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Decreasing prevalence of atopic dermatitis in Swedish schoolchildren: three repeated population-based surveys

Maja af Klinteberg,[1] Anna Winberg,[2] Martin Andersson,[3] Eva Rönmark[3] and Linnea Hedman[3]

[1]Department of Public Health and Clinical Medicine, Dermatology and Venereology, Umeå University, Umeå, Sweden; [2]Department of Clinical Sciences, Pediatrics, Umeå University, Umeå, Sweden; and [3]Department of Public Health and Clinical Medicine, Section of Sustainable Health, The OLIN Unit, Umeå University, Umeå, Sweden

Correspondence Maja af Klinteberg. Email: maja.af.klinteberg@umu.se

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Abstract

Background The prevalence of atopic dermatitis (AD) has increased over several decades and now affects about one-fifth of all children in high-income countries (HICs). While the increase continues in lower-income countries, the prevalence of AD might have reached a plateau in HICs.

Objectives To investigate trends in the prevalence of AD and atopic comorbidity in schoolchildren in Sweden.

Methods The study population consisted of three cohorts of children (median age 8 years) in Norrbotten, Sweden, for 1996 ($n=3430$), 2006 ($n=2585$) and 2017 ($n=2785$). An identical questionnaire that included questions from the International Study of Asthma and Allergies in Childhood (ISAAC) protocol was used in all three cohorts. Trends in AD prevalence were estimated, as well as trends in atopic comorbidity. AD prevalence was estimated both according to the ISAAC definition of AD and by adding the reported diagnosis by a physician (D-AD).

Results The prevalence of AD decreased in the last decade, from 22.8% (1996) and 21.3% (2006) to 16.3% (2017; $P<0.001$). The prevalence of D-AD was lower, but the same pattern of decrease was seen, from 9.3% (1996) and 9.4% (2006) to 5.7% (2017; $P<0.001$). In all three cohorts, AD was more common among girls than boys (18.9% vs. 13.8% in 2017; $P<0.001$). Children from the mountain inlands had a higher prevalence of AD than children from coastal cities (22.0% vs. 15.1% in 2017; $P<0.001$). In comparing D-AD, there were no significant differences between the sexes or between inland or coastal living. Concomitant asthma increased over the years from 12.2% (1996) to 15.8% (2006) to 23.0% (2017; $P<0.001$). Concomitant allergic rhinitis and allergic sensitization increased from 1996 (15.0% and 27.5%) to 2006 (24.7% and 49.5%) but then levelled off until 2017 (21.0% and 46.7%).

Conclusions The prevalence of AD among schoolchildren in Sweden decreased over the study period, whereas atopic comorbidity among children with AD increased. Although a decrease was seen, AD is still common and the increase in atopic comorbidity among children with AD, especially the increase in asthma, is concerning.

What is already known about this topic?

- Atopic dermatitis (AD) is a common chronic skin disorder, affecting about one-fifth of all children.
- The prevalence of AD has previously increased but may have reached a plateau in high-income countries.
- There are few recent studies on trends in the prevalence of AD in children.

What does this study add?

- This study provides current data on the prevalence of AD in Swedish children, as well as a time trend of prevalence over 20 years.
- It also provides prevalence and trends in atopic comorbidity.
- The study reports a decrease in the prevalence of AD and an increase in atopic comorbidity.

Atopic dermatitis (AD) is a common chronic dermatological disorder among children, causing a substantial burden of disease on the affected population.[1–4] Symptoms of AD consists of dry skin and recurrent itchy rashes with a distribution that is typically age related, where the flexural areas of the arms and legs are common areas of involvement in preadolescents.[4,5] AD most commonly starts in early childhood, often before the age of 2 years, and at this young age the

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eczema is sometimes more diffusely spread, involving the face, trunk and extensor areas of the limbs.[4,6,7]

Numerous studies have shown an increase in prevalence of AD in children over the last few decades; the current prevalence rate of AD in developed countries is estimated to be around 20%.[1,3,8–11] However, this increase in prevalence has recently levelled-off in several high-income countries. It has been suggested that the prevalence of AD has reached a plateau in these countries but that it continues to increase in lower-income countries.[4,11]

