

Original article

Diverging prevalence trends of atopic disorders in Norwegian children. Results from three cross-sectional studies

Background: During the last decades there has been extensive epidemiological research to explore the increasing prevalence of asthma and allergy in childhood. The worldwide variations in prevalence of these diseases necessitate regional reports. Furthermore, time-trend analyses with comparable methods are important in order to monitor the rapidly changing prevalence of these diseases.

Methods: Three cross-sectional questionnaire-based studies of asthma and allergy in schoolchildren were conducted in the counties of Troms and Finnmark, in northern Norway in 1985, 1995 and 2000. The two former studies included children from randomly selected primary schools ($n = 1794/1985$, $n = 1432/1995$). The latter study was a part of ISAAC-II Europe study ($n = 3853$). Identical items of asthma and allergy were employed. The analyses comprised only children 9–11 years of age.

Results: The prevalence of asthma was 9.3, 13.2 and 13.8% in 1985, 1995 and 2000, respectively. However, great gender differences were detected; the prevalence of asthma increased in males from 1995 to 2000, from 14.1 to 17.0%, $RR = 1.2$ (95% CI 1.0–1.5), but decreased in females 1995 to 2000, from 12.3 to 10.5%, $RR = 0.9$ (95% CI 0.7–1.1). Furthermore, in children with asthma, a changing trend was found in the external factors that perceived symptoms, from typical allergens towards other, unspecific agents. The prevalence of self-reported atopic eczema/dermatitis syndrome (AEDS) was 13.4, 21.1 and 20.8% in 1985, 1995 and 2000, respectively. The prevalence of self-reported allergic rhinoconjunctivitis was in 16.5, 24.7 and 29.6% 1985, 1995 and 2000, respectively, RR (2000/1995) = 1.2 (95% CI 1.1–1.3).

Conclusion: The prevalence of asthma in girls has reached a plateau and even decreased from 1995 to 2000 which is in contrast to the asthma prevalence in boys that tends to continuously increase. The prevalence of AEDS which increased substantially between 1985 and 1995 did not change from 1995 to 2000. However, the prevalence of allergic rhinoconjunctivitis increased steadily from 1985, 1995 to 2000.

A. Selnes¹, W. Nystad², R. Bolle³, E. Lund¹

¹Institute of Community Medicine, University of Tromsø, Tromsø; ²Norwegian Institute of Public Health, Oslo; ³University Hospital of Northern Norway, Tromsø, Norway

Key words: allergic rhinoconjunctivitis; asthma; atopic eczema/dermatitis syndrome; schoolchildren; time trends.

Dr Anders Selnes
Aker University Hospital HF
Trondheimsveien 235
N-0514 Oslo
Norway

Accepted for publication 16 November 2004

Epidemiological research on asthma and allergy in children has during the last decades focused on an increasing prevalence observed worldwide (1). Sooner or later this increase may reach a plateau, and only through repeated comparable studies, time trends in childhood asthma and allergy prevalence can be followed. There has been a significant reduction in the prevalence of reported asthma in Melbourne schoolchildren, whereas the prevalence of eczema and allergic rhinitis has continued to increase (2). Although several 10-year follow-up studies concerning this issue are published, only a few studies have a third comparable prevalence measurement made after another 5–10 years time period. Prevalence of asthma and allergy was studied in schoolchildren in Belmont, Australia: three

cross-sectional surveys over 20 years were conducted. The prevalence of hay fever, eczema, atopy, airway hyperresponsiveness or current asthma (defined as recent wheeze plus airway hyperresponsiveness) did not change significantly. These trends were in contrast with the substantial rise in the prevalence of most of these indicators during the period 1982–1992 (3).

We present a time trend study of asthma and allergy prevalence in primary schoolchildren in northern Norway. The present study is based on three separate cross-sectional written questionnaire-based studies orchestrated in 1985, 1995 and 2000. The objectives of this study were to assess whether or not the prevalence of these diseases was continuously increasing during the study period.

