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ORIGINAL ARTICLE

Epidemiology of Allergic Disease

WILEY

Increased prevalence of allergic asthma from 1996 to 2006 and further to 2016—results from three population surveys

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Summary

Background: During the latter half of the 20th century, the prevalence of asthma and many other allergic diseases has increased. Information on asthma prevalence trends among adults after 2010, especially regarding studies separating allergic asthma from non-allergic asthma, is lacking.

Objective: The aim was to estimate prevalence trends of current asthma among adults, both allergic and non-allergic, from 1996 to 2016.

Methods: Three cross-sectional samples from the same area of Sweden, 20-69 years, participated in surveys with the same questionnaire in 1996 (n=7104 participants, 85% response rate), 2006 (n=6165, 77%) and 2016 (n=5466, 53%), respectively. Allergic rhino-conjunctivitis (ARC) was used as a marker for allergic sensitization to define allergic asthma.

Results: The prevalence of current asthma increased from 8.4% (95% CI: 7.8-9.0) in 1996 to 9.9% (95% CI: 9.2-10.6) in 2006 and 10.9% (95% CI: 10.1-11.7) in 2016 ($P<.001$). Allergic asthma increased from 5.0% (95% CI: 4.5-5.5) in 1996 to 6.0% (95% CI: 5.4-6.6) in 2006 and further to 7.3% (95% CI: 6.6-8.0) in 2016 ($P<.001$), while the prevalence of non-allergic asthma remained stable around 3.4%-3.8%. The increase in current asthma was most pronounced among women and among the middle-aged. Physician-diagnosed asthma, asthma medication use and ARC also increased significantly, while the prevalence of symptoms common in asthma such as wheeze and attacks of shortness of breath decreased slightly or was stable. The prevalence of current smoking decreased from 27.4% in 1996 to 12.3% in 2016.

Conclusions and Clinical Relevance: The prevalence of allergic asthma increased from 1996 to 2006 and further to 2016, while the prevalence of non-allergic asthma remained on a stable prevalence level. The prevalence of symptoms common in asthma decreased slightly or was stable despite a substantial decrease in the prevalence of current smoking. Clinicians should be aware that the previously observed increase in prevalence of allergic asthma is still ongoing.

KEYWORDS
asthma, epidemiology, rhinitis

1 | INTRODUCTION

A worldwide total of >300 million people are estimated to have asthma.[1] It is mainly considered a chronic disease among adults, while remission is more common among children.[2] Asthma affects all ages, with the highest incidence in childhood and teenage[3-5] and highest prevalence in young adulthood,[2,6] and it contributes to high costs for the society.[7] Furthermore, asthma is a heterogenic disease with several phenotypes,[8] traditionally divided into allergic and non-allergic asthma. During the major part of the 20th century, the asthma prevalence has been increasing, while studies in the late 1990s and thereafter present differing prevalence trends, some increasing and some where the increase has levelled off,[6,9-15] the latter especially among children and adolescents.[16-20] The current trends may be associated with changes in environments, and many areas where there still is an ongoing increase are characterized by a Westernized lifestyle and rapid urbanization.[19,21]

The preferred method to estimate prevalence trends is to repeatedly survey large random samples in the same area, within the same age-span and with the same validated methods.[21] Such studies are costly and time-consuming, and as a consequence rarely performed. However, a few studies fulfilling these requirements have presented asthma prevalence trends among adults including results from the 21st century. A study comparing asthma prevalence in 2007 with 1996 in Stockholm, Sweden, reported that the asthma prevalence had reached a plateau,[13] while an Italian study with three cross-sectional surveys concluded that the asthma prevalence, especially for non-allergic asthma, was still increasing between 1991 and 2010.[14] In contrast, the prevalence of allergic asthma increased from 1989 to 1998 in Denmark.[22]

The asthma prevalence differs between regions and is high in north-western Europe including the British Isles and the Nordic countries,[1,21,23] estimated at about 10% of the adult population or even more in recent studies.[1,2,13,15,24] In Sweden, the smoking prevalence has been steadily decreasing by more than half over the last decades, and the prevalence of COPD has decreased.[25] On the other hand, the prevalence of allergic rhinitis, which is associated with asthma, has been increasing.[26] Furthermore, studies of allergic sensitization have shown a high prevalence [27,28] and the prevalence has been increasing in many areas including Sweden, especially among children and teenagers[29] but also among adults.[30-33]

The aim of this study is to estimate prevalence trends of asthma by comparing three cross-sectional surveys of the adult population performed in 1996, 2006 and 2016 in northern Sweden. A further aim is to estimate prevalence trends for both allergic and non-allergic asthma.

