

The clinical expression of asthma in schoolchildren has changed between 1996 and 2006

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Several studies have reported diverging trends in the prevalence of asthma and wheeze. The aim of this study was to investigate the clinical expression of childhood asthma in 1996 and 2006 by studying asthma morbidity, treatment, and environmental exposures in school children with physician-diagnosed asthma and wheeze, respectively. All children enrolled in first or second grade (7–8 yr-old) in three municipalities in northern Sweden were invited to a questionnaire study in 1996 and 2006, respectively. In 1996, 3430 (97%) participated; and in 2006, 2585 (96%) participated. The same parental completed questionnaire, including the ISAAC questions, was used in both surveys. Physician-diagnosed asthma was reported at 5.7% in 1996 and 7.4% in 2006. A significantly greater proportion of children with asthma were using inhaled corticosteroids (ICS) in 2006, 67% vs. 55% in 1996. This increase was parallel to a major decrease in severe asthma symptoms such as disturbed sleep because of wheeze (49% vs. 38%) and troublesome asthma (21% vs. 11%). The prevalence of current wheeze among the asthmatics decreased significantly; however, this was seen only among children not using ICS. Parental smoking decreased significantly as did the proportion living in damp buildings. In conclusion, although asthma remains a major public health issue in school age children, children with asthma had less respiratory symptoms and a better asthma control in 2006 compared to 1996. This parallels with an increase in treatment with ICS, more beneficial environmental conditions, and an increased diagnostic intensity resulting in a larger proportion of children with mild symptoms being diagnosed as having asthma.

**Martin Andersson^{1,2}, Anders Bjerg^{2,3},
Bertil Forsberg¹, Bo Lundbäck^{2,4}
and Eva Rönmark^{1,2}**

¹Department of Public Health and Clinical Medicine, Occupational and Environmental Medicine, Umeå University, Umeå, Sweden, ²The OLIN Studies, Department of Medicine, Sunderby Hospital, Norrbotten, Luleå, Sweden, ³Department of Public Health and Clinical Medicine, Respiratory Medicine and Allergy, Umeå University, Umeå, Sweden, ⁴Department of Internal Medicine/Krefting Research Centre, Institute of Medicine, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden

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Eva Rönmark, The OLIN Studies, Department of Medicine, Sunderby Hospital, Norrbotten, S-97180 Luleå, Sweden
Tel.: +46 70 5424431
Fax: +46 920 230843
E-mail: Eva.Ronmark@nll.se

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The prevalence of asthma has increased worldwide since the middle of the 20th century (1); and today, approximately 300 million people are affected (2). In the Western world, the increase in asthma, most prominent in children and young adults, has made the disease a major public health concern. Aside the obvious risks of hospitalization and fatal outcomes of severe asthma, the disease may also cause disturbed sleep and restrict daily activities. In children, school absenteeism increases with asthma

severity (3–5). Globally, leveling prevalence in traditionally high prevalence countries has been noticed (6), while the prevalence of asthma in Africa, Latin America, and parts of Asia is increasing (7). The diverse global trends in asthma prevalence make regional investigations important.

The perception of asthma may have changed over time, as may the diagnostic practices in identifying asthma. Recent guidelines from The Global Initiative for Asthma (GINA) suggest

asthma control as a way of approaching asthma management rather than asthma severity (2). Studies of childhood asthma often measure the prevalence of physician-diagnosed asthma together with prevalence of symptoms common in asthma. Wheezing has been suggested the most important symptom in identifying asthma in population studies (8). Asthma is a heterogeneous disease and there are different wheezing phenotypes in childhood (9).