Material and methods

Study area

Troms and Finnmark are localized in the subarctic area of Norway north of the polar circle. The population counts 223 000 inhabitants and the counties covers an area of 75 000 km². Around 57% of the population live in regional centres whereas 43% live in sparsely populated districts along the coastline. Although some live in a dry inland climate, the majority of people live in a coastal humid climate.

Studies

The questionnaire employed in the 1985 and 1995 studies. In 1985, a written, four-paged questionnaire was formulated by Bolle and Holt to assess the frequency of asthma and allergy among schoolchildren in northern Norway (4–6). The questionnaire targeted the subjects' childhood asthma, allergic rhinoconjunctivitis (AR) and atopic eczema/dermatitis syndrome (AEDS) and the symptoms associated with these conditions. In the questionnaire, two core questions concerning asthma were employed; 'Has the child ever had asthma?' and 'Does the child experience wheeze, periods with cough or attacks with shortness of breath (asthma) caused by external factors?' A clinical validation estimated the test–retest reliability (κ) to be 0.91 when these two questions were combined (and/or) as a definition of asthma (7). A letter accompanying the questionnaire broadened the descriptions of symptoms and signs of the diseases under investigation.

The 1985 study. In 1985, this questionnaire was distributed with the accompanying letter to schoolchildren aged 7–13 attending primary schools ($n = 11\ 200$). The schools were randomly selected within the three northernmost counties of Norway, i.e. Nordland, Troms and Finnmark. The local school nurse was in charge of the distribution of the questionnaire to the pupils. The questionnaire was filled in at home by the parents. Before delivery, a teacher controlled that all fields were filled in.

The 1995 study. The 1995 study was designed as a 10-year follow-up to the study conducted in 1985. Questions concerning symptoms and diseases the last 12 months were added to the questionnaire described above, which otherwise was identical. Similarly to the 1985 study, the questionnaire was distributed with the accompanying letter to the pupils in randomly selected primary schools in the three northernmost counties of Norway ($n = 9950$). Overall, an identical procedure to the one utilized in the 1985 study (and described above) was followed.

The 2000 (ISAAC) study. The 2000 study was part of an ISAAC-II Europe study. All 9–11 years old children in the counties of Troms and Finnmark were invited to participate. The study was arranged according to standard ISAAC procedures (8–12).

Comparability between the 1985, 1995 and 2000 study. In order to ensure comparability between the three studies, these steps were taken: (i) from the 1985 and 1995 studies, only children in third to fourth level (9–11 years) from Troms and Finnmark were included (ii) in the 2000 study, identical core questions from the Bolle/Holt questionnaire were added to the ISAAC questionnaire.

Variables compared between the 1985, 1995 and 2000 studies

The study is based on parental reports of asthma, allergic rhinoconjunctivitis (AR) and AEDS. Two core questions concerning

asthma (mentioned above) were employed; 'Has the child ever had asthma?' and 'Does the child experience wheeze, periods with cough or attacks with shortness of breath (asthma) caused by external factors?'. The first question is referred to as 'self-reported asthma', and the latter is referred to as 'asthma symptoms'. Affirmative answers to the questions 'Has the child ever had hay fever?' or 'Does the child experience periods with complaints from nose and/or eyes like a runny nose, nose stuffiness, sneezing, itchy nose/eyes swelling around eyes, red eyes?' were recorded as AR. AEDS was recorded in the cases of an itchy eruption lasting for more than 4 weeks combined with (i) lesions in face, elbow- or knee flexures or (ii) high degree of itching and lesions elsewhere. In the cases of missing answers to core questions, the answer was assumed to be non-affirmative (no disease/symptoms).

