

Original article

Are asthma and allergies in children and adolescents increasing? Results from ISAAC phase I and phase III surveys in Münster, Germany

Objective: To assess time trends in symptoms of asthma, allergic rhinitis, and atopic eczema among children in Münster, Germany.

Methods: Two cross-sectional surveys 5-years apart (1994/1995, 1999/2000) using ISAAC core written and video questionnaires and applying the ISAAC protocol. Two main age groups (6–7 and 13–14 year olds) were designated with information collected by parental and self-report for both age groups, respectively. A school-based sample of 7744 participants in the 1994/1995 survey and 7962 participants in the 1999/2000 survey was recruited. In the first and second surveys, response rates for the 6–7 year olds were 81 and 82%, respectively, while for the 13–14 year olds response rates were 94% in both. Analyses focus on the change in 12-month prevalence of symptoms of asthma, rhinitis, and eczema.

Results: There is a tendency towards an increase in current symptoms for all three conditions and in both age groups, but more so among girls. Indices of diagnosis either remained the same or increased in parallel to the increase in symptoms. Indices of severity also showed a homogenous increase in the 5-year study period.

Conclusions: Our study shows that symptoms of asthma, rhinitis, and eczema are increasing, reflecting a change in the morbidity of these conditions in our population.

**W. Maziak¹, T. Behrens¹,
T. M. Brasky², H. Duhme¹, P. Rzehak³,
S. K. Weiland³, U. Keil¹**

¹Institute of Epidemiology and Social Medicine, University of Münster, Germany; ²Department of Epidemiology, School of Public Health and Health Sciences, University of Massachusetts-Amherst, MA, USA; ³Department of Epidemiology, University of Ulm, Ulm, Germany

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Ulrich Keil
Institute of Epidemiology and Social Medicine
University of Münster
Domagkstr. 3, 48129 Münster
Germany

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There is a wide consensus that asthma and allergies are witnessing a rising trend among children especially in western societies (1, 2). In some western countries asthma and allergies have reached alarming proportions, affecting up to one-third of children within the general population (3). Although most of the information about the increase in asthma and allergies come from studies on school children, recent evidence from the UK suggests that wheezing disorders, including viral wheeze, are increasing in preschool children as well, indicating a generalized trend (4). Asthma and allergies rank high on the public health agenda in many countries, highlighting the need for continuous monitoring and assessment of the dynamics of these disorders and factors that influence their trends (5). In Leipzig, Germany, surveys conducted between 1991 and 1996 showed a substantial increase in the prevalence of hay fever and atopic sensitization, but not asthma (6).

While there is general agreement on the increasing trends of asthma and allergies in western countries, a lot of factors can affect our assessment of those trends such as changes in severity, changes in medical care practices,

and changes of diagnostic labelling of these disorders (7, 8). On the other hand, despite extensive research devoted to studying time trends in asthma and allergies, methodological problems, especially those related to comparability and generalizability of research results, still hinder the establishment of a reliable picture about the epidemiology of asthma and allergies worldwide (9, 10). Having such reliable data is instrumental for the generation of valid concepts about possible driving forces, intervention strategies, and for the assessment of costs of asthma and allergies within the society. A considerable amount of effort, therefore, has been devoted in the last decade or so to the development and refinement of standardized, sensitive, and practical survey tools that can be widely applied to measure the burden of, and factors associated with, these disorders in different populations and to allow for reliable assessment of disease trends spatially and secularly (9–11).

The International Study of Asthma and Allergies in Childhood (ISAAC) is one of the pioneer and most comprehensive efforts aiming at the creation of a reliable map on the international trends in asthma and allergies

that will foster better understanding of their patterns as well as hint towards possible etiological factors (12, 13). It is in brief a three-phase multi-centre, multi-national project, with phases I and III involving the conduction of identical surveys at least 5 years apart to look at the spread and time trends in childhood asthma and allergies worldwide (12). To the best of our knowledge, this is the first study within the ISAAC framework to report the time trends in symptoms of asthma, allergic rhinitis, and atopic eczema based on data collected from Phase I (1994/1995) and Phase III (1999/2000) in Münster, Germany.