2 | METHODS

2.1 | Study area

The study was performed in Norrbotten, the northernmost county of Sweden, where the climate is subarctic with long winters and short but warm summers. The county comprises 25% of the area of Sweden but is sparsely inhabited with a population of about 250 000 (about 48% women) the decades before and after the millennium shift. The study was performed as part of the Obstructive Lung Disease in Northern Sweden (OLIN) Studies and was approved by the Regional Ethical Review Board at Umeå University (Dnr:s 1996-123, 2005-157M and 2015-404-31).

2.2 | Study samples and questionnaire

Three randomly selected cross-sectional study samples, 20-69 years, participated in postal questionnaire surveys in 1996 (n=7104, 85% response rate),[15,34] 2006 (n=6165, 77%)[15] and 2016 (n=5466, 53%), respectively. Overlap between the samples was avoided in the selection procedure. The three surveys were all performed during the same time periods of the year with a starting point in January/February. Two reminders were sent in 1996 and 2006 and three in 2016. The questionnaire was focused on respiratory symptoms, asthma, rhinitis and factors associated with the conditions including smoking. The exact phrasing of the core questions has been identical and is described elsewhere.[15]

2.3 | Definitions

The main outcome *current asthma* was defined as a physician-diagnosed asthma in combination with at least one of (i) attacks of shortness of breath (SOB) last 12 months, (ii) any wheeze last 12 months or (iii) current asthma medication use. Subjects were defined as having allergic rhino-conjunctivitis (ARC) when giving affirmative response to the question "Do you have or have you had allergic nose or eye problems (hayfever)?". Current asthma was divided into *allergic asthma*, defined as current asthma with ARC, and *non-allergic asthma*, defined as current asthma without ARC.

Current smokers reported smoking during the 12 months preceding the survey, while *ex-smokers* reported having quit smoking at least 12 months prior to the study. *Non-smokers* did not report current smoking or ex-smoking. *Socio-economic status* was based on main occupation according to classifications by Statistics Sweden.

2.4 | Statistical analyses

The chi-square test was used to test for differences in proportions and the Mantel-Haenszel test was used for test of linear trend over the 3 years. The Student's *t* test was used for differences in means between two groups and ANOVA for means across more than two groups. *P*-values <.05 were considered statistically significant. The prevalence was age and sex adjusted to the distributions of the county each survey year.

Three different Poisson regression models with current asthma, allergic asthma and non-allergic asthma as outcomes, respectively, were utilized to estimate prevalence ratios (PR) and 95% CI with 1996 as a reference. The models were run both unadjusted and adjusted with (i) year, age and sex, and (ii) year, age, sex, smoking

habits, family history of asthma and socio-economic status included as covariates. These regression analyses were performed among all subjects and in subgroups based on sex, age and presence of ARC. The analyses were also performed by comparing year 2016 and 2006 only, with 2006 as a reference.

2.5 | Sensitivity analyses

An alternative definition of current asthma defined as having both attacks of shortness of breath last 12 months and current asthma medication use, without taking physician diagnosis into account, was analysed. An alternative definition of allergic asthma was also used, based on affirmative answers to getting recurrent breathlessness when exposed to pollen or furred animals. To adjust for differences in response rates, analyses were performed among respondents to the first mailing of the questionnaire only, as well as among respondents to the first and second mailings only. The Poisson regression analyses adjusted for age and sex were also performed with an additional adjustment for postal mailing numbering (number 1-4) in another attempt to adjust for non-response. In order to adjust for possible confounding due to differences in smoking habits between responders in the three surveys, analyses among non-smokers only were performed.

3 | RESULTS

3.1 | Participation and characteristics

The participation rates decreased by study year, from 85% in 1996 (n=7104) to 77% in 2006 (n=6165) and 53% in 2016 (n=5466), and women and subjects of older ages were more likely to participate all years (Table S1).