Handling of missing values. Missing values to the question 'Has the child ever had asthma?' was found in 2.2% in 1985, 1.0% in 1995 and 8.2% in 2000. Missing values to the question 'Wheeze, periods with cough or attacks with shortness of breath (asthma) caused by external factors?' was found in 4.8% in 1985, 3.7% in 1995 and 18.1% in 2000. By means of reducing the high percentage of missing answers to the asthma core questions in the 2000 study, this step was taken; in these cases we projected the answers to an additional question concerning asthma only present in the ISAAC questionnaire: 'Has the child ever had one of the following diseases: asthma, hay fever, adverse reactions to food, other kind of allergic reactions?'. If asthma was confirmed or denied in this question, the same value was applied to the asthma core questions. The missing in the 2000 study was thereby reduced to 0.5 % ($n = 20$).

Analyses

The comparison between the three studies was made by measurements of relative risk (RR) 1995/1985 and 2000/1995. These RR estimates were (alternatively to *P*-value) accompanied by a 95% confidence interval (95%CI) of the RRs and handled by Cochran–Mantel–Haenszel statistics based on table scores. Linear regression and trend analysis was only preferred in situations of probable linearity. The statistics were taken care of by SAS software package (13). All studies were based on informed consent from the child's parents. The studies were approved by the Ethical Committee in North-Norway and the Norwegian Data Inspectorate.

Results

The main results are presented in Tables 1–3.

Asthma

Overall, the prevalence of self-reported asthma increased from 1985 to 2000. On the contrary, the prevalence of self-reported asthma symptoms increased from 1985 to 1995 but decreased between 1995 and 2000. When the two questions were combined (self-reported asthma and/or asthma symptoms), the prevalence of asthma increased from 1985 to 2000. However, great gender differences were detected concerning asthma; in males, asthma prevalence increased more between 1995 and 2000 than it did between 1985 and 1995. In contrast, in females the prevalence of self-reported asthma was unchanged from 1995 to 2000.

Table 1. The prevalence of asthma, allergic rhinoconjunctivitis (AR) and atopic eczema/dermatitis syndrome (AEDS) in the studies from 1985, 1995 and 2000. Differences in prevalence between 1995/1985 and 2000/1995 are quantified with relative risk (RR) and corresponding 95% confidence interval (95% CI)

	Prevalence (%)						
	Study			1995/1985		2000/1995	
	1985 (n = 1794)	1995 (n = 1432)	2000 (n = 3853)	RR	95% CI	RR	95% CI
Response rate (%)	>90	87	80				
Gender distribution (male/female ratio)	1.0	1.0	1.0				
Asthma							
Self-reported asthma (1)	6.7	8.8	10.2	1.31	1.03–1.67	1.16	0.95–1.40
Wheeze, periods with cough or attacks with shortness of breath (asthma) caused by external factors? (2)	7.2	10.5	10.3	1.46	1.17–1.83	0.98	0.82–1.17
Asthma question (1) and/or (2)	9.3	13.2	13.8	1.42	1.17–1.73	1.04	0.89–1.22
Self-reported allergic rhinoconjunctivitis	16.5	24.7	29.6	1.49	1.30–1.72	1.20	1.08–1.33
Self-reported atopic eczema/dermatitis syndrome	13.4	21.1	20.8	1.57	1.35–1.83	0.99	0.88–1.11

Table 2. The prevalence of asthma, allergic rhinoconjunctivitis (AR) and atopic eczema/dermatitis syndrome (AEDS) in the studies from 1985, 1995 and 2000. Differences in prevalence between 1995/1985 and 2000/1995 are quantified with relative risk (RR) and corresponding 95% confidence interval (95% CI) (males)