Methods

Population and data collection

Methods of the international ISAAC and ISAAC Münster projects have been described in detail elsewhere (14, 15). Briefly, this study uses the information collected on two occasions 5 years apart (Phase I 1994/1995, Phase III 1999/2000), using identical methods on symptoms of asthma and allergies in two age groups referred to as 6–7 year olds and 13–14 year olds. A random sample of all schools in the city of Münster was selected, and all pupils in the two grades with the highest proportion of 6–7 and 13–14 year olds were approached. The number of schools participating in the two surveys was 90 and 91 in 1994/1995 and 1999/2000, respectively. The overall number of participants in the first survey was 7744 (3741 in the 6–7-year age group, 4003 in the 13–14-year age group) with response rates of 81 and 94%, for both age groups, respectively, while the overall number of participants in the second survey was 7962 (3830 in the 6–7-year age group, 4132 in the 13–14-year age group) with response rates of 82 and 94%, for both age groups, respectively. Information for the younger age group was collected by parental report, while for the older age group it was collected by self-report (14). Questionnaires used in both groups contained the ISAAC core questions on symptoms of asthma and allergies. During the design period of the ISAAC project, the German version of these questions was piloted and validated among schoolchildren in the city of Bochum (16). In both surveys, information was collected outside the main pollen season and within the same time of the year (August–January).

As recommended by the ISAAC protocol, we used for the 13–14-year-old age group the video questionnaire, which showed five sequences related to asthma symptoms and severity: (i) moderate wheezing at rest; (ii) wheezing and shortness of breath after exercise; (iii) nocturnal wheezing; (iv) nocturnal cough; and (v) severe wheezing and shortness of breath at rest (17, 18). For the two surveys, the Caucasian version of the video questionnaire was used after the written one, whereby participants answered specific questions after viewing each sequence (15, 17, 18).

Outcome measures

Main outcome measures used in this study were 12-month prevalence of symptoms of asthma (current wheeze), allergic rhinitis (current rhinitis), and atopic eczema (current eczema). According to ISAAC phase I and III main modules and consistent with previously published reports from the ISAAC project, these outcome measures were obtained from core questions about the presence of wheezing or whistling in the chest in the past 12 months (17–19), about having a problem with sneezing, or a runny/blocked nose

when the participant did not have a cold or flu in the past 12 months (20), and about the presence of an itchy rash in the last 12 months that affected the skin creases (21). To cover as much as possible the range of presenting symptomatology of childhood asthma, we included in the analyses responses to questions about the presence of exercise-induced wheeze, and about dry cough at night not due to cold or chest infection (14, 17, 18). Information related to lifetime diagnosis of the three disorders were obtained from answers to three questions about ever having had asthma, hay fever, or eczema (14, 17, 18). For the 13–14 year olds, responses to the five video sequences related to 12-month prevalence and severity of asthma symptoms are included in the current analyses.

Severity of asthma symptoms was assessed among children with current wheeze from responses to questions about the number of wheezing attacks in the last 12 months, about sleep disturbance due to wheezing, and about the presence of speech-limiting wheeze in the last 12 months (14, 17, 18). Severity of allergic rhinitis was assessed among children with current rhinitis from the responses to the questions on the presence of accompanying itchy-watery eyes, and about interference with daily activities because of the nose problem. Finally, severity of atopic eczema was assessed based on the response to a question about interference with sleeping because of the itchy rash (14, 17, 18). Consistent with an earlier report from Münster, severity indices were subcategorized into (none) and (any) (15).

Data analysis

Of the 15 706 total participants (phases I and III combined), 128 (0.81%) had missing values for sex or nationality, and could not be included in the analyses. To be able to assess time trends of symptoms of asthma and allergies in a rather homogenous population we opted to restrict our analyses to children with known German nationality. Accordingly, 1009 (6.42%) non-Germans were excluded from the analyses, leaving a total of 14 569 participants for subsequent analyses. A gender/age stratified description of the study participants is found in Table 1. Missing or inconsistent responses were included in the denominator for calculation of prevalence figures while they were excluded from subsequent bivariate analyses in accordance with ISAAC recommendations (19–22). Our prevalence estimates, therefore, are conservative; they are calculated by dividing positive responses to the given question by the total number of completed questionnaires for the corresponding stratum. Analyses were done using SAS 8.02 statistical package. Chi-square (χ^2) tests were done to test for statistical significance in comparisons of proportions between the two surveys, and prevalence odds ratios (POR) and 95% confidence intervals (95% CI) were calculated. To test whether the difference between odds ratios for time trends of different severity levels is significant, a test of homogeneity of the odds ratios was calculated and a resulting *P* value <0.05 was considered significant.