In clinical practice, the diagnosis of AD is often based on the UK Working Party or Hanifin and Raijka criteria.[12,13] However, in larger epidemiological studies, survey-based criteria for the diagnosis of AD are more feasible. The International Study of Asthma and Allergies in Childhood (ISAAC) items are widely used to estimate the prevalence of AD based on participants' reports.[3,10,14]

In children with AD there is a high comorbidity with asthma and allergic rhinitis, and the strength of the association increases with AD severity.[15–18] There is also an association between allergic sensitization and AD; however, far from all patients with AD have elevated allergen specific IgE measured in serum or (indirectly) by a skin prick test (SPT). It has previously been estimated that around two-thirds of patients with AD lack evidence of allergic sensitization.[19]

In this study we investigated time trends in the prevalence of AD in 8-year-old children in northern Sweden over a period of 21 years. We also investigated comorbidity with asthma, allergic rhinitis and allergic sensitization over time.

Materials and methods

Study area and sample

Three cohorts with 7–8-year-old children were recruited within the Obstructive Lung Disease in Northern Sweden (OLIN) studies, a large research programme for studies on obstructive airway diseases and allergy. In the municipalities of Kiruna, Piteå and Luleå, in the northernmost part of Sweden, all schoolchildren in the first and second grade were invited to participate in the study. Piteå and Luleå are situated in the coastal area of the Baltic Sea, whereas Kiruna is situated in the mountain inlands. The study design was identical in the three cohorts and is described in previous publications.[20–22] The children's parents completed a questionnaire. Response rates were 97% ($n=3430$) in 1996, 96% ($n=2585$) in 2006 and 91% ($n=2785$) in 2017. The median age was 8 years in all three cohorts. Forty-nine per cent ($n=1681$) of participants in 1996, 48.4% ($n=1252$) in 2006 and 48.3% ($n=1346$) in 2017 were female. The proportion reported living in a country outside Sweden in their first years of life was 2.7% ($n=91$) in 1996, 1.7% ($n=45$) in 2006 and 3.8% ($n=106$) in 2017.

Questionnaire

The questionnaire included the core questions about asthma, rhinitis and AD from ISAAC.[14] Additional questions about possible risk factors, heredity, physician diagnosis and medication for the above-mentioned diagnoses were included. The questions were identical for all three cohorts.

Skin prick test

All children in Kiruna and Luleå were invited to have a SPT with 10 common airborne allergens. A mean wheal of ≥ 3 mm was considered a positive reaction and defined as allergic sensitization. The testing procedure followed the recommendations of the European Academy of Allergology and Clinical Immunology. Allergic sensitization was defined as a positive test to any of the tested allergens specified in Table 2.

Definitions

AD was defined by answering 'yes' to all the three questions in the ISAAC questionnaire: 'Has the child ever had an itchy rash which was coming and going for at least 6 months?'; 'Has the child had this itchy rash at any time in the last 12 months?'; and 'Has this itchy rash at any time affected any of the following places: the folds of the elbows, behind the knees, in front of the ankles, under the buttocks, or around the neck, ears or eyes?'

Diagnosed atopic dermatitis
Diagnosed AD (D-AD) fulfilled the criteria for AD above and reported a physician diagnosed eczema by answering 'yes' to the question 'Has the child been diagnosed with eczema by a physician?'

Persistent rash
Has this rash cleared completely at any time during the last 12 months?

Physician-diagnosed asthma
Has the child been diagnosed as having asthma by a physician?

Ever asthma
Has the child ever had asthma? Any report of asthma was defined by answering 'yes' to either one or both of the two preceding questions.

Ever hay fever
Has the child ever had hay fever?

Physician-diagnosed allergic rhinitis
Has the child been diagnosed as having hay fever or allergic rhinitis by a physician? Any report of allergic rhinitis was defined by answering 'yes' to either one or both two preceding questions.