Among participants in 1996, 2006 and 2016, respectively, the mean age was 44.4, 46.4 and 48.5 years ($P<.001$), and 48.9%, 50.9% and 53.0% were women ($P<.001$). Between the surveys, there was a substantial and significant decrease in both the proportion reporting current smoking (27.4% in 1996, 19.3% in 2006 and 12.3% in 2016) and in the number of cigarettes smoked/day. The proportion of non-smokers increased from 51.1% in 1996 to 58.1% in 2006 and 65.3% in 2016 ($P<.001$). The distribution of socio-economic status also changed significantly between the surveys (Table 1). Among subjects with current asthma, the prevalence of current smoking was 25.5%, 20.3% and 11.5% ($P<.001$) in 1996, 2006 and 2016, respectively, compared to 23.8%, 20.1% and 9.5% ($P<.001$) among subjects with allergic asthma, and 27.9%, 20.7% and 15.2% ($P=.005$) among subjects with non-allergic asthma.

3.2 | Prevalence change

The prevalence of physician-diagnosed asthma, use of asthma medicines and current asthma, respectively, increased significantly over the 20-year period. In all surveys, the prevalence of current asthma was highest among the youngest subjects among which the prevalence did not change over time. The largest increase over time was found among the middle-aged, who also had the lowest prevalence in 1996, and among women. When analysing prevalence change in groups based on year of birth, the prevalence of current asthma increased from 6.7% in 1996 to 9.3% in 2006 and 8.8% in 2016 ($P=.038$) among those born 1947-1956, and from 9.2% in 1996 to 9.5% in 2006 and 12.4% in 2016 ($P=.008$) among those born 1957-1966, while no significant changes occurred among those born in 1967-1976. When analysing allergic and non-allergic asthma separately, the largest increases were seen among those born 1957-1966 but the results did not reach statistical significance. The prevalence of ARC increased significantly from 23.3% in 1996 to 25.1% in 2006 and 28.9% in 2016, but none of the respiratory symptoms increased in prevalence (Table 2). When dividing current asthma into allergic and non-allergic, the prevalence trends differed; non-allergic asthma remained on a constant level around 3.4%-3.8%, while allergic asthma increased, from 5.0% (95% CI: 4.5-5.5) in 1996 to 6.0% (95% CI: 5.4-6.6) in 2006 and 7.3% (95% CI: 6.6-8.0) in 2016 ($P<.001$), and the pattern was similar among men and women (Figures 1 and 2; Figures S1 and S2). The prevalence of having neither asthma nor ARC decreased from 73.5% in 1996 to 68.4% in 2016 ($P<.001$; Figure 2).

In the regression analyses adjusted for age and sex, the proportion with current asthma increased by 18% (95% CI: 6-32%) from 1996 to 2006 and by 32% (95% CI: 18-47%) from 1996 to 2016. When stratified by sex, the increase in current asthma to 2016 was significant among both men and women and was seen mainly among the middle-aged (Table 3). The trend for allergic asthma was more pronounced, with an increase from 1996 by 25% (95% CI: 8-44%) to 2006 and by 53% (95% CI: 33-75%) to 2016 (Table 4). These results remained almost identical after adjustment also for smoking habits, socio-economic status and family history of asthma (Tables S2 and S3). When limiting the adjusted regression analyses to changes from 2006 to 2016, an increase in current asthma by 11%, although non-significant ($P=.057$; Table S4), and in allergic asthma by 21% (95% CI: 6-39%) was observed (Table 4). When adjusted also for smoking habits, socio-economic status and family history, the increase from 2006 to 2016 in current asthma was 14% and significant (95% CI: 3-27%, $P=.015$) and the increase in allergic asthma remained significant (Tables S3 and S4).

3.3 | Prevalence change in subgroups with ARC and physician-diagnosed asthma

Among subjects with physician-diagnosed asthma, the prevalence of current asthma decreased because of a significant decrease in non-allergic asthma. Among subjects with ARC, the prevalence of current asthma increased (Table 5). When adjusted for age and sex in regression models, the prevalence of current asthma among subjects with ARC increased by 13% ($P=.062$) from 1996 to 2006 and by 21% (95% CI: 6.7-38%) from 1996 to 2016. Among subjects without ARC, the prevalence of current asthma remained stable (Table 5)

