

Accepted Manuscript

Increasing prevalence of asthma, respiratory symptoms, and allergic diseases: Four repeated surveys from 1993-2014

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PII: S0954-6111(15)00180-8

DOI: [10.1016/j.rmed.2015.05.010](https://doi.org/10.1016/j.rmed.2015.05.010)

Reference: YRMED 4716

To appear in: *Respiratory Medicine*

Received Date: 25 February 2015

Revised Date: 4 May 2015

Accepted Date: 11 May 2015

Please cite this article as: Brozek G, Lawson J, Szumilas D, Zejda J, Increasing prevalence of asthma, respiratory symptoms, and allergic diseases: Four repeated surveys from 1993-2014, *Respiratory Medicine* (2015), doi: 10.1016/j.rmed.2015.05.010.

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TITLE: Increasing prevalence of asthma, respiratory symptoms, and allergic diseases: Four repeated surveys from 1993-2014

RUNNING TITLE: Rising trend of asthma and allergic diseases in Poland

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ABSTRACT

Background: Published data shows different prevalence trends depending on the region of Europe.

Aim: The aim of the study was to analyze time trends of the frequency of the respiratory symptoms and allergic diseases in school children (Silesia, Poland) over the last 21 years.

Methods: We compared the results of four population-based surveys performed in a town of Chorzow in 1993, 2002, 2007 and 2014 in children aged 7-10 years. All four studies had the same study protocol, recruitment (cluster, school-based sampling), questionnaire (WHO respiratory health questionnaire) and the same principal investigator. The surveys included 1130 children in 1993, 1421 children in 2002, 1661 children in 2007 and 1698 in 2014.

Results: The results covered a 21 year span and showed a statistically significant ($p < 0.05$) increase in the prevalence of the following physician-diagnosed disorders (1993-2002-2007-2014): asthma (3.4%-4.8%-8.6%-12.6%); allergic rhinitis (4.3%-11.9%-15.9%-13.9%); atopic dermatitis (3.6%-7.9%-12.0%-13.9%); allergic conjunctivitis (4.3%-7.9%-8.3%-7.9%); A simultaneous increasing trend ($p < 0.05$) in the attacks of dyspnea (3.9%-5.9%-7.0%-7.3%) and symptoms (wheeze, dyspnea, cough) induced by exercise (7.5%-10.6%-22.0%-22.4%) and - at the same time - decrease ($p < 0.05$) in the prevalence of cough (31.6%-19.6%-15.4%-14.4%).

Among children with diagnosed asthma during the 21 year span there was significantly ($p < 0.05$) increased proportion of treated children (51.3%-51.3%-69.5%-60.7%) and a lower frequency of presenting current symptoms.

Conclusions: Our findings are in line with the concept of a real increase in the occurrence of asthma and allergic disease in children. The pattern involves not only physician-diagnosed

allergic diseases but also occurrence of symptoms related to respiratory disorders. Diagnosed asthma is better treated and better controlled.

INTRODUCTION

Allergic diseases are very common, especially among children. Over the second half of the 20th century, the prevalence of allergic diseases, including asthma, increased significantly worldwide with the highest increase observed in industrialized nations [1-3]. Currently, the frequency of allergic diseases varies geographically globally with different temporal patterns in the same populations. The best documented epidemiology of allergic disease is childhood asthma. Actual data shows significant differences in childhood asthma frequency between European countries, ranging from 1.4%-1.7% in Belarus [4] and Ukraine [5] through 7.7-9.6% in Sweden and Hungary and up to 21.6-29.7% in Ireland and the UK [2, 6-8]. In addition, the direction of the time trends of asthma and its symptoms differ with evidence of decline in Belgium, Sweden, and the UK; plateaus in Spain; and increases in countries including Finland, Romania and Ukraine [2, 9]. Similar differences are observed in case of atopic eczema and allergic conjunctivitis [3, 9]. These results suggest that there is not a common pattern for asthma and allergic disease prevalence in Europe. Monitoring prevalence changes over time should be completed and interpreted in regional populations such as within individual countries. Such summarized data gives a better picture of the epidemiology of allergic diseases and is helpful not only in planning national health care needs but also to predict trends in the future.

In a previous study we found statistically significant increases in the prevalence of allergic diseases diagnosed by a physician and respiratory symptoms suggestive of asthma tendency. In 2014 we expanded on the previous study by repeating a cross-sectional study as has been completed before to further investigate changes in asthma prevalence, now up to 21 years making use of four time points. We further expand on the previous investigation of temporal

trends by investigating changes in the management of asthma among children and profiling children with asthma with regard to report of respiratory symptoms and allergic conditions. More specifically, our objective was to determine whether increases in the prevalence of asthma and related conditions was continuing in this community and to identify if the profile of children with asthma changed between 1993 and 2014.

