdeen: questionnaire studies of a defined school population repeated over 35 years. *BMJ* 2004; **329**: 489–490.
10. Selnes A, Nystad W, Bolle R, Lund E. Diverging prevalence trends of atopic disorders in Norwegian children. Results from three cross-sectional studies. *Allergy* 2005; **60**:894–899.
11. Venn A, Lewis S, Cooper M, Hill J, Britton J. Increasing prevalence of wheeze and asthma in Nottingham primary schoolchildren 1988–1995. *Eur Respir J* 1998; **11**:1324–1328.
12. Anthracopoulos MB, Liolios E, Panagiotakos DB, Triantou K, Priftis KN. Prevalence of asthma among schoolchildren in Patras, Greece: four questionnaire surveys during 1978–2003. *Arch Dis Child* 2007; **92**: 209–212.
13. Bjerg-Bäcklund A, Perzanowski M, Platts-Mills T, Sandström T, Lundbäck B, Rönmark E. Asthma during the primary school ages—prevalence, remission and the impact of allergic sensitization. *Allergy* 2006; **61**: 549–555.
14. Sears MR, Greene JM, Willan AR, Wiecek EM, Taylor DR, Flannery EM et al. A longitudinal, population-based, cohort study of childhood asthma followed to adulthood. *N Engl J Med* 2003; **349**:1414–1422.
15. Asher MI, Keil U, Anderson HR, Beasley R, Crane J, Martinez F et al. International Study of Asthma and Allergies in Childhood (ISAAC): rationale and methods. *Eur Respir J* 1995; **8**:483–491.
16. Rönmark E, Lundbäck B, Jönsson E, Platts-Mills T. Asthma, type-1 allergy and related conditions in 7- and 8-year-old children in Northern Sweden: prevalence rates and risk factor pattern. *Respir Med* 1998; **92**:316–324.
17. Åberg N, Hesselmar B, Åberg B, Eriksson B. Increase of asthma, allergic rhinitis and eczema in Swedish schoolchildren between 1979 and 1991. *Clin Exp Allergy* 1995; **25**:815–819.
18. Rönmark E, Perzanowski M, Platts-Mills T, Lundbäck B. Four-year incidence of allergic sensitization among schoolchildren in a community where allergy to cat and dog dominates sensitization: report from the obstructive lung disease in northern Sweden study group. *J Allergy Clin Immunol* 2003; **112**:747–754.
19. Perzanowski MS, Rönmark E, Platts-Mills TAE, Lundbäck B. Effect of cat and dog ownership on sensitization and development of asthma among preteenage children. *Am J Respir Crit Care Med* 2002; **166**:696–702.
20. Rönmark E, Jönsson E, Platts-Mills T, Lundbäck B. Different pattern of risk factors for atopic and nonatopic asthma among children—report from the Obstructive Lung Disease in Northern Sweden Study. *Allergy* 1999; **54**:926–935.
21. Statistics Sweden's website. 31-01-2009 [cited 02-02-2009]; Available from: <http://www.scb.se>.
22. Dreborg S, Backman E, Basomba A, Bousquet J, Mallin D. Skin tests used in type I allergy testing. Position paper of European Academy of Allergology and Clinical Immunology. *Allergy* 1989; **44**(Suppl. 10):1–59.
23. Eder W, Ege MJ, von Mutius E. The asthma epidemic. *N Engl J Med* 2006; **355**:2226–2235.
24. Chinn S, Jarvis D, Burney P, Luczynska C, Ackermann-Liebrich U, Anto JM et al. Increase in diagnosed asthma but not in symptoms in the European Community Respiratory Health Survey. *Thorax* 2004; **59**:646–651.
25. Siersted HC, Boldsen J, Hansen HS, Mostgaard G, Hyldebrandt N, Rees PJ et al. Population based study of risk factors for underdiagnosis of asthma in adolescence: Odense schoolchild study. *BMJ* 1998; **316**:651–657.
26. Magnus P, Jaakkola J. Secular trend in the occurrence of asthma among children and young adults: critical appraisal of repeated cross sectional surveys. *BMJ* 1997; **314**:1795–1799.
27. Annus T, Riikjäär M-A, Rahu K, Björkstén B. Modest increase in seasonal allergic rhinitis and eczema over 8 years among Estonian schoolchildren. *Allergy* 2005; **16**:315–320.
28. Maziak W, Behrens T, Brasky TM, Duhme H, Rzehak P, Weiland SK et al. Are asthma and allergies in children and adolescents increasing? Results from ISAAC phase I and phase III surveys in Münster, Germany. *Allergy* 2003; **58**: 572–579.
29. Mandhane PJ, Greene JM, Cowan JO, Taylor DR, Sears MR. Sex differences in factors associated with childhood- and adolescent-onset wheeze. *Am J Respir Crit Care Med* 2005; **172**:45–54.
30. Strachan D, Butland B, Anderson H. Incidence and prognosis of asthma and wheezing illness from early childhood to age 33 in a national British cohort. *BMJ* 1996; **312**:1195–1199.
31. Braun-Fahrlander C, Gassner M, Grize L, Takken-Sahli K, Neu U, Stricker T et al. No further increase in asthma, hay fever and atopic sensitisation in adolescents living in Switzerland. *Eur Respir J* 2004; **23**:407–413.
32. Galassi C, De Sario M, Biggeri A, Bisanti L, Chellini E, Ciccone G et al. Changes in prevalence of asthma and allergies among children and adolescents in Italy: 1994–2002. *Pediatrics* 2006; **117**:34–42.
33. Weinmayr G, Weiland SK, Björkstén B, Brunekreef B, Buchele G, Cookson WOC et al. Atopic sensitization and the international variation of asthma symptom prevalence in children. *Am J Respir Crit Care Med* 2007; **176**:565–574.
34. Kurukulaaratchy R, Matthews S, Arshad S. Defining childhood atopic phenotypes to investigate the association of atopic sensitization with allergic disease. *Allergy* 2005; **60**:1280–1286.