The Obstructive Lung Disease in Northern Sweden (OLIN) pediatric study compared two large, population-based groups of 7- to 8-yr-olds using identical methods in 1996 and 2006, respectively (10–12). It demonstrated no further increase in several asthma-related symptoms including current wheeze (11), results in line with other European countries (13). Nevertheless, the prevalence of physician-diagnosed asthma and of users of asthma medication increased significantly (11). This discrepancy between prevalence trends in symptoms common in asthma and the diagnosis of asthma might be the result of a more effective treatment and/or an improved environment. Another explanation could be changes in diagnostic practice and increased awareness, resulting in more physician diagnoses of asthma among children with mild symptoms.

The aim of the present study was to investigate the reasons for the diverging trend in asthma diagnosis and symptoms common in asthma by analyzing the associations of physician-diagnosed asthma and symptoms of wheeze, respectively, with treatment, particularly inhaled corticosteroids (ICS), environmental exposures, and variables expressing morbidity in 7- to 8-yr-old children in 1996 and 2006.

Material and methods

Study population

As a part of the OLIN pediatric studies, a parental questionnaire was submitted in 1996 to all children in first and second grade (7–8 yr-old) in three municipalities of northern Sweden; Luleå, Piteå, and Kiruna (10). In 2006, again all children attending first or second grade were invited to a study using the same methodology (11, 12). In 1996, 3430 children participated (97% of invited). Because of a lower birth rate, 2585 children participated in 2006 (96% of invited).

Methods

The questionnaire, which mainly included questions about asthma, allergic diseases, symptoms,

medication use, and home environment, has been published in an online supplement (12). The International Study of Asthma and Allergy in Childhood (ISAAC) core questions were also included (14). The OLIN questionnaire was validated in 1997 with > 99% specificity and 70% sensitivity regarding the question of physician-diagnosed asthma (10).

The children in Kiruna and Luleå were also invited to a skin prick test with ten standard airborne allergens (10, 12). The tests were performed following the European Academy of Allergology and Clinical Immunology (EAACI) recommendations (15). In 1996, 2148 (88%) children were tested vs. 1700 (90%) in 2006. Allergic sensitization was defined as a mean wheal diameter of ≥ 3 mm to any of the tested allergens, and validations against specific IgE have been performed (12, 16). The studies were approved by the ethical committee at the University of Umeå, Sweden.

Definitions

The most commonly used terms in this article include the following:

Physician-diagnosed asthma: ‘Has your child been diagnosed by a physician as having asthma?’ (12).

Current wheeze: ‘Has your child had wheezing or whistling in the chest in the last 12 months?’ (14)

Current asthma: *Physician-diagnosed asthma* and either *current wheeze* or *current medication* (12).

Asthma medication: Use of any kind of asthma medicine. Use of ICS also includes the use of ICS when administered together with long-acting β -agonist (LABA) in combined inhalers (12). *Current medication* refers to usage in the last 12 months (12).

Disturbed sleep: ‘In the last 12 months, how often, on average, has your child’s sleep been disturbed due to wheezing?’ (14).

Speech-limiting wheeze: ‘In the last 12 months, has wheezing ever been severe enough to limit your child’s speech to only one or two words at a time between breaths’ (14).

Troublesome asthma: Either *speech-limiting wheeze* or *disturbed sleep* or ≥ 1 /wk in the last 12 months.

Asthma severity score: Based on four ISAAC core questions and one of the OLIN questions about asthma medication, an arbitrary asthma severity score ranging from 0 to 5 was developed. The score included *current wheeze*, *daily asthma medication*, ≥ 1 nights per wk with *disturbed*

sleep, at least one episode of *speech-limiting wheeze*, and *> 12 episodes of wheezing* and during the last 12 months. Each item yielded one point.

Statistical analysis

Data were analyzed utilizing the Statistical Package for Social Science Software 16.0 (SPSS Inc, Chicago, IL, USA). Chi square test, and Fisher's exact test when appropriate, was used for bi-variate comparisons of categorical variables and one-way ANOVA for test for trend. A p -value < 0.05 was considered statistically significant. Analyses of symptoms and morbidity variables were also performed after stratification for use of ICS and for allergic sensitization, respectively.