METHODS

Study design and study population

This study consisted of four repeated cross-sectional surveys in the same location and using the same survey with identical methodology. This protocol has been described previously as part of our earlier investigation of the temporal trends in asthma prevalence [10, 11]. In brief, this study was completed in Chorzow, Poland in 1993, 2002, 2007, and 2014. Chorzow is an industrial center, part of the Silesian Agglomeration in the Upper Silesian Industrial Zone with coal mining and metallurgical operations. Over the 21 years of study, Chorzow's population ranged between 127,049 and 111,168 [12]. No major changes in the population structure occurred during the study period [12]. For example, the proportion of children 14 years and younger ranged between 16.6% in 1995 to 14.5% in 2013 with no noticeable migration.[12] In Chorzow, as well as in the whole Silesia region there was observed significant reduction of air pollution [14].

Schools were randomly selected for inclusion to the study in 1993. In subsequent survey years, the same schools were included in order to remove any bias that may occur by resampling schools. All children between 7 to 10 years of age attending selected schools were eligible for inclusion. A study package, which included a letter explaining the study objectives, a written consent form, and a survey were sent home through the schools for self-completion by the parent or guardian. Once completed, the survey was returned to the school where it was picked up study staff.

Study instrument and operational definitions

The same study instrument was used in each round of data collection. This was a 17 item survey asking about age, sex, doctor's diagnosis of asthma, respiratory symptoms, and allergic disorders. The survey was based on the Polish version [15] of a validated children's lung health questionnaire [16] that was also used in the Central European Study of Air Pollution and Respiratory Health [17].

The list of diagnosed allergic disorders was based on self-report and included asthma, obstructive bronchitis, allergic rhinitis, allergic conjunctivitis, atopic dermatitis, pollen-, dust- and food- allergy each asking about a previous physician diagnosis ever in the past. Asthma and other diagnoses of allergic diseases/disorders were defined according to the answer to the question "Has a child ever had [*given disease*] diagnosed by physician?". In addition to this, information about the age of diagnosis and current treatment was ascertained for a report of an asthma diagnosis or an obstructive bronchitis diagnosis.

Chest wheezing (ever) was defined according to the answer to the question: "Has a child ever had wheezing or whistling in the chest at any time in the past?". Current chest wheezing was defined according to the answer to the question: "Has a child's chest sounded wheezy or whistling in the last 12 months?". Attacks of dyspnea (ever) were defined according to the answer to the question "Has a child ever had attacks of dyspnea?". Current dyspnea attacks were defined based on the answer to the question "Has a child had attacks of dyspnea during the last 12 months?" Dry cough during the night was defined according to the answer to the question "Has a child had a dry cough at night in the last 12 months, apart from coughing with a cold or chest infection?". Morning cough was defined according to the answer to the question "Does a

child usually cough in the morning in autumn/winter season?” while chronic cough was based on the question “ Did a child cough on most days for at least 3 months consecutively in the last autumn/winter season?”.

Statistical analysis

All analyses were completed using SPSS 20. Statistical significance was defined by an alpha level of 0.05. Descriptive analysis of condition frequency was conducted through the calculation and presentation of prevalence [95% confidence intervals (CI)]. All analyses were completed to investigate the temporal trends in condition prevalence. This was completed overall then stratified by sex given the different patterns in allergic disease prevalence between boys and girls and the gender switch around puberty. Initially, statistical analysis was completed using a chi-square test for trends.

Following this initial analysis, a multiple logistic regression model was fitted with calendar year as the primary independent variable and the medical condition as the outcome with adjustment for age and sex. Because of results seen in a Canadian population where diagnostic differences in girls may have been occurring but not among boys [18], effect modification between calendar year and sex was assessed.

In order to investigate a potential labeling effect, the ratio of children with current wheeze to ever-diagnosed asthma was calculated. In addition to this, we examined the characteristics of those with diagnosed asthma including age of diagnosis, use of treatment strategies, and report of respiratory and allergic symptoms by study year. The Kruskal-Wallis

test was used to test differences in age of diagnosis by study year and the chi-squared test was used to test differences in report of treatment and respiratory symptoms by study year.