TABLE 1 Basic characteristics (%) by age group, sex and among all subjects

		Age groups						Sex			
	Year	20-29 y	30-39 y	40-49 y	50-59 y	60-69 y	*P*-value**	Women	Men	*P*-value***	All
Women	1996	48.8%	47.8%	47.3%	48.9%	52.2%	.103	[a]	[a]	[a]	48.9%
	2006	50.6%	49.5%	52.1%	50.9%	50.8%	.819	[a]	[a]	[a]	50.9%
	2016	53.1%	52.9%	55.3%	52.9%	51.6%	.487	[a]	[a]	[a]	53.0%
	P-value*	.151	.082	<.001	.106	.794					<.001
Non-smokers	1996	69.3%	55.0%	41.3%	42.0%	50.8%	<.001	51.9%	50.3%	.182	51.1%
	2006	75.8%	74.0%	56.8%	45.6%	48.1%	<.001	55.2%	61.2%	<.001	58.1%
	2016	76.9%	76.1%	75.5%	60.8%	51.6%	<.001	63.1%	67.7%	<.001	65.3%
	P-value*	<.001	<.001	<.001	<.001	.161		<.001	<.001		<.001
Ex-smokers	1996	9.3%	17.9%	24.9%	26.5%	27.8%	<.001	18.6%	24.1%	<.001	21.5%
	2006	7.8%	13.3%	20.5%	30.1%	34.0%	<.001	22.0%	23.1%	.326	22.5%
	2016	8.3%	12.8%	13.4%	23.9%	29.5%	<.001	21.3%	18.1%	.003	19.8%
	P-value*	.416	.001	<.001	.001	.002		.002	<.001		.001
Current smokers	1996	21.4%	27.1%	33.7%	31.5%	21.3%	<.001	29.4%	25.5%	<.001	27.4%
	2006	16.4%	12.7%	22.7%	24.3%	17.9%	<.001	22.8%	15.7%	<.001	19.3%
	2016	11.1%	8.3%	9.3%	13.3%	15.9%	<.001	13.3%	11.3%	.026	12.3%
	P-value*	<.001	<.001	<.001	<.001	.001		<.001	<.001		<.001
Socio-economic groups based on occupation											
Manual work in industry	1996	20.4%	24.8%	25.9%	23.0%	25.6%	.004	4.2%	42.9%	<.001	24.0%
	2006	12.1%	18.2%	20.3%	25.6%	23.1%	<.001	3.3%	38.4%	<.001	20.6%
	2016	13.1%	15.6%	13.7%	15.8%	15.5%	.312	2.9%	28.4%	<.001	14.9%
	P-value*	<.001	<.001	<.001	<.001	<.001		.015	<.001		<.001
Manual work in service	1996	26.5%	30.3%	27.8%	28.3%	30.2%	.140	42.4%	15.4%	<.001	28.6%
	2006	24.4%	27.7%	30.2%	25.6%	29.1%	.008	38.4%	16.2%	<.001	27.5%
	2016	24.1%	26.1%	23.5%	25.7%	19.3%	<.001	30.8%	14.7%	<.001	23.2%
	P-value*	.368	.097	.002	.163	<.001		<.001	.306		<.001
Assistant non-manual employees	1996	7.8%	11.2%	15.8%	15.9%	14.6%	<.001	16.9%	9.7%	<.001	13.2%
	2006	8.0%	9.3%	14.3%	15.0%	17.4%	<.001	17.2%	9.3%	<.001	13.3%
	2016	8.2%	9.3%	10.4%	11.8%	11.2%	.057	12.9%	7.7%	<.001	10.5%
	P-value*	.953	.192	<.001	.006	<.001		<.001	.024		<.001
Intermediate non-manual employees	1996	10.3%	16.4%	17.3%	19.8%	12.6%	<.001	17.7%	13.4%	<.001	15.5%
	2006	6.0%	21.8%	20.3%	20.3%	16.9%	<.001	20.4%	14.8%	<.001	17.6%
	2016	9.9%	20.0%	28.4%	23.2%	21.2%	<.001	25.8%	15.9%	<.001	21.1%
	P-value*	.001	.003	<.001	.062	<.001		<.001	.025		<.001
Professionals, executives, self-employed non-Professionals	1996	3.0%	7.3%	8.1%	8.3%	7.7%	<.001	4.4%	9.4%	<.001	7.0%
	2006	2.9%	8.7%	8.5%	9.0%	7.0%	<.001	5.4%	9.6%	<.001	7.5%
	2016	3.3%	11.0%	15.5%	14.0%	11.1%	<.001	8.5%	14.7%	<.001	11.4%
	P-value*	.886	.015	<.001	<.001	<.001		<.001	<.001		<.001
Students, housewives or unable to classify	1996	32.0%	9.9%	5.0%	4.7%	9.3%	<.001	14.3%	9.1%	<.001	11.7%
	2006	46.7%	14.4%	6.5%	4.5%	6.6%	<.001	15.2%	11.7%	<.001	13.5%
	2016	41.4%	18.0%	8.6%	9.5%	21.8%	<.001	19.2%	18.6%	.653	18.9%
	P-value*	<.001	<.001	.001	<.001	<.001		<.001	<.001		<.001

*P-value, chi-square test of difference in prevalence between years.