The association between study year and severity of asthma was analyzed in a multiple logistic regression model including all subjects with physician-diagnosed asthma from the two cohorts. Other independent variables included in the model were current use of ICS, ever dampness at home, current cat at home, and a currently smoking mother.

Results

In 1996, 197 (5.7%) children had physician-diagnosed asthma vs. 191 (7.4%) in 2006 ($p < 0.001$). The prevalence of current wheeze was similar in 1996 and 2006; 400 (11.7%) and 335 (13.0%), respectively ($p = 0.128$) (11). Allergic sensitization measured by skin prick test

increased from 20.6% to 29.9%, $p < 0.001$ (12). In the present study, we investigated the subgroups of children with physician-diagnosed asthma and children with wheeze.

Respiratory symptoms and morbidity

Among children with physician-diagnosed asthma, the prevalence of current wheeze decreased from 81.2% in 1996 to 69.6% in 2006 ($p = 0.008$), and current use of any asthma medicines decreased from 87.8% to 80.1% ($p = 0.038$). More severe symptoms, such as disturbed sleep because of wheeze, as well as troublesome asthma, also decreased significantly. Among children with current asthma, the proportion of children with disturbed sleep because of wheeze, as well as the proportion of troublesome asthma, decreased significantly from 1996 to 2006. Among children with current wheeze but without physician-diagnosed asthma, no change in their presentation of symptoms was seen (Table 1). This was true also for all children with current wheeze (data not shown).

Consistently, the proportion having current asthma among those with physician-diagnosed asthma decreased from 91.9% in 1996 to 82.2% in 2006 ($p = 0.004$). The asthma severity score indicated a decrease in the proportion of children with more severe symptoms, $p = 0.006$ (Fig. 1). Neither in 1996 nor in 2006, any gender difference in asthma severity was found.

Both in 1996 and 2006, two-thirds of the children with physician-diagnosed asthma reported that respiratory symptoms affected their

Table 1. Prevalence (%) of respiratory symptoms and conditions among children with physician-diagnosed asthma, current asthma, and current wheeze among children without physician-diagnosed asthma in 1996 and 2006, respectively. Difference by year (p -value) calculated by chi-square test and anova test for trend*

Conditions	Physician-diagnosed asthma			Current asthma			Current wheeze without physician-diagnosed asthma		
	1996 (n = 197)	2006 (n = 191)	p-value	1996 (n = 181)	2006 (n = 157)	p-value	1996 (n = 240)	2006 (n = 202)	p-value
Current wheeze	81.2	69.6	0.008	88.4	84.7	0.320	—	—	—
Number of wheezing episodes during the last 12 months									
0	27.9	37.2	0.073*	21.5	23.6	0.565*	15.8	20.8	0.256*
1–3	27.4	25.1		29.8	30.6		66.3	62.9	
4–12	30.5	26.2		33.1	31.8		12.9	12.4	
> 12	14.2	11.5		15.5	14.0		5.0	4.0	
Number of nights with disturbed sleep during the last 12 months									
Never	50.8	62.3	0.002*	46.4	54.1	0.021*	67.9	60.4	0.241*
< 1 night per wk	38.1	34.6		41.4	42.0		26.3	34.7	
≥ 1 night per wk	11.2	3.1		12.2	3.8		5.8	5.0	
Speech-limiting wheeze last 12 months	13.2	8.9	0.178	14.4	10.8	0.330	7.5	7.4	0.976
Current asthma	91.9	82.2	0.004	—	—	—	—	—	—
Any current asthma medication	87.8	80.1	0.038	95.6	97.5	0.354	21.7	26.7	0.214
Troublesome asthma	21.3	11.0	0.006	23.2	13.4	0.021	12.5	11.9	0.843