	Prevalence (%)						
	Study			1995/1985		2000/1995	
	1985 (n = 1794)	1995 (n = 1432)	2000 (n = 3853)	RR	95% CI	RR	95% CI
Males							
Asthma							
Self-reported asthma (1)	8.9	10.0	12.7	1.13	0.83–1.53	1.27	0.99–1.63
Wheeze, periods with cough or attacks with shortness of breath (asthma) caused by external factors? (2)	10.1	10.6	12.5	1.05	0.78–1.40	1.18	0.93–1.51
Asthma question (1) and/or (2)	12.4	14.1	17.0	1.13	0.88–1.46	1.20	0.98–1.48
Self-reported allergic rhinoconjunctivitis	18.5	27.2	32.2	1.47	1.23–1.76	1.18	1.03–1.36
Self-reported atopic eczema/dermatitis syndrome	12.7	18.2	18.2	1.44	1.14–1.81	1.00	0.83–1.20

Table 3. The prevalence of asthma, allergic rhinoconjunctivitis (AR) and atopic eczema/dermatitis syndrome (AEDS) in the studies from 1985, 1995 and 2000. Differences in prevalence between 1995/1985 and 2000/1995 are quantified with relative risk (RR) and corresponding 95% confidence interval (95% CI) (females)

	Prevalence (%)						
	Study			1995/1985		2000/1995	
	1985 (n = 1794)	1995 (n = 1432)	2000 (n = 3853)	RR	95% CI	RR	95% CI
Females							
Asthma							
Self-reported asthma (1)	4.4	7.6	7.6	1.71	1.15–2.55	1.00	0.74–1.35
Wheeze, periods with cough or attacks with shortness of breath (asthma) caused by external factors? (2)	4.2	10.5	8.1	2.49	1.71–3.65	0.77	0.59–1.00
Asthma question (1) and/or (2)	6.0	12.3	10.5	2.04	1.47–2.82	0.86	0.68–1.08
Self-reported allergic rhinoconjunctivitis	14.5	22.1	27.0	1.53	1.24–1.89	1.22	1.04–1.42
Self-reported atopic eczema/dermatitis syndrome	14.2	23.9	23.5	1.68	1.37–2.07	0.98	0.84–1.14

The prevalence decreased from 1995 to 2000 when asthma was defined by the combination of both core questions.

In children with asthma, we investigated with trend analysis which external factor(s) that made the children perceive symptoms (Table 4); there was a decreasing tendency of reporting grass pollen as a trigger of asthma

attacks from 1985 to 2000 and an opposite, increasing trend for reporting other (and unspecific) factors. Again gender differences were apparent; in females these trends were more predominant with additionally animal dander decreasingly notified as a causative factor to perceive asthma symptoms.

Table 4. External factors which made the asthmatic children ($n = 674$) perceive asthma symptoms (see text). Time trend is given in per cent change in frequency by year Δ (%), statistical significance tested by probability (P -value)

	All					Males					Females				
	Study			Time trend		Study			Time trend		Study			Time trend	
	1985 ($n = 128$)	1995 ($n = 151$)	2000 ($n = 395$)	Δ (%)	P -value	1985 ($n = 91$)	1995 ($n = 75$)	2000 ($n = 241$)	Δ (%)	P -value	1985 ($n = 37$)	1995 ($n = 76$)	2000 ($n = 154$)	Δ (%)	P -value
Animal dander	50.0	50.1	43.5	-0.47	0.16	45.1	45.3	45.6	0.03	0.92	62.2	56.6	40.3	-1.61	<0.01
Grass pollen	49.2	38.4	33.9	-1.02	<0.01	48.4	41.3	36.5	-0.79	<0.05	51.4	35.5	29.9	-1.41	<0.05
Infections	23.4	26.5	27.3	0.26	0.39	25.3	21.3	26.6	0.10	0.77	18.9	31.6	28.6	0.05	0.32
Weather	28.1	26.5	29.9	0.14	0.66	28.6	22.7	30.7	0.02	0.65	27.0	30.3	28.6	0.01	0.90
Food	7.0	15.2	12.4	0.33	0.14	4.4	14.7	13.3	0.58	<0.05	13.5	15.8	11.0	-0.23	0.57
Other factors	14.1	23.2	30.4	1.10	<0.01	13.2	21.3	29.5	1.10	<0.01	16.2	25.0	31.8	1.07	<0.05