**P-value, chi-square test of difference in prevalence between age groups.

***P-value, chi-square test of difference in prevalence between women and men.

[a]Not applicable. Approximately 1% lacks data on smoking habits each survey.

TABLE 2 Prevalence (%) of asthma, asthma medicine use and respiratory symptoms, by age groups, sex and among all subjects

		Age groups						Sex				
	Year	20-29 y	30-39 y	40-49 y	50-59 y	60-69 y	*P*-value**	Women	Men	*P*-value***	All	All[a]
Current asthma	1996	10.4%	9.2%	6.7%	6.2%	10.0%	<.001	8.6%	8.1%	.451	8.4%	8.4%
	2006	12.6%	10.0%	9.5%	9.3%	8.6%	.025	10.8%	8.8%	.007	9.8%	9.9%
	2016	12.5%	10.2%	11.2%	12.4%	8.8%	.010	12.1%	9.4%	.001	10.8%	10.9%
	P-value*	.104	.429	<.001	<.001	.277		<.001	.087		<.001	
Physician-diagnosed asthma	1996	11.8%	10.1%	7.7%	6.8%	10.7%	<.001	9.4%	9.3%	.899	9.3%	9.4%
	2006	15.6%	12.1%	10.8%	10.6%	9.5%	<.001	12.4%	10.5%	.020	11.5%	11.5%
	2016	16.6%	13.1%	13.7%	13.7%	10.1%	<.001	14.4%	11.5%	.002	13.0%	13.3%
	P-value*	.001	.030	<.001	<.001	.654		<.001	.004		<.001	
Asthma medicine use	1996	11.8%	11.8%	9.5%	10.0%	11.7%	.101	12.2%	9.7%	.001	10.9%	10.9%
	2006	14.1%	11.9%	11.7%	12.6%	12.0%	.426	13.7%	11.0%	.001	12.4%	12.3%
	2016	14.0%	13.1%	14.3%	14.2%	12.3%	.518	14.9%	11.9%	.001	13.5%	13.4%
	P-value*	.120	.432	<.001	.001	.637		.001	.005		<.001	
Asthmatic wheeze last 12 months	1996	7.8%	7.8%	6.3%	8.1%	9.6%	.031	7.6%	8.1%	.446	7.9%	7.8%
	2006	8.3%	5.8%	7.3%	8.2%	7.1%	.159	7.6%	7.2%	.519	7.4%	7.4%
	2016	8.2%	6.9%	7.3%	7.2%	6.8%	.794	7.9%	6.5%	.051	7.2%	7.3%
	P-value*	.730	.256	.292	.404	.008		.703	.016		.175	
Recurrent wheeze	1996	12.1%	13.6%	12.2%	13.8%	15.6%	.056	14.1%	12.8%	.119	13.4%	13.3%
	2006	10.3%	11.1%	11.8%	13.8%	12.3%	.082	11.9%	12.2%	.765	12.1%	12.0%
	2016	10.7%	10.5%	12.2%	12.1%	11.8%	.697	11.8%	11.3%	.555	11.6%	11.5%
	P-value*	.252	.021	.961	.197	.003		.006	.082		.002	
Any wheeze last 12 months	1996	18.4%	19.1%	16.5%	19.0%	20.3%	.116	19.6%	17.6%	.030	18.6%	18.5%
	2006	20.8%	17.7%	17.5%	19.7%	17.6%	.147	19.0%	18.2%	.423	18.6%	18.6%
	2016	19.4%	16.7%	18.2%	18.7%	17.5%	.630	19.4%	16.7%	.010	18.1%	18.0%
	P-value*	.454	.156	.266	.857	.065		.797	.408		.517	
Attacks of shortness of breath	1996	13.7%	14.3%	13.7%	14.4%	16.2%	.345	16.4%	12.6%	<.001	14.4%	14.4%
	2006	15.2%	13.0%	13.3%	13.5%	12.3%	.363	14.3%	12.4%	.033	13.3%	13.3%
	2016	14.5%	12.4%	14.4%	14.2%	11.3%	.065	15.2%	10.9%	<.001	13.2%	13.2%
	P-value*	.536	.187	.706	.833	<.001		.162	.061		.038	
Allergic rhino-conjunctivitis	1996	30.1%	27.9%	21.9%	18.8%	16.4%	<.001	24.3%	21.8%	.014	23.0%	23.3%
	2006	30.4%	30.1%	27.4%	23.2%	15.9%	<.001	26.6%	23.0%	.001	24.8%	25.1%
	2016	31.7%	31.2%	33.2%	28.9%	20.1%	<.001	27.8%	27.8%	.993	27.8%	28.9%
	P-value*	.445	.094	<.001	<.001	.007		.001	<.001		<.001	