Results

Apart from eczema among 13–14-year-old boys, there was a general increase in current symptoms for all three conditions and in both age groups (Tables 2 and 3). The increase was generally more marked among girls compared to boys for all three conditions and in both age groups (Fig. 1A,B). Indices of severity also showed a general increase in the 5-year study period, with the increase being generally homogenous across all severity

Table 1. Descriptive statistics of the study population*

	1994/1995 survey (phase I)		1999/2000 survey (phase III)	
	N (%)	Mean age $\pm$ SD	N (%)	Mean age $\pm$ SD
6–7-year age group				
Male	1754 (50.6)	6.90 $\pm$ 0.78	1863 (52.8)	6.85 $\pm$ 0.76
Female	1713 (49.4)	6.87 $\pm$ 0.76	1666 (47.2)	6.84 $\pm$ 0.73
Total	3467 (100)	6.88 $\pm$ 0.77	3529 (100)	6.84 $\pm$ 0.75
13–14-year age group				
Male	1865 (49.6)	13.43 $\pm$ 0.93	1894 (49.6)	13.34 $\pm$ 0.84
Female	1892 (50.4)	13.28 $\pm$ 0.89	1922 (50.4)	13.24 $\pm$ 0.94
Total	3757 (100)	13.35 $\pm$ 0.91	3816 (100)	13.29 $\pm$ 0.94

* German nationals with known sex.

Table 2. Time trends of symptoms, severity, and diagnosis of asthma, allergic rhinitis, and atopic eczema among 6–7 year olds* in Münster

	Boys			Girls		
	1994/1995 survey (N = 1754)	1999/2000 survey (N = 1863)	POR** (95% CI)	1994/1995 survey (N = 1713)	1999/2000 survey (N = 1666)	POR (95% CI)
	n (%)	n (%)		n (%)	n (%)	
<i>12-Month prevalence of asthma symptoms</i>						
Wheeze	210 (12.0)	254 (13.6)	1.2 (0.95–1.41)	128 (7.5)	212 (12.7)	1.8 (1.42–2.28)
Night cough	263 (15.0)	303 (16.3)	1.1 (0.91–1.31)	223 (13.0)	257 (15.4)	1.2 (0.99–1.48)
Exercise-induced wheeze	132 (7.5)	146 (7.8)	1.0 (0.80–1.32)	81 (4.7)	100 (6.0)	1.3 (0.93–1.73)
Number of wheeze attacks						
None	38 (2.2)	40 (2.1)	1.0 (0.62–1.59)	17 (1.0)	31 (1.9)	1.9 (1.01–3.57)
Any	167 (9.5)	211 (11.3)	1.2 (0.97–1.51)	105 (6.1)	179 (10.7)	1.8 (1.42–2.38)
Speech-limiting wheeze						
None	150 (8.6)	197 (10.6)	1.3 (1.0–1.59)	111 (6.5)	180 (10.8)	1.8 (1.35–2.25)
Any	55 (3.1)	54 (2.9)	0.9 (0.62–1.37)	14 (0.8)	31 (1.9)	2.3 (1.17–4.55)
Sleep disturbance due to wheeze						
None	90 (5.1)	116 (6.2)	1.2 (0.91–1.64)	52 (3.0)	85 (5.1)	1.7 (1.19–2.47)
Any	111 (6.3)	133 (7.1)	1.1 (0.87–1.49)	69 (4.0)	123 (7.4)	1.9 (1.39–2.60)
<i>Lifetime diagnosis</i>						
Asthma ever	86 (4.9)	96 (5.2)	1.1 (0.77–1.42)	46 (2.7)	60 (3.6)	1.4 (0.90–2.03)
<i>12-Month prevalence of rhinitis symptoms</i>						
Rhinitis	272 (15.5)	337 (18.1)	1.2 (1.01–1.44)	165 (9.6)	241 (14.5)	1.6 (1.29–1.98)
Rhino-conjunctivitis	130 (7.4)	150 (8.0)	1.1 (0.85–1.41)	66 (3.9)	98 (5.9)	1.6 (1.12–2.17)
Interference with daily activities						
None	94 (5.4)	135 (7.2)	1.4 (1.05–1.83)	65 (3.8)	108 (6.5)	1.8 (1.26–2.43)
Any	174 (9.9)	193 (10.4)	1.1 (0.84–1.31)	92 (5.4)	130 (7.8)	1.5 (1.12–1.98)
<i>Lifetime diagnosis</i>						
Hay fever ever	123 (7.0)	137 (7.4)	1.1 (0.81–1.36)	71 (4.1)	74 (4.4)	1.1 (0.76–1.52)
<i>12-Month prevalence of eczema symptoms</i>						
Eczema	128 (7.3)	123 (6.6)	0.9 (0.69–1.17)	114 (6.7)	163 (9.8)	1.5 (1.18–1.97)
Average nights of sleeplessness						
None	87 (5.0)	90 (4.8)	1.0 (0.71–1.33)	68 (4.0)	114 (6.8)	1.8 (1.29–2.45)
Any	38 (2.2)	31 (1.7)	0.8 (0.46–1.26)	45 (2.6)	49 (2.9)	1.1 (0.73–1.73)
<i>Lifetime diagnosis</i>						
Eczema ever	251 (14.3)	253 (13.6)	0.9 (0.77–1.13)	250 (14.6)	282 (16.9)	1.2 (0.99–1.44)