Allergic rhinoconjunctivitis and atopic eczema/dermatitis syndrome

The prevalence of self-reported AR increased steadily in the studies from 1985, 1995 and 2000. Unlike asthma, the increase in self-reported AR showed no gender differences. The prevalence of self-reported AEDS increased substantially from 1985 to 1995, but no further prevalence changes were observed from 1995 to 2000. Again, no gender differences were apparent concerning prevalence changes in self-reported AEDS.

Discussion

According to this study of 9–11 years old schoolchildren from northern Norway, somewhat new and surprising trends have occurred in the context of prevalence of atopic disorders. In spite that the asthma prevalence in boys tends to continuously increase over the 15 years studied from 1985 to 2000, the prevalence of asthma in girls has reached a plateau and has even decreased from 1995 to 2000. Moreover, the prevalence of AEDS which increased substantially between 1985 and 1995 did not change from 1995 to 2000. However, the prevalence of allergic rhinoconjunctivitis increased continuously among schoolchildren in northern Norway in these cross-sectional studies from 1985, 1995 to 2000.

The increasing prevalence of asthma and AEDS is considered a major worldwide health problem (14, 15). Several epidemiological studies on the prevalence of asthma and allergy in childhood are orchestrated in our region from the beginning of the 1980s to date (7, 12, 16–25). According to the Norwegian lifetime prevalence studies, both AEDS and AR continued to increase during the period 1981–1995 (4, 7, 16). On the contrary, a review of these studies showed that the prevalence of asthma culminated in the beginning of the 1990s after an increase in the 1980s. Furthermore, recent published studies have shown a stabilization of the prevalence rates of allergic diseases among primary school children other than allergic rhinitis (26, 27). The prevalence of asthma and AEDS has even showed declining trends in children from

the first half of the nineties (28–30). The rate of hospitalizations for asthma is on the decline or low and stable in children aged 3 years or older in a study from 1984 to 2000 in Rogaland, Norway (31). No increase in hospital admission due to asthma was detected in schoolchildren in Oslo during 1980–1995 (32).

Nevertheless, despite the interesting and encouraging changes to AEDS and asthma prevalence, we did find that the prevalence of AR, which above of all is associated with IgE-mediated allergy, is continuously increasing. Obviously, these differences in prevalence changes between asthma, AR and AEDS in our study are not easy to explain. Atopy and atopic disorders arise from a multifactor origin with an interaction between environment and genetics (33). It is hypothesized that the increased prevalence of asthma and allergy is connected to the wealth increase and a higher prevalence is found in rich families (34). The differences in prevalence rate in 1985, 1995 and 2000 we observe in our study may reflect the changes in standard of living in Norway the last decades; similarly to other industrialized countries, the socioeconomic conditions in Norway improved greatly in the 1960s and 1970s, but reached a plateau in the 1980s. Consequently, as AEDS and asthma occur earlier in life, it is expected that the prevalence of AEDS and asthma will first culminate, and later this will also be the case with AR. On the contrary, the differences between asthma, AEDS and AR in prevalence changes over time may also reflect a better understanding in public in avoidance of offending allergens; Whereas (typical) allergens connected to asthma and AEDS are in part possible to avoid (animal dander/food), the allergens typically causing AR (pollen) are however impossible to avoid. The causative factor when the children perceive asthma symptoms have over the 15 years studied transitioned from traditional allergens to other and unspecific external factors, which may reflect that asthmatics today are a more heterogenic group than 'yesterdays' asthmatics. This observation that especially girls with asthma to a lesser extent experience symptoms due to allergens in 2000 than in 1985, may point towards a changing expression of asthma. However, the great difference between girls and boys observed

in asthma trends from 1995 to 2000 does not favour an environmental or public opinion (avoidance) explanation to the changes. Yet, physical activity can possibly lay behind the expression 'other factors' when asthma symptoms are perceived. We do know that children are increasingly inactive and that asthmatic symptoms are associated with physical activity in children with increased body mass index (35–37).