Atopic comorbidity
Any report of asthma or any report of allergic rhinitis as defined above.

Statistical analyses

SPSS version 28.0 (IBM, Armonk, NY, USA) was used for all statistical analyses. The level of significance was set at a *P*-value of <0.05. Missing answers to individual questions were regarded as negative responses. To compare groups, χ^2 tests were used for comparisons of proportions, and the Mantel–Haenszel test was used for to test for a linear trend. ANOVA was used for the comparison of means between the three groups.

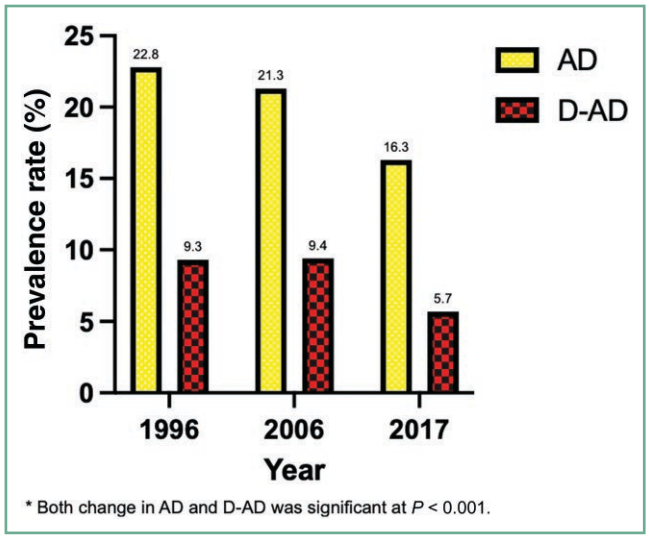

Figure 1 Change in prevalence of atopic dermatitis (AD) and in prevalence of AD with a reported physician diagnosis of AD (D-AD).

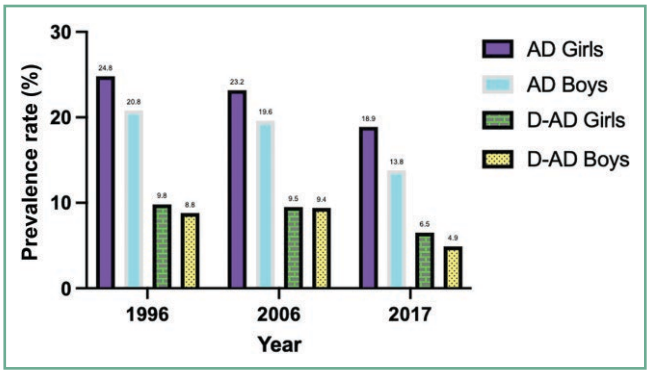

Figure 2 Change in prevalence of atopic dermatitis (AD) and AD with a physician diagnosis (D-AD), by sex.

Results

Prevalence trends for atopic dermatitis

The prevalence rate of reported AD among the children was 22.8% ($n=781$) in the 1996 cohort, 21.3% ($n=551$) in the 2006 cohort and 16.3% ($n=453$) in 2017 cohort (Figure 1). This decreasing trend was statistically significant ($P<0.001$). Also, D-AD decreased over the years [9.3% ($n=318$) in 1996, 9.4% ($n=244$) in 2006 and 5.7% ($n=159$) in 2017; $P<0.001$].

AD was more common in girls than in boys in all three cohorts, a significant difference of 24.8% vs. 20.8% in 1996 ($P=0.005$), 23.2% vs. 19.6% in 2006 ($P=0.03$) and 18.9% vs. 13.8% in 2017 ($P<0.001$; Figure 2). However, as shown in Figure 2, the difference between boys and girls in prevalence of D-AD was less pronounced and was not statistically significant in any of the cohorts.

Comparing the prevalence of AD among the children from the coastal cities of Luleå and Piteå, with that of the children from Kiruna in the mountain inlands, the children in Kiruna had a significantly higher prevalence of AD (Figure 3). However, when comparing the prevalence of D-AD between inland and coastal areas, no statistically significant difference was found.