RESULTS

There were 1,137 participants in 1993, 1,487 participants in 2002, 1,661 participants in 2007, and 1,698 participants in 2014, which was at least 25% of the total target population in the community. Participation rates for the study were 72% in 1993, 82% in 2002, 83% in 2007 and 76% in 2014. There was no difference in the sex distribution between years with 49.3%, 50.5%, 48.4%, and 50.5% females in 1993, 2002, 2007, and 2014, respectively ($p=0.5$). There were also no differences in mean age by year of study [1993: 8.7 years (SD=0.9); 2002: 8.6 years (SD=1.2); 2007: 8.7 years (SD=1.1); 2014: 8.6 years (SD=1.2)].

Table 1 presents the prevalence of diagnosed asthma, respiratory symptoms, and allergic conditions. Overall, the prevalence of asthma increased from 3.4% in 1993 to 12.6% in 2014. This distinct rise in asthma prevalence was not observed for current wheeze. Symptoms of current dyspnea attacks, exercise-induced respiratory symptoms, specific allergic conditions, and report of any allergy or allergic condition also showed steady increases in prevalence although there was less consistency with the specific allergic conditions. In contrast, both chronic cough and dry cough at night showed relatively consistent reductions in prevalence between 1993 and 2014.

Among children with current wheeze, the proportion of children who also reported a previous diagnosis of asthma increased by study year. In 1993, 17.1% of children with wheeze in the past 12 months had a previous diagnosis of asthma while this increased to 20.3%, 31.3%, and 45.1% in 2002, 2007, and 2014, respectively.

When stratified by sex (Table 2) both males and females showed steady increases in asthma prevalence where in a given year, males had a higher prevalence of asthma than females

(Males: 4.3% in 1993 to 15.1% in 2014; Females: 2.5% in 1993 to 10.1% in 2014). Similar trends in symptoms over time were observed for both males and females although males generally had a higher prevalence of a given symptom or condition (Table 2).

After completing an adjusted analysis, the results were consistent with the descriptive analyses. As seen in Table 3, there was an increased risk of having a previous diagnosis of asthma as calendar year increased while there was generally a weak, non-significant association between current wheeze and calendar year, with the exception of 2007, which showed an increased risk of report of current wheeze compared to 1993. Clear increases by calendar year were seen for current dyspnea attacks, exercise-induced respiratory symptoms, and any allergy or allergic condition while there was a clear inverse trend observed for chronic cough over time. Females were at a statistically significant lower risk of each identified outcome with the exception of current dyspnea attacks. We examined a potential interaction between sex and calendar year and found that inclusion of an interaction term did not significantly improve any model suggesting that the temporal trends were similar between males and females (data not shown).

Among those children with a previous diagnosis of asthma, there was a statistically significant difference in the age of diagnosis by study year ($p=0.04$). While the median age of diagnosis in each year was 4, the mean age of diagnosis varied without a consistent pattern and with differences that did not appear to be clinically important [1993: 3.5 years (SD=2.0); 2002: 3.7 years (SD=1.8); 2007: 4.6 years (SD=2.5); 2014: 4.0 years (SD=2.3)]. Table 4 presents the prevalence of asthma treatment, respiratory symptoms, and allergic conditions among children with asthma in order to assess changes in management or presentation of disease over time while Table 5 repeats these analyses stratified by sex. Among children with asthma, overall there was a

higher proportion of children who received treatment for asthma in recent years although this was not observed after stratification by sex. However, in general, over the study period there was a statistically significant reduction in the prevalence of current wheeze, exercise-induced symptoms, chronic cough, and dry cough at night among children with asthma. There were no statistically significant changes over the study period for specific allergic conditions among children with asthma but there was an increase in the proportion of any allergy or allergic condition being present among children with asthma over the study period. As seen in Table 5, the temporal trends are consistent between males and females. Among those with a previous diagnosis of asthma, there was not a statistically significant difference between males and females with regard to the prevalence of reported respiratory symptoms or allergic diseases.

DISCUSSION

The results of our study suggest an increasing prevalence of asthma and other allergic conditions among children over a 21 year period from 1993 to 2014. This was observed along with a generally increasing prevalence of those being treated for asthma among those with asthma and a decreasing prevalence of respiratory symptoms among those who have asthma. Through this investigation of temporal patterns we were able to expand on previous studies by a thorough investigation of multiple time points, reporting of patterns over time among those with asthma, formal evaluation of effect modification in time trends by sex, and adjustment for age and sex.