Although the Bolle/Holt-asthma-questionnaire has been validated and the combination of the two core questions provides a high sensitivity and specificity (0.96 and 0.88, respectively) (7), systematic bias concerning the asthma label must be expected in a cross-sectional, written questionnaire-based design that is employed in these studies. We have no information neither if the children suffer a mild, moderate or severe asthma, nor do we know about the use of antiasthmatic medication. Furthermore, in a cross-sectional setting, it is impossible to do judgement about causality. This is especially true in case of the finding of the trend changes in asthma symptoms due to allergens and 'other factors'. We do not know if these changes are due to increasing knowledge about allergy and allergens in families with allergies (and hence avoidance) or if the population of asthmatic children over the 15 years studied has transitioned in direction of a greater percentage of children with mild, 'intrinsic' asthma.

The prevalence of asthma is difficult to follow over time owing to changes in diagnostic practice and information bias may explain the trends (38). There is a methodological difference between the two former and the latest (ISAAC) study that is a potential source of bias. The ISAAC questionnaire was more profound with multiple questions and the core questions employed in this study did not have the same central position like in the two former studies. This may be an explanation to the differences in missing answers to core questions. Additionally, the response rate has been declining during our study period. An interpretation may be decreasing motivation in the public to participate in such epidemi-

ological studies. A lack of motivation may also be partly responsible to the high rate of missing data to the asthma questions in the 2000 (ISAAC) study. However, some of the missing data can be explained by uncertainties by the responders, an expression of doubt whether the child is asthmatic or not. Lastly, the trend of falling response rate from 1985 to 2000 must inevitable decrease the reliability of the latter studies.

The high rate of missing responses to the asthma core questions in the 2000 (ISAAC) study could potentially be handled by three ways; by excluding the missing data from analysis, by employing an interpretation that the missing data represents no disease and hence can be treated as such, and lastly, by applying the additional asthma-question available in the ISAAC questionnaire and subsequently reduce the number of missing. In our opinion, excluding all subjects with missing responses to the asthma core question would result in serious misinterpretation of the asthma prevalence in the 2000 (ISAAC) study and lead to a false high prevalence. Epidemiological studies on prevalence of disease in persons who do not complete questionnaires have shown that this mode of response implies no disease (Professor Eiliv Lund, personal communication). In cases of missing answers to core questions we therefore could had chosen to interpret these values as nonaffirmative in order to avoid false over reporting. However, we choose the third and applied the additional asthma-question available in the ISAAC questionnaire and thereby reduced the high rate of missing without obvious misinterpretation of the data and the results.

We conclude that the prevalence of childhood asthma shows diverging trends in northern Norway; although it tends to increase in boys, the prevalence has ceased in girls from 1995 to 2000. Furthermore, our study indicates that after a substantial increase in the prevalence of AEDS from 1985 to 1995, no further increase has occurred from 1995 to 2000. However, the prevalence of allergic rhinoconjunctivitis has been continuously increasing over the 15 years studied.