* Parental report. ** Prevalence odds ratio.

levels (Tables 2 and 3). For the 13–14 year olds, responses to the video sequences about 12-month prevalence of symptoms of asthma showed similar time trends as was

observed from the written questionnaires, although on a smaller scale (Table 4). The test of homogeneity of odds ratios was statistically significant only in two subgroups,

Table 3. Time trends of symptoms, severity, and diagnosis of asthma, allergic rhinitis, and atopic eczema among 13–14 year olds* in Münster

	Boys			Girls		
	1994/1995 survey (N = 1865)	1999/2000 survey (N = 1894)	POR (95% CI)	1994/1995 survey (N = 1892)	1999/2000 survey (N = 1922)	POR (95% CI)
	n (%)	n (%)		n (%)	n (%)	
<i>12-Month prevalence of asthma symptoms</i>						
Wheeze	241 (12.9)	288 (15.2)	1.2 (1.0–1.46)	289 (15.3)	378 (19.7)	1.4 (1.15–1.62)
Night cough	303 (16.2)	332 (17.5)	1.1 (0.90–1.28)	451 (23.8)	549 (28.6)	1.3 (1.09–1.47)
Exercise-induced wheeze	359 (19.2)	429 (22.7)	1.2 (1.04–1.44)	441 (23.3)	558 (29.0)	1.3 (1.14–1.54)
Number of wheeze attacks						
None	21 (1.1)	33 (1.7)	1.6 (0.87–2.78)	36 (1.9)	25 (1.3)	0.7 (0.39–1.17)
Any	208 (11.2)	253 (13.4)	1.2 (1.0–1.49)	246 (13.0)	345 (18.0)	1.5** (1.22–1.76)
Speech limiting wheeze						
None	146 (7.8)	170 (9.0)	1.2 (0.92–1.47)	173 (9.1)	209 (10.9)	1.2 (0.97–1.51)
Any	88 (4.7)	111 (5.9)	1.2 (0.93–1.69)	110 (5.8)	165 (8.6)	1.5 (1.17–1.97)
Sleep disturbance due to wheeze						
None	177 (9.5)	220 (11.6)	1.3 (1.01–1.55)	189 (10.0)	249 (13.0)	1.3 (1.09–1.65)
Any	54 (2.9)	63 (3.3)	1.2 (0.78–1.69)	94 (5.0)	121 (6.3)	1.3 (0.97–1.71)
<i>Lifetime diagnosis</i>						
Asthma ever	166 (8.9)	166 (8.8)	1.0 (0.78–1.24)	95 (5.0)	132 (6.9)	1.4 (1.05–1.84)
<i>12-Month prevalence of rhinitis symptoms</i>						
Rhinitis	508 (27.2)	524 (27.7)	1.0 (0.88–1.18)	582 (30.8)	695 (36.2)	1.3 (1.11–1.46)
Rhino-conjunctivitis	248 (13.3)	210 (11.1)	0.8 (0.66–0.99)	298 (15.8)	366 (19.0)	1.3 (1.05–1.49)
Interference with daily activities						
None	204 (10.9)	211 (11.1)	1.0 (0.82–1.25)	258 (13.6)	315 (16.4)	1.2 (1.02–1.46)
Any	258 (13.8)	282 (14.9)	1.1 (0.90–1.30)	262 (13.8)	347 (18.1)	1.4 (1.13–1.61)
<i>Lifetime diagnosis</i>						
Hay fever ever	424 (22.7)	468 (24.7)	1.1 (0.93–1.27)	360 (19.0)	429 (22.3)	1.2 (1.04–1.43)
<i>12-Month prevalence of eczema symptoms</i>						
Eczema	93 (5.0)	85 (4.5)	0.9 (0.66–1.22)	178 (9.4)	214 (11.1)	1.2 (0.98–1.50)
Average nights of sleeplessness						
None	71 (3.8)	49 (2.6)	0.7 (0.46–0.99)	115 (6.1)	132 (6.7)	1.1 (0.87–1.49)
Any	20 (1.1)	32 (1.7)	1.6** (0.88–2.89)	60 (3.2)	81 (4.2)	1.3 (0.94–1.91)
<i>Lifetime diagnosis</i>						
Eczema ever	153 (8.2)	206 (10.9)	1.4 (1.09–1.71)	233 (12.3)	334 (17.4)	1.5 (1.22–1.77)