Asthma prevalence has increased over the past few decades although the increases have not been consistent by location making it important to consider asthma epidemiology at a regional level. Most regions that have experienced an increase in asthma prevalence were those of industrialized or “Westernized” nations. However, more recently, there have been several studies suggesting a plateau in the prevalence of asthma and related conditions, although this has not been consistent either, again justifying the importance of investigating time trends in asthma prevalence at a regional level given its impact on the individual and society. In our study, asthma prevalence increased relatively consistently across the period of observation. Over the past 25 years, Poland has undergone political, social, and environmental transformation as it moved towards more Westernized practices and into the European Union. Some of these changes in lifestyle could account for the increases in asthma prevalence observed. In a previous study of children living in villages compared to a town in Poland, there was a significant increase in the prevalence of atopy in villages between 2003 and 2012 (7.3 to 19.6%) but no difference in the

town (20.0 to 19.9%) [19]. Asthma prevalence was relatively stable between the time points (approximately 4-5%) [19]. Similar to these results, previous comparisons of the prevalence of asthma and allergic disease in East Germany shortly after unification (1995-6 vs 1991-2) showed increases in the prevalence of allergic disorders but no differences in the prevalence of asthma [20]. The prevalence of asthma in our study was higher and increased over time compared to the previous studies. A difference between the previous studies and ours were that different overall time periods were considered. A different study, however, showed increases in both asthma prevalence and the prevalence of allergic disorders between three time points in Eastern Germany after unification (1992-3, 1995-6, and 1008-9) [21]. When considering changes post-unification, between 1989 and 2014, in general, levels of asthma prevalence in the former Eastern Germany have increased and converged to levels of Western Germany [22].

More similar to our work, results from Poland, and most of Eastern and Northern Europe, from the ISAAC study also showed increases in asthma symptoms between repeated phases in the early 1990's and 2002-03. The prevalence of asthma in our study was more comparable to the results reported in the ISAAC study which ranged between 7.8 and 13.6% [9]. We expanded on the temporal investigation by examining trends up to 2014. Despite the similarity with ISAAC results, the prevalence of asthma observed in our study was still higher than what has been observed in previous studies of Eastern Europe [17].

It has previously been suggested that diagnostic shift from related conditions such as spastic bronchitis to asthma may account for the increases in prevalence [17, 23]. While some of the increase in asthma prevalence observed in our study could be linked to diagnostic shift, we believe that the increase in asthma prevalence reflects a true increase in the disease frequency for several reasons. First, with the exception of chronic cough, there has been a parallel increase in

respiratory symptoms including dyspnea attacks and exercise-induced symptoms. Second, there has also been a parallel increase in any allergy or allergic disease, conditions related to asthma, especially among children where asthma is more often allergy linked. Third, a higher proportion of children with asthma have been treated for asthma in recent years and a higher proportion of children with asthma reported allergic conditions in recent years. While the prevalence of respiratory symptoms has decreased in recent years among children who had a diagnosis of asthma, this could result from improved management, more accurate diagnosis and subsequent management, or a milder form of disease. Fourth, among children who had current wheeze, there was an increase in the proportion of those who also reported a diagnosis of asthma. Finally, the basic characteristics of asthma including age of diagnosis and sex distribution have remained relatively consistent over the time period under study. Similar findings were reported from Canada in the 1980's and 90's where there was some evidence of diagnostic exchange explaining the rise of asthma prevalence [13]. However, the diagnostic exchange could not explain the whole increase in asthma prevalence suggesting true increases in the prevalence of disease.

We also observed increases in the prevalence of allergic conditions. This is similar to previous reports from other countries in Europe [2, 3, 9, 19, 20, 22] and more globally with some variation by geographic location [9, 24, 25]. The explanation of the observed trend of allergic diseases is difficult because many factors may play role such as environment, socio-economic status, and lifestyle changes. The impact of genetic factors on the trend is highly unlikely given the time frame of the surveys. Furthermore, in the study area the population is very stable and in/out migration is virtually non-existent. Between-survey differences cannot be convincingly attributed to changes in clinical practices over the reported period - diagnostic guidelines were introduced at the beginning of that period and have been followed since. Moreover, in the study

area, the availability of pediatric allergology services is stable and meets the needs in the field of pediatric asthma and allergic disorders. In our study, there was a high proportion of children with asthma who also had an allergic condition such as rhinitis or atopic dermatitis. During the 21 years of observation, the proportion of children with asthma who suffered from any allergic diseases increased from 53% up to 82%. This may support the idea that asthma and allergic rhinitis are different clinical manifestations of chronic inflammation of the upper and lower respiratory tracts with the same pathological mechanism where it has previously been reported that the proportion of patients with asthma who also suffer from allergic rhinitis ranges between 30-90% or that rhinitis may be a risk factor for asthma [26,27].