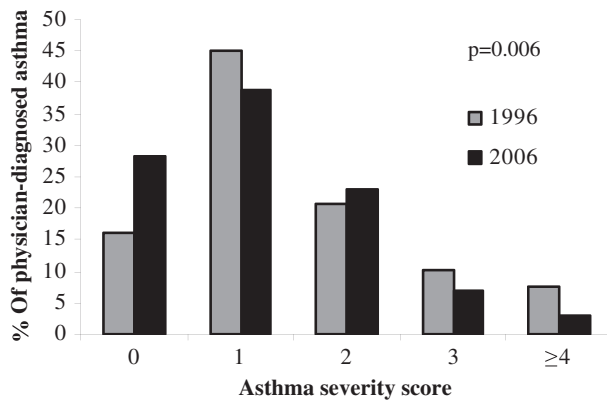


Fig. 1. Asthma severity score among children with physician-diagnosed asthma in 1996 and 2006. Difference by study was calculated by one-way ANOVA.

daily life and one-third reported worsened respiratory symptoms when being at school. However, the proportion of children who had to stay home from school because of breathing problems decreased from 40.9% to 31.1% ($p = 0.047$). Each year, the large majority of the children with

Table 2. Prevalence (%) of conditions expressing asthma morbidity and co-morbidity among children with physician-diagnosed asthma in 1996 and 2006. Difference by year (p -value) calculated by chi-square test

Conditions	Physician-diagnosed asthma		
	1996 (n = 197)	2006 (n = 191)	p-value
Take full part in physical activities in school	97.9	97.9	0.982
Same physical fitness as the schoolmates	70.4	74.7	0.349
Worsening of respiratory symptoms in school	33.0	30.8	0.655
Stayed home from school due to respiratory symptoms/asthma	40.9	31.1	0.047
Respiratory symptoms/asthma interfering with daily life	65.6	63.6	0.686
Regular doctor visits for asthma	62.8	58.6	0.401
Current rhinitis	46.7	41.9	0.340
Current medication for rhinitis/conjunctivitis	34.5	32.5	0.668
Current itchy rash	46.7	39.3	0.139

asthma took part in the physical activities in schools despite 25–30% reporting less physical fitness compared to their schoolmates. Neither the prevalence of rhinitis nor eczema did change significantly (Table 2). Among children with current asthma, a similar distribution of morbidity variables was found but without any statistically significant changes between the study year. Among the group with current wheeze, the prevalence of variables expressing asthma morbidity was generally lower compared to the group with current asthma, and the figures were almost similar in 1996 and 2006 (data not shown).

Asthma medication

The proportion of children with physician-diagnosed asthma using ICS increased from 54.8% in 1996 to 67.0% in 2006 ($p = 0.014$), while the corresponding proportion of users of short-acting β -agonists (SABA) decreased from 85.3% to 77.0%, $p = 0.036$ (Table 3).

The prevalence of symptoms in 1996 and 2006 in children with physician-diagnosed asthma was analyzed after stratification by ICS treatment (Table 4). In those using ICS, the prevalence of current wheeze was level, while troublesome asthma decreased from 29.6% in 1996 to 14.1% in 2006 ($p = 0.004$). Further, among the children using ICS, a lower proportion reported both speech-limiting wheeze and nights with disturbed sleep because of wheeze in 2006, the latter statistically significantly so. Among the children with physician-diagnosed asthma but without ICS treatment, current wheeze decreased significantly from 70.8% in 1996 to 36.5% in 2006 ($p < 0.001$), and similarly the frequency of wheezing episodes and nights with sleep disturbing wheeze decreased significantly (Table 4).

Allergic sensitization and environmental exposure

From 1996 to 2006, the proportion of sensitized children increased from 40.2% to 54.0%

Table 3. Proportion of users of medication (%) among children with physician-diagnosed asthma and current wheeze in 1996 and 2006, respectively. Difference by year (p -value) calculated by chi-square test.