* Self-report.

** $P < 0.05$ for the difference in odds ratios corresponding to the two levels of severity (none vs any) using the test of homogeneity of the odds ratios.

indicating a greater increase in the higher severity category (any vs none, Table 3). In the younger age group, indices related to lifetime diagnosis (ever asthma, ever hay fever, ever eczema) either remained the same or increased to a lower extent than indices related to current symptoms (Table 2), while in the older age group indices of medical diagnosis either increased in parallel to the increase in symptoms (asthma, rhinitis) or surpassed the increase in symptoms (eczema) (Table 3).

Discussion

With the rigorous application of identical study methods, attainment of high and similar response rates in both surveys and for both age groups, and the use of a large

sample representative of children within the general population, we believe that we have arrived at credible estimates of time trends of the prevalence of symptoms of asthma, allergic rhinitis, and atopic eczema within the studied population. Our data show that there is a general tendency towards an increase in the symptoms of these disorders among children in Münster, remarkably more so among girls than boys.

The two main concerns about questionnaire-based surveys for the epidemiological study of asthma and allergies are the ability of questionnaires to catch the clinical spectrum of the problem of interest, and the liability of questionnaire-gathered information to the change in awareness or diagnostic labelling (23–25). These concerns are particularly relevant for the study of childhood asthma, where presentation can vary across a

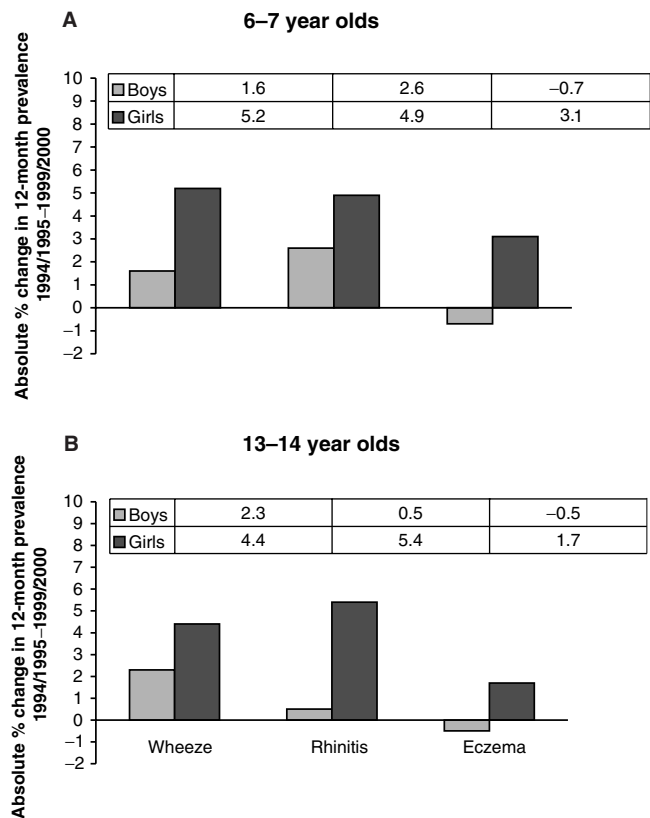


Figure 1. Absolute percentage change in 12-month prevalence of symptoms of asthma, allergic rhinitis, and atopic eczema for boys and girls in both age groups.