While the proportion of children with asthma who reported being treated increased and the proportion of children with asthma reporting current symptoms reduced, a large proportion of children with asthma still reported symptoms indicating that their condition may not be adequately controlled. From a public health perspective, this represents a target for improvement. However, it also represents a limitation in the present study and a focus of future research to identify the impact of asthma on daily living and quality of life of children in this region as well as to better describe the level of asthma severity.

There are several limitations that should be considered when interpreting the results of our study. While we believe there is evidence to support the temporal trends observed and that the increase in asthma prevalence is true, we are not able to investigate the explanations for these results. As this was a study of prevalence, our primary interest was a high response rate with sufficient numbers to consider the research questions under study. As such, the survey we used was short and we could not include information on risk factors such as smoking or indoor environmental conditions. In addition to this, we were not able to address some important

potential confounders including family history, socio-economic status nor parental education. There is some potential bias due to the differing participation rates. However, we anticipate that this is minimal given that participation in each year was relatively high and stable across the years. Another limitation is that these questionnaires were based on self-report. However, these questions were based on standardized questionnaires used in other epidemiological studies. In order to address these problems, future studies should be conducted to corroborate these results in other areas of the country. Also, there should be further investigation into the reasons for the increases in asthma prevalence including an assessment of risk factors. Conducting some research into the diagnostic accuracy should also be completed.

Our study also had several strengths. We were able to conduct this study at four time points over 21 years allowing for excellent investigation of temporal patterns. By using the same community, schools, and age groups, we were able to reduce any bias that could result from selection issues. We used the same survey at each phase allowing for valid comparisons of responses. We experienced good participation rates with large sample sizes allowing for robust estimates. Finally our analyses were appropriate for an investigation of prevalence including a presentation of results by subgroup, with confidence intervals, and with adjustment of age and sex.

We were able to continue our investigation of the prevalence of asthma and related conditions in this community allowing for more accurate and up to date assessment of temporal trends. The results of our study suggest an increase in asthma prevalence in this region of Poland over the past 21 years. This provides evidence that asthma is an increasing problem, at least in this region, of Eastern Europe. If increases continue in this region and in other areas of Eastern Europe asthma could emerge as a major child health problem with immense health care resource

use as it has become in Westernized nations. Monitoring of the situation and investigation of explanations for these findings is critical for the future well-being of the individual and economic impact on the health care system. In addition to this, we were able to improve our analytic assessment of the trends by controlling for some key confounders and to investigate the temporal trends in the characteristics among children with asthma

CONCLUSIONS

Our findings are in line with the concept of a real increase in the occurrence of asthma and allergic disease in children in this part of Europe. The pattern involves not only physician-diagnosed allergic diseases but also occurrence of symptoms related to respiratory disorders. In the same time diagnosed asthma is better treated and better controlled.

ACKNOWLEDGEMENTS

Funds for all four studies were from the Medical University of Silesia.

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Table 1 Prevalence of self-reported diagnosed asthma, respiratory symptoms, and diagnosed allergic conditions by year of study

	1993	2002	2007	2014	
	n=1137 % (95%CI)	n=1487 % (95%CI)	n=1661 % (95%CI)	n=1698 % (95%CI)	p-value*
Ever diagnosed asthma	3.4 (2.4-4.5)	4.8 (3.7-5.8)	8.6 (7.2-9.9)	12.6 (11.0-14.2)	<0.001
Diagnosed obstructive bronchitis	8.5 (6.9-10.1)	21.2 (19.2-23.2)	15.1 (13.4-16.9)	15.1 (13.4-16.8)	0.04
Current wheeze	21.2 (18.8-23.6)	27.3 (25.1-29.4)	26.3 (24.2-28.4)	25.1 (23.0-27.2)	0.10
Current dyspnea attacks	3.9 (2.7-5.0)	5.9 (4.7-7.1)	7.0 (5.7-8.2)	7.3 (5.7-8.3)	<0.001
Exercise-induced symptoms	7.5 (5.5-8.5)	10.6 (9.1-12.2)	22.0 (20.0-24.0)	22.4 (20.4-24.4)	<0.001
Chronic cough	31.6 (28.9-34.3)	19.6 (17.7-21.6)	15.4 (13.7-17.1)	14.3 (12.6-15.9)	<0.001
Morning cough	36.2 (33.4-39.0)	34.1 (28.0-32.7)	28.0 (24.9-29.2)	24.0 (26.5-30.8)	<0.001
Dry cough at night	43.6 (40.7-46.5)	30.3 (28.0-32.5)	27.0 (24.9-29.1)	28.6 (26.5-30.8)	<0.001
Diagnosed allergic rhinitis	4.3 (3.1-5.5)	11.9 (10.3-13.5)	15.9 (14.1-17.7)	13.9 (12.3-15.6)	<0.001
Diagnosed allergic conjunctivitis	4.3 (3.1-5.5)	8.3 (6.9-9.7)	8.9 (7.5-10.3)	7.9 (6.7-9.2)	<0.001
Diagnosed allergic dermatitis	3.6 (2.5-4.7)	7.9 (6.5-9.2)	12.0 (10.4-13.6)	13.9 (12.3-15.6)	<0.001
Any allergy or allergic disease	13.1 (11.1-15.1)	26.4 (24.2-28.7)	32.0 (29.7-34.2)	32.7 (30.5-34.9)	<0.001