References

1. Nga NN, Chai SK, Bihn TT, Redding G, Takaro T, Checkoway H et al. ISAAC-based asthma and atopic symptoms among Ha Noi school children. *Pediatr Allergy Immunol* 2003;**14**:272–279.
2. Robertson CF, Roberts MF, Kappers JH. Asthma prevalence in Melbourne schoolchildren: have we reached the peak? *Med J Aust* 2004;**180**:273–276.
3. Toelle BG, Ng K, 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.
4. Selnes A, Bolle R, Holt J, Lund E. Cumulative incidence of asthma and allergy in north-Norwegian schoolchildren in 1985 and 1995. *Pediatr Allergy Immunol* 2002;**13**:58–63.
5. Selnes A, Bolle R, Holt J, Lund E. Atopic diseases in Sami and Norse schoolchildren living in northern Norway. *Pediatr Allergy Immunol* 1999;**10**:216–220.
6. Selnes A, Odland JO, Bolle R, Holt J, Dotterud LK, Lund E. Asthma and allergy in Russian and Norwegian schoolchildren: results from two questionnaire-based studies in the Kola Peninsula, Russia, and northern Norway. *Allergy* 2001; **56**:344–348.

7. Steen-Johnsen J, Bolle R, Holt J, Benan K, Magnus P. Impact of pollution and place of residence on atopic diseases among schoolchildren in Telemark County, Norway. *Pediatr Allergy Immunol* 1995;**6**:192–199.
8. 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.
9. Worldwide variations in the prevalence of asthma symptoms: the International Study of Asthma and Allergies in Childhood (ISAAC) *Eur Respir J* 1998;**12**:315–335.
10. Asher MI, Weiland SK. The International Study of Asthma and Allergies in Childhood (ISAAC). ISAAC Steering Committee. *Clin Exp Allergy* 1998;**28**(Suppl. 5):52–66.
11. Strachan D, Sibbald B, Weiland S, Ait-Khaled N, Anabwani G, Anderson HR et al. Worldwide variations in prevalence of symptoms of allergic rhinoconjunctivitis in children: the International Study of Asthma and Allergies in Childhood (ISAAC). *Pediatr Allergy Immunol* 1997;**8**:161–176.
12. Worldwide variation in prevalence of symptoms of asthma, allergic rhinoconjunctivitis, and atopic eczema: ISAAC. The International Study of Asthma and Allergies in Childhood (ISAAC) Steering Committee. *Lancet* 1998;**351**:1225–1232.
13. SAS INSTITUTE. SAS/STAT guide for personal computers. Cary, NC (USA): SAS Institute, 1992.
14. Masoli M, Fabian D, Holt S, Beasley R. The global burden of asthma: executive summary of the GINA Dissemination Committee report. *Allergy* 2004;**59**:469–478.
15. Leung DY, Bieber T. Atopic dermatitis. *Lancet* 2003;**361**:151–160.
16. Nystad W, Magnus P, Gulsvik A, Skarpaas IJ, Carlsen KH. Changing prevalence of asthma in school children: evidence for diagnostic changes in asthma in two surveys 13 yrs apart. *Eur Respir J* 1997;**10**:1046–1051.
17. Braback L, Appelberg J, Jansson U, Kalvesten L. Changes in prevalence and severity of asthma among schoolchildren in a Swedish district between 1985 and 1995. *Acta Paediatr* 2000;**89**:465–470.
18. Ulrik CS, von Linstow ML, Backer V. Prevalence and predictors of rhinitis in Danish children and adolescents. *Allergy* 2000;**55**:1019–1024.
19. Forsberg B, Pekkanen J, Clench-Aas J, Martensson MB, Stjernberg N, Barto-nova A et al. Childhood asthma in four regions in Scandinavia: risk factors and avoidance effects. *Int J Epidemiol* 1997;**26**:610–619.
20. Nystad W, Magnus P, Roksund O, Svidal B, Hetlevik O. The prevalence of respiratory symptoms and asthma among school children in three different areas of Norway. *Pediatr Allergy Immunol* 1997;**8**:35–40.