considerable range of symptoms and where we have no gold standard against which we can validate our questionnaires (26, 27). Furthermore, increased public attention to asthma in recent years can affect awareness or perception of symptoms, rendering studying time trends troublesome. Indeed, Man Kwong et al. have recently found, using the ISAAC questionnaire, that the increase in 12-month symptoms of asthma among children aged 8–9 years in Sheffield, England, was confined to mild symptoms, arguing for a possible contribution of over-reporting of mild symptoms, as a result of increased awareness, to the increasing trends of asthma in their

population (28). Furthermore, improvement in treatment can affect the severity profile of asthma symptoms, leading to an increase in the reporting of less severe symptoms (28, 29). However, we believe that the overall increase in the three conditions we report here reflects for the most part a genuine increase in their morbidity within the community. First, we focused in our assessment of time trends on the change in symptoms of the three disease entities, which should be less susceptible to change in the diagnostic behaviour of health-care providers. In addition, for most of the studied strata the 5-year increase in current symptoms (12 months) surpassed the increase in indices related to the diagnosis of these conditions, which argues against a change in diagnostic behaviour of physicians as an important contributor to the noticed time trends. Second, the fact that in the case of asthma the 5-year increase of symptoms within each stratum was homogenous for all assessed symptoms, and that in all three conditions the noticed increase in prevalence did not generally show a differential severity profile, rules out the possibility of an important contribution of change in severity or awareness of mild symptoms to the noticed time trends. Finally, for the 13–14 year olds, responses to the written and video questionnaires draw an analogous picture of the general trends towards an increase in asthma symptoms and severity, mostly among girls, giving further support to the validity of our observed trends.

Intriguingly, the most pronounced pattern found in this study was gender-related, with girls having more pronounced increase in the prevalence of symptoms of all three conditions compared to boys. For example, current wheeze among girls in the 6–7-year age group witnessed a 70% relative increase within the 5-year study period compared to only 13% increase for boys in the same age group. This is an important finding that can be overlooked by reporting figures of time trends without stratification by gender (28, 30). The same pattern was also seen for allergic rhinitis and atopic eczema although on a smaller scale for eczema. Venn and colleagues looked at time trends (1988–1995) in asthma among schoolchildren aged 4–11 years in Nottingham, England, and found that the increase in asthma symptoms was greater in girls than in boys (31). Similar gender-related

Table 4. Time trends of 12-month (current) symptoms of asthma among 13–14 year olds from the video questionnaire

	Boys			Girls		
	1994/1995 survey (N = 1865)	1999/2000 survey (N = 1894)	POR (95% CI)	1994/1995 survey (N = 1892)	1999/2000 survey (N = 1922)	POR (95% CI)
	n (%)	n (%)		n (%)	n (%)	
Wheeze while at rest	111 (6.0)	122 (6.4)	1.1 (0.83–1.43)	105 (5.5)	142 (7.4)	1.4 (1.04–1.78)
Wheeze with exercise	238 (12.8)	286 (15.1)	1.2 (1.0–1.46)	380 (20.1)	406 (21.1)	1.1 (0.91–1.25)
Sleep disturbance due to wheeze	72 (3.9)	74 (3.9)	1.0 (0.72–1.43)	69 (3.6)	105 (5.5)	1.5 (1.11–2.12)
Sleep disturbance due to cough	135 (7.2)	174 (9.2)	1.3 (1.02–1.66)	262 (13.8)	378 (19.7)	1.5 (1.27–1.81)
Severe wheeze	84 (4.5)	80 (4.2)	0.9 (0.68–1.30)	72 (3.8)	108 (5.6)	1.5 (1.10–2.07)

trends in the occurrence of asthma and allergies were reported among 7–13-year-old schoolchildren in Norway (32). Generally, the natural history of asthma and allergic rhinitis points towards male predominance in childhood but a female predominance from adolescence onward (25, 33). Considering this natural history, our results show that the noticed gender-related time trend works to mitigate the gender difference in respiratory and nasal symptoms in childhood, while probably augmenting it (towards more female dominance) in adolescent years. Atopic eczema, on the other hand, has a known female predominance and a tendency towards subsiding in adolescence (24). This corresponds with our results, which show that the increase of symptoms of eczema was only noticed among girls in both age groups, but more so in the younger age group. In addition, the described age–gender pattern of atopic eczema explains why among the older age group indices of medical diagnosis, which reflect mostly lifetime morbidity, surpassed those related to current symptoms. It is of note that atopic eczema among boys was the only condition that did not increase within the 5-year interval in both age groups.