Symptoms, treatment and diagnosis

Among the study participants with AD, fewer than half presented with AD symptoms before the age of 2 years. Early symptom debut was less frequent in 2017 (Table 1). In the cohort for 1996, early symptom debut was more common among boys than among girls. No other significant difference by sex was seen in AD symptoms or treatment, but a tendency toward more frequent sleep disturbance caused by itchy rash was found in boys (Table 1). Disturbance of sleep at least one night per week was more common in all cohorts of children with AD and atopic comorbidity than in those without (38.1% vs. 22.9%; $P<0.001$). Disturbance of sleep due to itchy rash at least one night a week peaked in 2006 (prevalence rate of 32.8% in participants with AD) but was lower in 2017 (29.1%; Table 1). In all three cohorts, sleep disturbance was significantly more common among children with D-AD compared with those with AD [31.8% vs. 15.8% (1996); 41.0% vs. 26.4% (2006); 42.8% vs. 21.8% (2017); all $P<0.001$]. About one-fifth of participants with AD had a persistent rash.

Treatment with topical corticosteroids (TCS) increased significantly from 1996 to 2006 and 2017, where the 2006 cohort had the highest rate of TCS use (Table 1). Among those with D-AD, a similar proportion in the three cohorts reported use of TCS in the last 12 months (89.3% in 1996, 88.1% in 2006 and 90.6% in 2017). There were no significant differences when comparing children with AD from the mountain inlands with children with AD from the coastal area with respect to age of symptom debut, sleep disturbance, persistent rash or use of TCS. Among all children with AD, fewer than half reported a diagnosis of AD by a physician, with the lowest prevalence rate reported by the most recent cohort [40.7% (1996), 44.3% (2006), 35.1% (2017); $P=0.01$].

Trends in atopic comorbidity

The proportions of comorbidity of asthma, allergic rhinitis and allergic sensitization to airborne allergens are presented

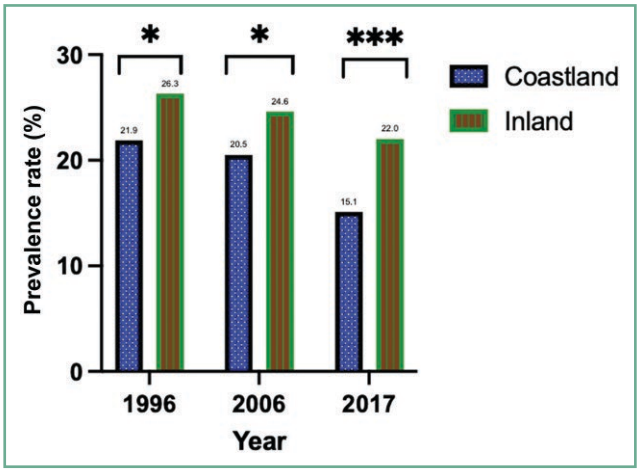

Figure 3 Prevalence of atopic dermatitis among children living near the coast vs. those living the mountain inland areas. *$P=0.02$, **$P=0.05$, ***$P<0.001$.

Table 1 Symptoms, treatment and reported diagnosis among those with atopic dermatitis (AD) in 1996, 2006 and 2017

	1996			Difference by sex	2006			Difference by sex	2017			Difference by sex	Difference by year
	All with AD ($n=781$), %	Male ($n=364$),%	Female ($n=417$), %	*P*-value[a]	All with AD ($n=551$), %	Male ($n=261$), %	Female ($n=290$), %	*P*-value[a]	All with AD ($n=453$), %	Male ($n=198$), %	Female ($n=255$), %	*P*-value[a]	*P*-value[a]
Symptom debut at < 2 years of age	44.4	48.6	40.8	**0.03**	47.4	46.4	48.3	0.65	38.6	36.9	40.0	0.50	**0.02**
Persistent rash in last 12 months	20.6	22.8	18.6	0.15	20.3	18.9	21.6	0.44	19.6	18.3	20.6	0.53	0.92
Disturbed sleep ≥ 1 night a week in last 12 months due to itchy rash	22.3	23.4	21.3	0.50	32.8	36.0	30.0	0.13	29.1	33.3	25.9	0.08	< **0.001**
Use of TCS in last 12 months	62.7	65.1	60.7	0.20	73.1	73.9	72.4	0.68	70.6	71.2	70.2	0.69	**0.001**
Physician-diagnosed AD	40.7	42.3	39.3	0.40	44.3	47.9	41.0	0.12	35.1	35.9	34.5	0.77	**0.01**