* Based on chi-squared test for trends

Table 2 Prevalence of self-reported diagnosed asthma, respiratory symptoms, and diagnosed allergic conditions by year of study and sex

	Males				Females			
	1993 n=576 % (95% CI)	2002 n=736 % (95% CI)	2007 n=857 % (95% CI)	2014 n=840 % (95% CI)	1993 n=561 % (95% CI)	2002 n=751 % (95% CI)	2007 n=804 % (95% CI)	2014 n=858 % (95% CI)
Ever diagnosed asthma	4.3 (2.7-6.0)	6.0 (4.3-7.7)	10.1 (8.0-12.0)	15.1 (12.7-17.5) [†]	2.5 (1.2-3.8)	3.5 (2.1-4.8)	6.7 (5.0-8.4)	10.1 (8.0-12.0) [†]
Diagnosed obstructive bronchitis	8.7 (6.4-11.0)	22.3 (19.1-25.1)	18.1 (15.5-20.7)	17.6 (15.0-20.2)*	8.2 (5.9-10.5)	19.6 (16.7-22.4)	11.7 (9.5-13.9)	12.7 (10.5-14.9)
Current wheeze	13.7 (10.9-16.5)	15.2 (12.6-17.8)	14.8 (12.3-17.1)	14.4 (12.0-16.8)	10.9 (8.3-13.4)	13.8 (11.2-16.2)	15.6 (13.0-18.0)	9.9 (7.9-11.9)
Current dyspnea attacks	4.3 (2.7-6.0)	7.5 (5.6-9.4)	6.7 (5.0-8.3)	7.7 (5.9-9.5)*	3.2 (1.7-4.7)	4.2 (2.7-5.5)	7.3 (5.4-9.0)	6.9 (5.2-8.6)*
Exercise-induced symptoms	7.3 (5.2-9.4)	13.3 (10.9-15.8)	23.1 (20.3-25.9)	23.3 (20.5-26.2) [†]	7.5 (5.3-9.7)	8.2 (6.3-10.2)	21.1 (18.3-24.0)	21.6 (18.8-21.6) [†]
Chronic cough	33.7 (29.8-37.5)	23.5 (20.4-26.6)	16.8 (14.3-19.3)	15.3 (12.8-17.7) [†]	29.8 (26.0-33.5)	16.1 (13.5-18.7)	13.8 (11.4-16.2)	13.2 (10.9-15.4) [†]
Morning cough	36.1 (32.2-40.0)	37.1 (33.6-40.6)	29.2 (26.1-32.2)	25.5 (22.5-28.4) [†]	36.7 (32.7-40.7)	30.5 (27.2-33.8)	26.9 (23.8-29.9)	22.5 (19.7-25.3) [†]
Dry cough at night	42.9 (38.8-46.9)	31.1 (27.8-34.4)	28.2 (25.0-31.0)	31.0 (27.9-34.1) [†]	44.4 (40.3-48.5)	29.5 (26.2-32.7)	26.1 (23.1-29.1)	26.3 (23.4-29.3)*
Diagnosed allergic rhinitis	4.5 (2.8-6.2)	12.8 (10.3-15.2)	18.1 (15.4-20.5)	18.3 (15.7-20.9) [†]	4.1 (2.5-5.7)	10.4 (8.1-12.4)	13.7 (11.2-15.9)	9.6 (7.6-11.5)
Diagnosed allergic conjunctivitis	4.0 (2.4-5.6)	8.7 (6.7-10.7)	9.8 (7.3-11.2)	9.9 (7.8-11.9) [†]	3.2 (1.7-4.7)	7.5 (5.6-9.3)	8.0 (5.9-9.7)	6.1 (4.5-7.7)
Diagnosed allergic dermatitis	2.3 (1.0-3.5)	7.1 (5.2-8.9)	13.2 (10.8-15.3)	15.7 (13.2-18.2) [†]	2.3 (1.1-3.6)	8.5 (6.5-10.5)	10.7 (8.5-12.8)	12.1 (9.9-14.3) [†]