Medication	Physician-diagnosed asthma			Current wheeze		
	1996 (n = 197)	2006 (n = 191)	p-value	1996 (n = 400)	2006 (n = 335)	p-value
Ever SABA	90.4	92.1	0.533	68.5	69.9	0.693
Current SABA	85.3	77.0	0.036	49.5	52.5	0.412
Current LABA	—	7.9	—	—	4.8	—
Ever ICS	56.3	77.0	< 0.001	29.0	46.0	< 0.001
Current ICS	54.8	67.0	0.014	26.2	41.2	< 0.001

ICS, inhaled corticosteroids, LABA, long-acting β -agonist, SABA, short-acting β -agonist.

Table 4. Prevalence (%) of respiratory symptoms and conditions among children with physician-diagnosed asthma, currently using and not using ICS in 1996 and 2006, respectively. Difference by year (p-value) calculated by chi-square test and ANOVA test for trend

	Users of ICS			Non-users of ICS		
	1996 (n = 108)	2006 (n = 128)	p-value	1996 (n = 89)	2006 (n = 63)	p-value
Current wheeze	89.8	85.9	0.366	70.8	36.5	< 0.001
Number of nights with disturbed sleep						
Never	38.0	50.0	0.008*	66.3	87.3	0.001*
< 1 night per wk	47.2	45.3		27.0	12.7	
≥ 1 night per wk	14.8	4.7		6.7	0	
Speech-limiting wheeze	18.5	10.9	0.098	6.7	4.8	0.736
Number of wheezing episodes						
0	19.4	21.1	0.183*	38.2	69.8	0.005*
1–3	25.0	32.8		30.3	9.5	
4–12	34.3	31.3		25.8	15.9	
> 12	21.3	14.8		5.6	4.8	
Troublesome asthma	29.6	14.1	0.004	11.2	4.8	0.240
Respiratory symptoms/asthma interfering with daily life	80.2	78.6	0.762	47.7	32.8	0.071

ICS, inhaled corticosteroids.

Table 5. Prevalence (%) of allergic sensitization measured by skin prick test (SPT) and some environmental exposures among children with physician-diagnosed asthma and current wheeze in 1996 and 2006, respectively. Difference by year (p-value) calculated by chi-square test

	Physician-diagnosed asthma			Current wheeze		
	1996 (n = 197)	2006 (n = 191)	p-value	1996 (n = 400)	2006 (n = 335)	p-value
Any positive SPT	49.3	56.6	0.241	40.2	54.0	0.002
Positive SPT to dog	33.6	45.1	0.058	25.2	42.3	< 0.001
Positive SPT to cat	39.9	48.4	0.168	29.5	43.2	0.002
Positive SPT to birch	22.6	25.4	0.600	17.2	26.8	0.010
Ever dog at home	28.6	35.8	0.129	30.4	34.2	0.267
Currently dog at home	10.7	18.4	0.032	10.1	19.5	< 0.001
Ever cat at home	19.4	23.7	0.304	23.8	22.2	0.615
Currently cat at home	3.1	14.2	< 0.001	6.8	12.3	0.011
Mother smokes currently	38.7	18.6	< 0.001	36.6	15.5	< 0.001
Father smokes currently	25.7	13.9	0.005	22.1	12.9	0.002
Ever damp housing	28.3	19.0	0.035	27.3	20.5	0.034
Current damp housing	9.9	8.2	0.545	9.9	9.3	0.795
Pertussis infection	49.2	3.7	< 0.001	53.3	4.3	< 0.001

($p = 0.002$) among those with current wheeze and tended to increase among those with physician-diagnosed asthma. The prevalence of currently having a cat or a dog at home increased among both children with physician-diagnosed asthma and among wheezers, while life-time prevalence of cat and dog ownership did not change significantly over the 10-yr period (Table 5).