**P*-value, Mantel-Haenszel test for trend over the 3 y.
***P*-value, chi-square test of difference in prevalence between age groups.
****P*-value, chi-square test of difference in prevalence between women and men.
[a]All, Standardized according to the age and sex distribution of the population in the county of Norrbotten.

and the adjusted regression analyses confirmed the unchanged prevalence.

3.4 | Sensitivity analyses

The sensitivity analyses confirmed the main findings of an increase in allergic asthma, and a constant prevalence of non-allergic asthma. These main findings were not affected to any relevant or significant magnitude by differences in response rates, smoking or the definitions of asthma or allergic asthma used in the main analyses (Table S5).

4 | DISCUSSION

The main results of this study were that the prevalence of current asthma increased from 8.4% in 1996 to 9.9% in 2006 and to 10.9% in 2016. The increase was mainly observed among the middle-aged and women and was explained by a continuing increase in allergic asthma, from 5.0% in 1996 to 6.0% in 2006 and further to 7.3% in 2016, while the prevalence of non-allergic asthma remained stable around 3.4%-3.8%. The use of asthma medication and the prevalence of ARC also increased, while the prevalence of wheeze and

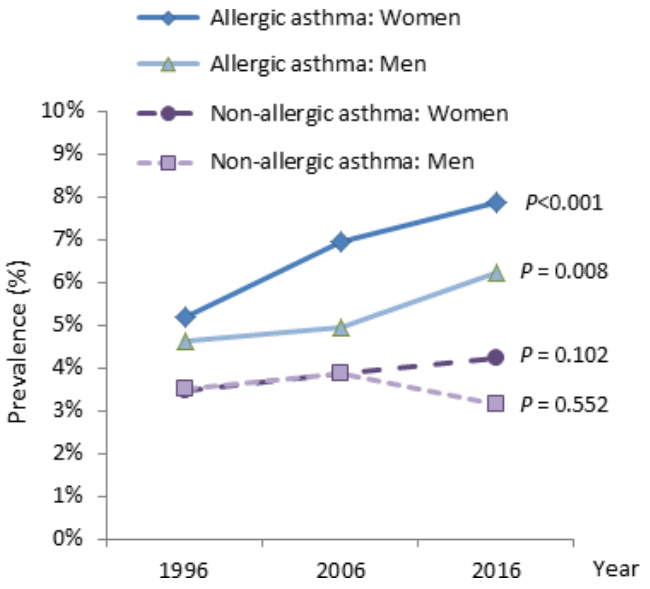

FIGURE 1 Prevalence of allergic and non-allergic asthma, respectively, among men and women. *P*-value for trend across the 3 y