Any allergy or allergic disease	13.2 (10.4-15.9)	27.0 (23.8-30.2)	34.7 (31.5-37.8)	37.5 (34.2-40.8) [†]	12.8 (10.1-15.6)	26.4 (23.2-29.5)	29.4 (26.2-32.5)	28.0 (25.0-31.0) [†]
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* p<0.05 for a linear trend using the chi-squared test for trends

[†] p<0.001 for a linear trend using the chi-squared test for trends

Table 3 Adjusted associations between calendar year, age, and sex with self-reported diagnosed asthma, respiratory symptoms, and diagnosed allergic conditions

	Ever diagnosed asthma	Current wheeze	Current dyspnea attacks	Exercise induced symptoms	Chronic cough	Any allergy or allergic disease
	Odds Ratio (95%CI)	Odds Ratio (95%CI)	Odds Ratio (95%CI)	Odds Ratio (95%CI)	Odds Ratio (95%CI)	Odds Ratio (95%CI)
Year						
1993	1.00	1.00	1.00	1.00	1.00	1.00
2002	1.40 (0.94-2.09)	1.21 (0.96-1.52)	1.58 (1.09-2.30)	1.50 (1.13-1.97)	0.53 (0.44-0.63)	2.54 (1.99-3.02)
2007	2.52 (1.75-3.63)	1.28 (1.02-1.59)	1.91 (1.33-2.73)	3.56 (2.77-4.58)	0.39 (0.32-0.47)	3.16 (2.58-3.86)
2014	4.09 (2.88-5.81)	0.98 (0.78-1.23)	2.01 (1.41-2.87)	3.62 (2.82-4.65)	0.35 (0.29-0.43)	3.26 (2.67-3.98)
Sex						
Male	1.00	1.00	1.00	1.00	1.00	1.00
Female	0.62 (0.51-0.75)	0.85 (0.73-0.98)	0.82 (0.66-1.02)	0.84 (0.73-0.97)	0.77 (0.67-0.88)	0.80 (0.71-0.89)
Age	0.97 (0.89-1.06)	0.89 (0.83-0.96)	0.99 (0.90-1.09)	0.94 (0.87-1.01)	0.91 (0.85-0.96)	0.98 (0.93-1.03)

Adjusted for each variable in the table.

Table 4 Prevalence of self-reported asthma treatment, respiratory symptoms, and diagnosed allergic conditions by year of study among children who have had a previous diagnosis of asthma

	1993	2002	2007	2014	
	n=39 % (95%CI)	n=76 % (95%CI)	n=141 % (95%CI)	n=214 % (95%CI)	p-value*
Asthma treated	51.3 (35.6-67.0)	51.3 (40.1-62.5)	69.5 (61.9-77.1)	60.7 (60.0-72.7)	0.03
Current wheeze	61.5 (46.3-76.8)	63.5 (52.5-74.5)	57.7 (49.4-65.9)	43.5 (36.8-50.1)	0.001
Current dyspnea attacks	41.0 (25.6-56.5)	49.3 (38.0-60.6)	43.5 (35.2-51.7)	36.5 (30.4-42.9)	0.15
Exercise-induced symptoms	79.5 (66.8-92.1)	92.1 (86.0-98.2)	80.0 (73.2-86.7)	62.2 (55.7-68.7)	<0.001
Chronic cough	69.2 (54.7-83.7)	69.3 (58.0-78.9)	48.5 (40.1-56.9)	42.5 (35.9-49.1)	<0.001
Morning cough	61.5 (46.3-76.8)	79.7 (71.3-89.2)	71.5 (64.2-79.1)	57.1 (50.4-63.6)	0.01
Dry cough at night	74.4 (60.7-88.1)	75.0 (65.3-84.7)	71.0 (63.4-78.6)	61.7 (55.2-68.2)	0.02
Diagnosed allergic rhinitis	17.9 (5.9-30.0)	53.7 (42.7-65.2)	61.6 (53.7-69.7)	43.5 (36.8-50.1)	0.26
Diagnosed allergic conjunctivitis	10.3 (0.7-19.8)	39.7 (28.5-50.5)	32.8 (24.9-40.4)	37.4 (30.9-43.9)	0.58
Diagnosed allergic dermatitis	15.4 (4.1-26.7)	36.1 (24.7-46.3)	31.9 (24.2-39.6)	22.0 (16.4-27.5)	0.11
Any allergy or allergic disease	53.8 (38.2-69.5)	84.2 (76.0-92.4)	86.5 (80.9-92.2)	82.7 (77.6-87.8)	0.003