Apart from time trends, a comparison of the frequency of asthma symptoms with asthma diagnosis at each point of time (1994/1995 and 1999/2000 surveys) suggests that adolescent girls are less likely to report asthma diagnosis compared to adolescent boys. Similar findings have been reported from 13–14-year-old students in Belgium using the ISAAC questionnaire, where the prevalence of asthma symptoms among girls was higher than among boys while the opposite was true for asthma diagnosis (34). Wieringa et al. suggest that their finding can be due either to under-diagnosis of asthma among girls or under-reporting of symptoms by boys in this age group (34). However, given the homogenous picture arising from comparing all responses between boys and girls, our data suggest that the discrepancy between reporting of symptoms and diagnosis of asthma among adolescent girls is most likely to reflect under-diagnosis of asthma among girls. Evidence from Switzerland and Denmark looking at asthma symptoms and diagnosis among school children suggest that asthma is particularly under-diagnosed among girls (35, 36).

In addition to the concerns mentioned earlier about measuring asthma and allergies in questionnaire-based surveys (9), we ought to remember that although incidence can be inferred from prevalence the cross-sectional design gives no direct information about the incidence of asthma or allergy. Prevalence, in turn, can be influenced by a variety of factors, such as remission, exacerbation, and treatment. However, given the chronic nature of the three studied conditions and the length of the inquiry period (12 months), the calculated estimates reflect to a good extent the morbidity of these conditions within the society at each point in time. In addition, differential recall due to a multitude of disease-related

(i.e. severity) or personal (i.e. socio-economic) factors can influence the quality of gathered information, but this would have minimal effect on the current analyses, since it is unlikely that these factors have changed considerably within 5 years. On the other hand, the use of identical methodology and the full compliance with the strict methodological and quality control measures of the ISAAC study in both surveys make us quite positive about the validity of our assessment and conclusions.

Trying to speculate on the reasons behind the observed time trends however, especially the female predominance, is not a simple task. We recently looked at the smoking habits of adolescents in the same surveys and found that the increase in current smoking was more marked among girls compared to boys (37). Smoking, however, is not likely to be of much importance in explaining the observed gender difference in time trends as it cannot explain the steeper increase in symptoms of asthma and eczema, in the younger age group. Recent evidence has shown that although genetic factors influence susceptibility to sensitization and allergic disease, identical twins show discordance in their expression of atopic symptoms (38). Furthermore, atopy (the propensity to mount IgE-mediated responses to common allergens), which is the strongest risk factor for asthma and allergies, seems to play a minor role in some populations, as studies from Africa and China suggest (39, 40). In a broader sense, there is ample evidence showing that children with more dynamic lifestyles (children in rural areas, more physically active, raised on a farm, in some traditional cultures) seem to be relatively protected from asthma and allergy (41–46). Accordingly, it seems that some environmental influences associated with more traditional lifestyles can confer resistance to the development of allergies even in susceptible individuals, and that the expression of asthma and allergies is governed by a dynamic balance between protective/risk factors at each stage of development. It is plausible, therefore, that, due to a mixture of social and biological factors, girls, especially in western/urban settings, can be more vulnerable to lifestyle factors that will interfere with their ability to develop normal resistance to allergy (47). Indeed, evidence from the two largest studies to date, looking at the effect of siblings on the occurrence of allergy, found a stronger protective effect for brothers than for sisters (48, 49), which can reflect the influence of male siblings (especially older ones) in determining the level of physical activity of his brother/sister as well as their ability to spend more time outdoors. Furthermore, Andrew-Aligne and colleagues have been able to show recently that the higher prevalence of asthma among inner city black children is not due to race or low income per se, but more so due to their living in an urban setting (50), highlighting the importance of the social context within which asthma and allergy develop. Thus, although this view does not give specific mechanisms/answers to the noticed gender-related time trends, it can provide a useful framework for future research looking in depth

into factors influencing different trends of asthma and allergies within the population.

Back to our main question, is the prevalence of asthma and allergies increasing? Recent evidence from children in Italy and adults in Great Britain suggests that the increase in asthma observed in the 1970s and 1980s may be coming to an end (51, 52). We show in this report, however, that symptoms of asthma and allergies in our population continue to show an increasing trend. This trend is likely to reflect a real change in the morbidity of

these conditions within our population as it spans the whole spectrum of symptoms and severity levels.

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