Among the children who had both physician-diagnosed asthma and were sensitized, the prevalence of troublesome asthma decreased from 23.5% in 1996 to 10.1% in 2006 ($p = 0.036$), while the prevalence of current use of ICS increased from 60.3% in 1996 to 75.4% in 2006 ($p = 0.059$). Among the children with physician-diagnosed asthma but without allergic sensitization, current use of ICS was level while current

wheeze decreased significantly from 71.4% in 1996 to 52.8% in 2006 ($p = 0.034$).

The prevalence of maternal smoking among children with physician-diagnosed asthma decreased considerably from 38.7% in 1996 to 18.6% in 2006 ($p < 0.001$), and a similar decrease in smoking was found among fathers. Further, the proportion of ever having lived in a damp house decreased from 28.3% in 1996 to 19.0% in 2006 ($p = 0.035$). Infection of pertussis decreased substantially because of a general immunization of the children in the 2006 cohort (Table 5).

Factors related to severe asthma

The associations of environmental factors to severe (asthma score ≥ 3) compared to

non-severe asthma (asthma score < 3) were analyzed. Smoking habits of the parents and having cat or dog in the home did not significantly impact asthma severity neither in 1996 nor in 2006. Ever having had dampness at home was significantly related to severe asthma in 1996, RR 2.10 (1.10–3.63), but not in 2006. In a multiple logistic regression model including use of ICS, smoking mother, cat at home, and home dampness as independent variables, severe asthma was significantly associated to the study year yielding an odds ratio of 0.44 (0.23–0.87) for 2006 using 1996 as reference.

Discussion

We have shown that children with physician-diagnosed asthma reported significantly less respiratory symptoms in 2006 compared to 1996. The most pronounced decrease in symptoms was found among the children without treatment with ICS. Thus, it seems that the diverging trend with an increase in asthma prevalence and no increase in symptoms from 1996 to 2006 (11) was mainly explained by an increased awareness among physicians and parents about asthma, resulting in a greater proportion of children with mild or temporary symptoms being diagnosed as having asthma. The increase in the proportion of children with asthma using ICS and the introduction of long-acting β -2-agonists (LABA) parallels with a major decrease of severe symptoms and probably explains this decrease.

Studies worldwide show diverse trends in the prevalence of asthma. Until recently, the prevalence has steadily increased in industrialized countries. Recent studies, however, indicate a leveling trend in the prevalence of asthma, and some studies even suggest a decrease (7, 17). The change in prevalence of current wheeze in the ISAAC III study was small in most countries (7). According to ISAAC III, the prevalence of wheeze in age 6–7 and age 13–14 did not increase in most study areas in Western Europe, while an increase was noticed in most areas in Eastern Europe (6). Although there are several hypotheses, the reasons for the past rise in asthma prevalence as well as for the recent presumed leveling are still unclear (18). A change in diagnosing asthma over time has been discussed as a contributing explanation for the increased asthma prevalence (19). Our results indicate a change in diagnostic intensity as the decrease in presentation of symptoms was only seen among the children with a diagnosis of asthma and among those without ICS treatment, while the

symptom presentation among those with current wheeze without physician-diagnosed asthma was level.

In line with our results, a recent study among Swedish children found an increase in diagnosed asthma and a decrease in symptoms common in asthma (20). Also in Norway, geographically close to Sweden and with a similar life-style, a study among children showed a level prevalence of symptoms common in asthma while the prevalence of asthma tended to increase from 1995 to 2000 (21). The same trend was found also among children in Austria (22). In contrast to our results, a recent study in Lithuania, geographically close to Sweden but with a different socio-economic situation, found an increase in prevalence of both respiratory symptoms and asthma (23).

In our study, the proportion among children with a physician-diagnosed asthma using ICS increased parallel to a decrease in use of inhaled SABA and other anti-asthmatic medication such as chromoglycate. Also, among children having current wheeze, the use of ICS increased from 1996 to 2006. During the past decade, the guidelines for treatment of asthma in children in Sweden were changed. ICS can now be prescribed also in mild asthma, and the combination therapy with ICS and LABA was introduced. This may at least in part explain the decrease in the use of SABA.