* Based on chi-squared test for trends

Table 5 Prevalence of self-reported asthma treatment, respiratory symptoms, and diagnosed allergic conditions by year of study and sex among children who have had a previous diagnosis of asthma

	Males				Females			
	1993 n=25 % (95% CI)	2002 n=44 % (95% CI)	2007 n=85 % (95% CI)	2014 n=127 % (95% CI)	1993 n=14 % (95% CI)	2002 n=26 % (95% CI)	2007 n=52 % (95% CI)	2014 n=87 % (95% CI)
Asthma treated	48.0 (28.4-67.6)	56.8 (42.2-71.5)	70.6 (60.9-80.3)	62.2 (53.8-70.6)	57.1 (31.2-83.1)	53.9 (34.7-73.0)	69.2 (56.7-81.8)	58.6 (48.3-69.0)
Current wheeze	60.0 (40.8-79.2)	71.4 (57.8-85.1)	53.7 (42.9-64.5)	48.8 (40.1-57.5) [‡]	64.3 (39.2-89.4)	50.0 (30.8-69.2)	66.7 (53.7-79.6)	35.6 (25.6-45.7)*
Current dyspnea attacks	36.0 (17.2-54.8)	58.1 (43.4-72.3)	39.0 (28.5-49.6)	38.6 (30.1-47.1)	50.0 (23.8-76.2)	38.5 (19.8-57.2)	51.9 (38.3-65.5)	33.3 (23.4-43.2)
Exercise-induced symptoms	80.0 (64.3-95.7)	93.2 (85.7-100.0)	80.3 (71.6-88.9)	63.0 (54.6-71.4)*	78.6 (57.1-100)	92.3 (82.1-100)	82 (72.4-93.0)	60.9 (50.7-71.2)*
Chronic cough	76.0 (59.3-92.7)	79.6 (67.6-91.5)	47.6 (46.8-58.4)	45.7 (37.0-54.3) [†]	57.1 (31.2-83.1)	56.0 (36.5-75.5)	50.0 (36.1-63.9)	37.9 (27.7-48.1) [‡]
Morning cough	64.0 (45.2-82.8)	86.1 (75.7-96.2)	69.5 (78.6-93.4)	59.8 (51.3-68.4)*	57.1 (31.2-83.1)	76.0 (60.1-93.1)	76.0 (65.5-88.4)	52.9 (42.4-63.4)
Dry cough at night	80.0 (64.3-95.7)	77.3 (64.9-89.7)	69.5 (59.6-79.5)	63.0 (54.6-71.4)*	64.3 (39.2-89.4)	69.2 (51.5-87.0)	76.9 (65.5-88.4)	59.8 (49.5-70.1)
Diagnosed allergic rhinitis	16.0 (1.6-30.4)	53.8 (39.8-69.3)	56.0 (45.9-67.0)	48.8 (40.1-57.5)*	21.4 (0.0-42.9)	52.2 (34.7-73.0)	71.7 (58.8-83.5)	35.6 (25.6-45.7)
Diagnosed allergic conjunctivitis	16.0 (1.6-30.4)	41.2 (26.4-55.4)	27.5 (17.6-36.5)	23.6 (16.2-31.0)	14.3 (0.0-32.6)	28.6 (9.9-44.0)	40.9 (27.0-53.7)	19.5 (11.2-27.9)
Diagnosed allergic dermatitis	8.0 (0.0-18.6)	43.8 (28.5-57.8)	37.1 (26.2-46.7)	37.0 (28.6-45.4) [‡]	14.3 (0.0-32.6)	38.1 (19.8-57.2)	27.9 (16.5-41.2)	37.9 (27.7-48.1)
Any allergy or allergic disease	44.0 (24.5-63.5)	86.4 (76.2-96.5)	84.7 (77.1-92.4)	84.3 (77.9-90.6)*	71.4 (47.8-95.1)	80.8 (65.6-95.9)	92.3 (85.1-99.6)	80.5 (72.1-88.8)

* $p < 0.05$ for a linear trend using the chi-squared test for trends

† $p < 0.001$ for a linear trend using the chi-squared test for trends

‡ $p = 0.05$