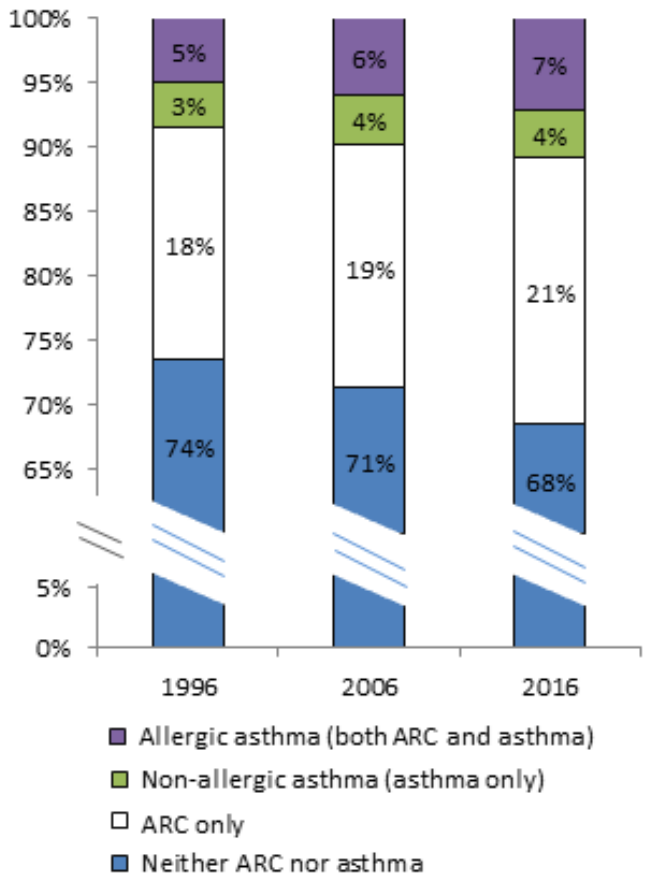

FIGURE 2 Prevalence of allergic asthma, non-allergic asthma, allergic rhino-conjunctivitis only and never asthma or allergic rhino-conjunctivitis in 1996, 2006 and 2016

attacks of shortness of breath decreased slightly or remained stable over the three surveys despite a major reduction in smoking.

The results showed that the prevalence of current asthma among the youngest subjects, who also had the highest prevalence already in 1996, did not increase. Instead, the prevalence of current asthma increased most among the middle-aged (40-59 years) and reached similar levels in 2016 as among 20-29 year olds in 1996. Thus, it is possible that the worldwide increase which previously has been most pronounced among younger subjects[21] has persisted into the middle ages of today. Changes in, for example, lifestyle and urbanization patterns may have affected the younger and middle ages of today at different time-points in their lives. The increase in current asthma was driven by increased prevalence among subjects born 1947-1966, that is after the Second World War when the living conditions improved considerably in the society, in line with results of increased prevalence especially among children after the 1950s.[21] The observed increase in asthma prevalence could not be explained by parallel changes in smoking habits, age and sex distributions, family history of asthma or socio-economic status. However, several other factors associated with asthma which were not included in our study have changed during the last decades, including dietary habits, sedentary lifestyle and obesity, which could contribute to the increased asthma prevalence.[2,21,35,36] On the other hand, decreased exposure to environmental tobacco smoke, occupational exposures and air pollution levels could hypothetically have led to a lower prevalence.[35,37] Before 1997 asthma medication was entirely subsidized in Sweden and it is possible that subjects with, for example, COPD received an asthma diagnosis in 1996 due to several reasons, one of them being the free medicines. Thus, the increased use of asthma medication after 1996 implies a real increase in demand, although increased marketing of asthma medications and disease mongering also may have contributed.

Specifically, our results showed that it was the allergic asthma that increased, while the non-allergic asthma remained on a constant prevalence level. As smoking is not a risk factor for allergic sensitization,[28,30] the diverging trends in ARC and allergic asthma vs smoking were unsurprising. Therefore, it is likely that the allergic asthma phenotype will remain a public health concern also in the future. Allergic sensitization is an important risk factor for asthma, especially among children and teenagers, and the prevalence of allergic sensitization has increased markedly in north-western Europe.[28-33,38-41] In the entire cohorts, we lacked objective measurements of allergic sensitization why we used ARC as a marker for sensitization. However, in randomly selected samples of the cohorts from 1996 and 2006, we have analysed allergic sensitization objectively. Among subjects aged 20-40 years in the 2006 cohort, 83% of those reporting allergic rhinitis had elevated specific IgE levels to any allergen which implies that ARC was a good marker for allergic sensitization.[42] Our definition of allergic asthma is also supported by a recent publication where 65% of subjects with asthma and ARC were polysensitized.[43]

There are few studies of asthma prevalence change over time among adults, but some large studies in Europe[6,9,10,14,24,44-46] and in other countries[11,12] have repeatedly surveyed large enough random samples in the same area, within the same age-span and with the same validated methods. Studies on male Swedish conscripts have

TABLE 3 Unadjusted and adjusted prevalence ratios (PR) for current asthma in 2006 and 2016 with 1996 as reference, by age group, sex and among all subjects