Bold denotes statistical significance. TCS, topical corticosteroids. [a]χ^2 test.

in Table 2. The comorbidity of asthma among the children with AD steadily increased over the last two decades. About 1 in 10 of the children with AD in 1996 also had asthma vs. almost 1 in 5 in 2017. In all three cohorts, asthma comorbidity was more common in boys than in girls (Table 2).

In children with AD, comorbidity with allergic rhinitis and allergic sensitization to airborne allergens increased during the study period, although they both peaked in 2006. In 2017, 21.0% of children with AD also had allergic rhinitis, while almost half of them were sensitized to at least one aeroallergen (Table 2). Comorbidity with allergic rhinitis was approximately twice as common in boys than in girls in 1996 and again in 2017, but in 2006 there were no significant differences according to sex. Compared with girls, boys with AD had a higher prevalence of allergic sensitization on SPT in 1996 but not in 2006 and 2017 (Table 2).

The prevalence of atopic comorbidity and/or allergic sensitization among the children with AD increased between the three surveys from 36.2% (1996) to 56.3% in 2006 and 58.4% in 2017 ($P<0.001$). There was a stable prevalence rate in combined comorbidity of allergic rhinitis and asthma in children with AD: 5.9% in 1996, 7.4% in 2006 and 7.7% in 2017 ($P=0.37$). Comorbidity overlap of AD, asthma and allergic rhinitis is provided in Figure 4.

Discussion

In this population-based study of three cohorts of 8-year-old children from the same geographical area, recruited 10 years apart, we found that the prevalence of self-reported AD decreased between 1996, 2006 and 2017, while atopic comorbidity increased.

The prevalence of AD has previously increased in Europe, and studies of trends in prevalence have been encouraged.[10,23] In our study, the prevalence rate of AD remained unchanged between 1996 and 2006, but there was a decrease between 2006 and 2017. It has previously been suggested that a plateau might have been reached in developed countries.[4] In a large study from the USA, the prevalence of AD increased from 1997 to 2011 but remained at about the same level in 2018.[24] Although the increase in AD seems to have levelled off, about 1 in 5 schoolchildren are affected by AD, making it a common paediatric disease.[3,25]

The prevalence of D-AD has previously been reported from other countries,[3] but – to our knowledge – our study is the first Swedish study to provide estimated prevalence trends of both D-AD and reported AD. Among our study participants with AD, only around 40% reported a physician diagnosis of AD. It has previously been found that D-AD reflects a group of children with moderate-to-severe AD.[3] In accordance with this, most of the children with D-AD in our study used TCS. Children with D-AD also reported more frequent disturbance of sleep than children with AD and no physician diagnosis. Disturbance of sleep at least one night a week because of an itchy rash has been suggested as an indicator of a moderate-to-severe AD, as children with mild AD more seldom have a sleep-disturbing itch.[18,26]

Our study showed a lower prevalence rate of AD (16.3%) and D-AD (5.7%) among the children in the 2017 cohort vs. the overall AD and D-AD prevalence rates reported from other countries, and especially compared with other