ICS is an effective treatment for asthma and the increasing use of ICS could have resulted in a decrease in respiratory symptoms among the asthmatics. However, despite the increased proportion of asthmatics using ICS, a similar and a high proportion of the asthmatics using ICS reported current wheeze both in 2006 and in 1996. On the other hand, a decrease in severe symptoms was found, which probably was a result of improved and changed treatment regimes. The most significant decrease in respiratory symptoms was seen among those without treatment with ICS, why other factors must be considered as a reason for the decrease in asthma severity.

A dramatic change in the indoor environment had occurred during the 10-yr period. Parental smoking and living in a damp house had decreased significantly in the whole cohort as well as among the children with asthma. Environmental tobacco smoke (ETS) is a well-known factor influencing asthma severity; and in children, an association between ETS and peak-flow variability, respiratory symptoms, and use of asthma medicines has been demonstrated (24). The marked decrease in smoking among the

parents may have contributed to better respiratory health in the asthmatic children, even though longitudinal studies are needed to confirm this. As respiratory infections has been identified as a significant risk factor for asthma (9, 10), we would not expect an increase in asthma prevalence as the prevalence of respiratory infections decreased considerably during the 10 yr. Particularly, pertussis infections decreased because of re-introduction of a general immunization program. Further, there is so far no evidence that vaccination against pertussis would increase the risk for developing asthma (25). Also, this argues against a true increase in asthma prevalence.

Surprisingly, significantly more children had furred pets in their homes in 2006 compared with 1996, and because the prevalence of 'ever pet at home' was unchanged, it can be concluded that less families choose to take away the animals from the homes even if their children have asthma. This may be an effect of the ongoing discussions about effects of having pets at home in relation to the development of asthma and allergy (26–28). However, despite the increase in keeping pets in homes, no increase in prevalence of asthma symptoms or variables reflecting asthma morbidity was found. Among the sensitized children with physician-diagnosed asthma, a trend towards an increasing proportion of children using ICS could be seen that was not present among non-sensitized children. Our study population is too small to allow stratified analyses with sufficient statistical power of symptoms in sensitized asthmatic children keeping pets or not in their homes. However, it has been shown that removal of pets reduces airway hyper-responsiveness in pet allergic asthmatics (29).

Still, few studies have been conducted on asthma morbidity on a population level. Our results show a decrease in asthma morbidity during the study period. In 2006, a lower proportion of asthmatic children reported speech-limiting wheeze, sleep disturbance, and absence from school because of asthma. A better asthma control may thus contribute to a better educational situation for the affected children (3–5). However, the findings are not univocal: there are also studies demonstrating equal academic achievements by asthmatic and non-asthmatic children, and no difference in school absence because of severity (30). Also, the probability of remission from asthma is greater among asthmatics having a mild disease (31). Despite improvements in morbidity, a large proportion of the children have their daily life affected by the

disease. A better asthma control is thus still a major goal in the care and treatment of asthma.

There are several strengths with our study. The two large population-based cohorts of children of the same age (7–8 yr) living in the same areas were examined 10 yr apart. The cohorts were examined with identical methods including validated and internationally used questionnaires, and skin prick testing. The participation rates were very high in both surveys. The limitations are attributed to epidemiologic questionnaire surveys including a lack of objective and more detailed measurements of severity of asthma and symptoms. Thus, the possibility of over-diagnosis of asthma in 2006 is not explored. Further, our investigation of asthma medication did not include doses of ICS and other medications.

In conclusion, we found that children with diagnosed asthma in 2006 had less respiratory symptoms, particularly severe symptoms, compared to 1996. This parallels with an increased treatment with ICS and an improved indoor environment, and to an increased diagnostic intensity resulting in a greater proportion being diagnosed as having asthma. Still, because of a high prevalence and its impact on daily life, asthma remains a major health problem in schoolchildren.

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