21. Bjorksten B, Dumitrescu D, Foucard T, Kheturiani N, Khaitov R, Leja M et al. Prevalence of childhood asthma, rhinitis and eczema in Scandinavia and Eastern Europe. *Eur Respir J* 1998;**12**:432–437.
22. Mortz CG, Lauritsen JM, Bindeslev-Jensen C, Andersen KE. Prevalence of atopic dermatitis, asthma, allergic rhinitis, and hand and contact dermatitis in adolescents. The Odense Adolescence Cohort Study on Atopic Diseases and Dermatitis. *Br J Dermatol* 2001;**144**:523–532.
23. Lindbaek M, Wefring KW, Grangard EH, Ovsthus K. Socioeconomical conditions as risk factors for bronchial asthma in children aged 4–5 yrs. *Eur Respir J* 2003;**21**:105–108.
24. Ronmark E, Perzanowski M, Platts-Mills T, Lundback B. Incidence rates and risk factors for asthma among school children: a 2-year follow-up report from the obstructive lung disease in Northern Sweden (OLIN) studies. *Respir Med* 2002;**96**:1006–1013.
25. Ronmark E, Perzanowski M, Platts-Mills T, Lundback B. Different sensitization profile for asthma, rhinitis, and eczema among 7–8-year-old children: report from the Obstructive Lung Disease in Northern Sweden studies. *Pediatr Allergy Immunol* 2003;**14**:91–99.
26. Kalyoncu AF, Selcuk ZT, Enunlu T, Demir AU, Coplu L, Sahin AA et al. Prevalence of asthma and allergic diseases in primary school children in Ankara, Turkey: two cross-sectional studies, five years apart. *Pediatr Allergy Immunol* 1999;**10**:261–265.
27. Lee SL, Wong W, Lau YL. Increasing prevalence of allergic rhinitis but not asthma among children in Hong Kong from 1995 to 2001 (Phase 3 International Study of Asthma and Allergies in Childhood). *Pediatr Allergy Immunol* 2004;**15**:72–78.
28. Camelo-Nunes IC, Wandalsen GF, Melo KC, Naspitz CK, Sole D. Prevalence of atopic eczema and associated symptoms in school children. *J Pediatr (Rio J)* 2004;**80**:60–64.
29. Wang XS, Tan TN, Shek LP, Chng SY, Hia CP, Ong NB et al. The prevalence of asthma and allergies in Singapore; data from two ISAAC surveys seven years apart. *Arch Dis Child* 2004;**89**:423–426.
30. Sunderland RS, Fleming DM. Continuing decline in acute asthma episodes in the community. *Arch Dis Child* 2004;**89**:282–285.
31. Engelsen DH, Oymar K. Hospital admissions for childhood asthma in Rogaland, Norway, from 1984 to 2000. *Acta Paediatr* 2003;**92**:610–616.
32. Jonasson G, Lodrup Carlsen KC, Leegaard J, Carlsen KH, Mowinkel P, Halvorsen KS. Trends in hospital admissions for childhood asthma in Oslo, Norway, 1980–95. *Allergy* 2000;**55**:232–239.
33. Klucken H, Wienker T, Bieber T. Atopic eczema/dermatitis syndrome – a genetically complex disease. New advances in discovering the genetic contribution. *Allergy* 2003;**58**:5–12.
34. Schafer T, Ruhdorfer S, Weigl L, Wessner D, Heinrich J, Wichmann HE et al. School education and allergic sensitization in adults. *Allergy* 2001;**56**:1206–1210.
35. Nystad W, Nafstad P, Harris JR. Physical activity affects the prevalence of reported wheeze. *Eur J Epidemiol* 2001;**17**:209–212.
36. Nystad W, Stigum H, Carlsen KH. Increased level of bronchial responsiveness in inactive children with asthma. *Respir Med* 2001;**95**:806–810.
37. Nystad W, Meyer HE, Nafstad P, Tverdal A, Engeland A. Body mass index in relation to adult asthma among 135,000 Norwegian men and women. *Am J Epidemiol* 2004;**160**:969–976.
38. Magnus P, Jaakkola JJ. Secular trend in the occurrence of asthma among children and young adults: critical appraisal of repeated cross sectional surveys. *BMJ* 1997;**314**:1795–1799.