Table 2 Comorbidity in those with atopic dermatitis (AD) in 1996, 2006 and 2017

	1996				2006				2017				
	All (*n*=781), %	**Male (*n*=364), %**	**Female (*n*=417), %**	**Difference by sex *P*-value[a]**	**All (*n*=551), %**	**Male (*n*=261), %**	**Female (*n*=290), %**	**Difference by sex *P*-value[a]**	**All (*n*=453), %**	**Male (*n*=198), %**	**Female (*n*=255), %**	**Difference by sex *P*-value[a]**	**Difference by year *P*-value[a]**
Physician-diagnosed asthma	10.5	13.7	7.7	**0.01**	12.3	15.7	9.3	**0.02**	18.1	25.3	12.5	**< 0.001**	**< 0.001**
Ever asthma	11.5	14.0	9.4	**0.04**	15.4	19.9	11.4	**0.01**	22.1	27.8	17.6	**0.01**	**< 0.001**
Any report of asthma[b]	12.2	15.1	9.6	**0.02**	15.8	20.7	11.4	**0.003**	23.0	29.3	18.0	**0.01**	**< 0.001**
Physician-diagnosed allergic rhinitis	11.5	15.1	8.4	**0.003**	16.9	17.2	16.6	0.83	11.5	14.1	9.4	0.117	**0.008**
Ever hay fever	10.6	15.4	6.5	**< 0.001**	20.1	20.7	19.7	0.76	18.3	25.8	12.5	**< 0.001**	**< 0.001**
Any report of allergic rhinitis[c]	15.0	20.6	10.1	**< 0.001**	24.7	24.5	24.8	0.93	21.0	27.8	15.7	**0.002**	**< 0.001**
Any atopic comorbidity[d]	21.3	28.6	14.9	**< 0.001**	33.0	36.4	30.0	0.11	36.2	47.0	27.8	**< 0.001**	**< 0.001**
Any allergic sensitization[e]	27.5	32.1	23.4	**0.02**	49.5	51.6	47.5	0.42	46.7	49.3	47.5	0.39	**< 0.001**
Birch	12.8	14.5	11.0	0.18	25.9	28.8	23.2	0.21	21.7	26.6	17.6	0.06	**< 0.001**
Timothy grass	8.7	13.3	4.7	**< 0.001**	18.3	20.1	16.7	0.38	21.7	26.6	17.6	0.06	**< 0.001**
Mug wort	1.1	1.1	1.0	0.88	4.5	4.9	4.0	0.69	3.5	4.2	3.0	0.55	**0.004**
Cat	19.9	23.0	16.8	0.06	31.7	33.2	30.3	0.55	29.7	37.3	23.4	**0.007**	**< 0.001**
Horse	10.5	14.8	6.7	**0.002**	17.1	17.5	16.8	0.85	14.1	19.1	10.0	**0.02**	**0.01**
Dog	13.7	16.2	11.4	0.10	28.5	33.7	23.7	**0.03**	26.3	33.1	20.6	**0.01**	**< 0.001**
Any mite[f]	1.6	2.7	0.7	0.06	2.4	4.4	0.5	**0.01**	3.0	2.2	3.6	0.47	0.42
Any mould[g]	2.5	4.3	1.0	**0.02**	4.5	7.7	1.5	**0.004**	3.9	5.1	3.0	0.35	0.24
Allergic sensitization or atopic comorbidity[h]	36.2	42.3	30.8	**0.005**	56.3	59.8	53.0	0.18	58.4	64.6	53.2	**0.04**	**< 0.001**

Bold denotes statistical significance. [a]χ^2 test. [b]Reported physician-diagnosed asthma and/or reported ever asthma. [c]Reported physician-diagnosed allergic rhinitis or reported hay fever. [d]Any report of asthma or allergic rhinitis. [e]Allergic sensitization in any of the allergens in skin prick test (SPT). Among patients with AD, 563 (299 females, 264 male), 382 (198 females, 184 males) and 313 (170 females, 143 males) participated in SPTs in 1996, 2006 and 2017, respectively. [f]Mites: *Dermatophagoides pteronyssinus* and *Dermatophagoides farinae*. [g]Moulds: *Cladosporium* sp. and *Alternaria* sp. [h]Any atopic comorbidity and/or any allergic sensitization.

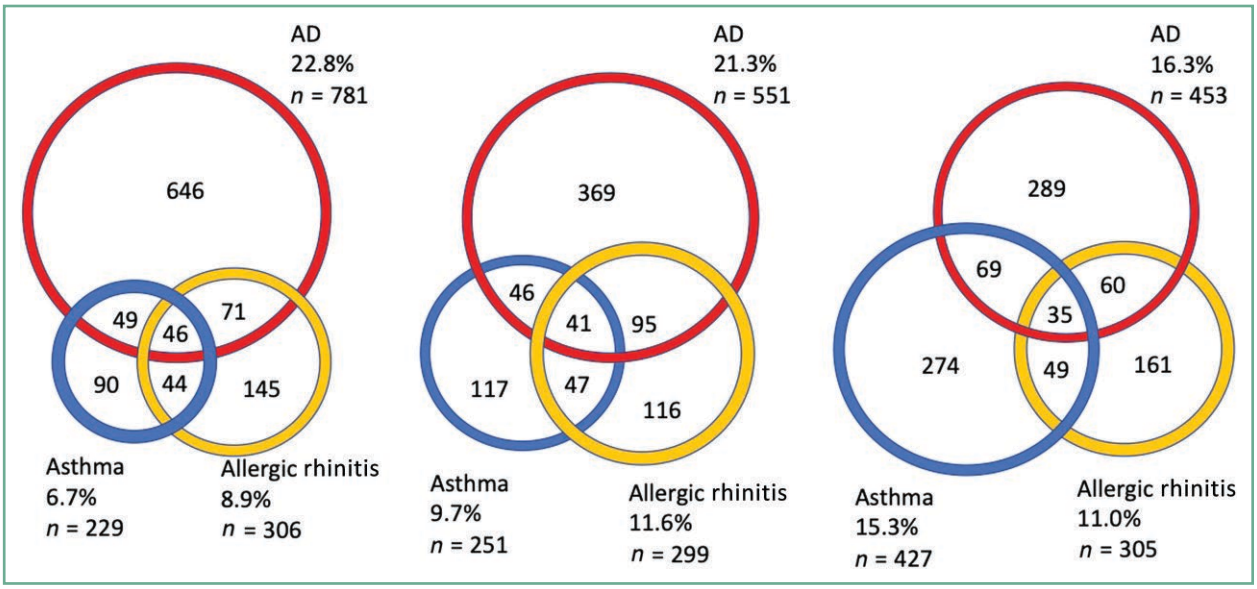

Figure 4 Atopic dermatitis (AD) comorbidity overlap with asthma and allergic rhinitis over 20 years among 8-year-old children.

European countries.[3] In a recent international multicentre study, a D-AD prevalence rate of 13.0% was found among children of similar age (6–12 years) to those who participated in our study. In this study, which involved many countries worldwide, Germany had the lowest prevalence among participating European countries, with a D-AD prevalence rate of 9.3%, whereas Italy had the highest prevalence rate (19.5%). Investigating AD according to ISAAC only, the prevalence rate ranged from 11.6% (Israel) to 41.9% (Italy).[3] In a meta-analysis of studies of AD in the Arctic region, the 1-year prevalence rate of AD was estimated to be 19%.[27] However, this meta-analysis also included studies from the twentieth century.

According to previous studies, a cold and dry climate is considered to be a risk factor for AD.[28] Our study population lives in the most northern part of Sweden, Norrbotten, a large district that constitutes about a quarter of the total area of Sweden. The district includes different climate zones. Among children living in Kiruna, located in the mountain inlands north of the Arctic Circle, the prevalence of AD was higher than among the children living near the coast. This is in contrast to a previous Swedish study that compared the prevalence of eczema in children living in Kiruna and Gothenburg in the south of Sweden, which found no geographical difference in the prevalence of AD.[29] Although we found that symptoms of AD were more common among children from the inland area, these children did not have a higher prevalence of physician-diagnosed AD than children living in the coastal area. It is possible that there are more children with milder symptoms of AD living in the mountain inland area. However, no significant differences were found in the use of TCS, disturbance of sleep or reports of persistent rash when comparing children with AD from these areas. Another explanation could be that care-seeking is less frequent in people from the mountain inland areas, possibly due to longer distances to healthcare centres or a lack of specialized care.

We have previously shown an increase in allergic sensitization among 8-year-old children, from 21% in 1996 to 30% in 2006,[20] but the prevalence rate remained at 30% in 2017.[22] Among children with AD in our study, the prevalence rate of sensitization followed the same pattern, from 28% in 1996 to 50% in 2006, plateauing at about half the population in 2017. The prevalence of asthma among children with AD steadily increased over the years, almost doubling from 1996 to 2017. This has also been seen in other studies, and possible explanations include better awareness, changes in asthma treatment routines and the availability of diagnostic tools.[30–34] An increase is the prevalence of asthma was also seen in children without AD (Figure 4). Therefore, the increase in comorbidity could reflect an increase in asthma in general. It is possible that the decrease seen in the prevalence of AD could be explained by earlier treatment, prevention and self-resolution in early childhood. However, this needs to be further investigated. In our study, the prevalence of allergic rhinitis in children with AD appeared to have reached a plateau, which has also been seen in other studies.[22,35,36] Any type of atopic comorbidity increased from 21% in 1996 to 36% in 2017. As asthma, allergic rhinitis and AD all negatively affect quality of life and sleep in both the children and their families, this is a concerning development.[1,15,37–39] Therefore, trends in the prevalence of atopic comorbidity need further study.

In line with other findings,[18,40] AD was more common among girls than boys. However, there was no difference according to sex in the prevalence of D-AD. Among our study participants with AD, atopic comorbidity was more common in boys than in girls. A comorbidity with asthma was about twice as common among boys; similar results were seen for comorbidity with allergic rhinitis. As eczema is often diagnosed by a physician during healthcare visits for other atopic diseases like asthma, the higher prevalence of atopic comorbidity among boys could be a possible explanation for the absence of significant differences according to sex in D-AD. Previous studies have also shown that comorbid asthma and allergic rhinitis are associated with more severe AD.[18,41] In accordance, children with AD and comorbid asthma or allergic rhinitis in our study reported

significantly higher disturbance of sleep due to eczema. Boys with AD had a tendency toward more frequent disturbances of sleep, although this difference was not statistically significant.

Strengths of this study are that it included a large sample size and that the response rates were high. The three surveys were performed with age-equivalent study populations, in the same geographical areas and with identical methods, enabling reliable data on time trends in prevalence. As the study included self-reported data using parental questionnaires, there could be a potential risk of recall or reporting bias. Although AD is a clinical diagnosis where a physician's examination is the gold standard,[4] in larger, population-based studies it is reasonable to use a questionnaire to estimate prevalence. Comparison of prevalence rates between studies can be difficult because different definitions of AD are used in different studies.[10] Using the criteria for diagnosing AD based on the ISAAC questionnaire is a strength as the ISAAC questions are well validated and commonly used in larger studies, facilitating the comparison of prevalence rates between populations and countries.[3,11,25,42–45]

In conclusion, this study found a decreasing trend in prevalence of AD among 8-year-old schoolchildren in the northernmost county of Sweden. The decrease was seen in the last cohort, whereas a plateau seemed to be reached between the two preceding surveys. We also found an increasing trend in atopic comorbidity with asthma and allergic rhinitis, and a high prevalence of allergic sensitization among children with AD in the two most recent cohorts. Although this study showed a decrease in prevalence, AD is still common and has a substantial impact on affected children. The decreasing prevalence of AD and increasing prevalence of atopic comorbidity among schoolchildren in northern Sweden calls for further studies investigating possible risk factors and protective factors in the development of AD.

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Conflicts of interest

A.W. reports consulting fees from Danone Nutricia Sweden for scientific lectures outside the submitted work. The other authors declare no conflicts of interest.

Data availability

The data underlying this study are available from the authors upon reasonable request and after a confidentiality evaluation.

Ethics statement

Ethical approval was given for the research project by The Swedish Ethical Review Authority. The parents of all children provided written informed consent for their child to participate.

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