		Unadjusted analyses				Adjusted analyses			
		Year 2006 vs 1996		Year 2016 vs 1996		Year 2006 vs 1996		Year 2016 vs 1996	
		n=6165		n=5466		n=6165		n=5466	
	Strata	PR	(95% CI)	PR	(95% CI)	PR	(95% CI)	PR	(95% CI)
Age group	20-29 y	1.22	(0.97-1.53)	1.20	(0.95-1.53)	1.23	(0.97-1.55)	1.20	(0.95-1.53)
	30-39 y	1.08	(0.85-1.38)	1.11	(0.84-1.45)	1.08	(0.85-1.37)	1.10	(0.84-1.43)
	40-49 y	**1.41**	**(1.10-1.81)**	**1.66**	**(1.29-2.13)**	**1.40**	**(1.09-1.79)**	**1.63**	**(1.26-2.10)**
	50-59 y	**1.50**	**(1.16-1.92)**	**1.98**	**(1.55-2.53)**	**1.51**	**(1.18-1.94)**	**1.99**	**(1.56-2.53)**
	60-69 y	0.86	(0.68-1.10)	0.88	(0.70-1.10)	0.87	(0.68-1.10)	0.88	(0.70-1.11)
Sex	Women	**1.25**	**(1.08-1.45)**	**1.40**	**(1.21-1.62)**	**1.27**	**(1.09-1.47)**	**1.43**	**(1.24-1.66)**
	Men	1.08	(0.92-1.27)	1.15	(0.98-1.35)	1.10	(0.94-1.29)	**1.19**	**(1.01-1.40)**
All subjects		**1.17**	**(1.05-1.31)**	**1.29**	**(1.16-1.44)**	**1.18**	**(1.06-1.32)**	**1.32**	**(1.18-1.47)**

Adjustment by Poisson regression with current asthma as outcome and year of study, age (continuous) and sex as covariates.
In the separate models for women and men, the models are not adjusted for sex.
Bold figures indicate statistical significance ($P<.05$).

TABLE 4 Adjusted prevalence ratios (PR) for allergic and non-allergic asthma in 2006 and 2016, by sex and among all subjects

		Year 2006 vs 1996		Year 2016 vs 1996		Year 2016 vs 2006	
	Strata	PR	(95% CI)	PR	(95% CI)	PR	(95% CI)
Allergic asthma	Women	**1.37**	**(1.13-1.36)**	**1.59**	**(1.32-1.92)**	1.15	(0.96-1.37)
	Men	1.11	(0.90-1.38)	**1.47**	**(1.19-1.31)**	**1.32**	**(1.06-1.63)**
	All subjects	**1.25**	**(1.08-1.44)**	**1.53**	**(1.33-1.75)**	**1.21**	**(1.06-1.39)**
Non-allergic asthma	Women	1.11	(0.87-1.43)	1.20	(0.93-1.54)	1.09	(0.85-1.40)
	Men	1.07	(0.84-1.37)	0.84	(0.64-1.11)	0.79	(0.60-1.05)
	All subjects	1.09	(0.91-1.30)	1.02	(0.85-1.23)	0.95	(0.79-1.14)

Allergic asthma, current asthma with allergic rhino-conjunctivitis.
Non-allergic asthma, current asthma without allergic rhino-conjunctivitis.
Adjustment by Poisson regression with asthma as outcome and year of study, age (continuous) and sex as covariates.
In the separate models for women and men, the models are not adjusted for sex.
Bold figures indicate statistical significance ($P<.05$).

shown a continuous increase in the prevalence of asthma from the 1960s to the 1990s (Figure 3).[44,46] Among adults in Norway and Denmark, the prevalence of asthma increased from the 1970s to the 1990s[6,10] and in Denmark further to 2004.[45] A study from 1996 to 2006, very similar to ours, in the capital of Finland reported an increase in physician-diagnosed asthma partly due to increased diagnostic recognition but also a parallel increase in ARC which supported a true increase in asthma prevalence.[24] Italy is a country with an average asthma prevalence and rather high smoking prevalence where a large proportion of people with asthma lack treatment, and a continuing increase in both current asthma and allergic rhinitis was observed from 1991 to 2010 in three cross-sectional studies of subjects aged 20-44 years.[14] The prevalence of wheezing and shortness of breath was stable between the first two surveys, while it increased between the second and third survey.[14,47] In that Italian study, the increase in current asthma was observed mainly among subjects without a report of allergic rhinitis,[14] which contrasts to our results. Another Italian study over 25 years also found an increase in asthma prevalence until 2011.[48] Results on asthma prevalence trends among adults are lacking for the time-period after 2011, why our up-to-date results of an ongoing increase add important knowledge to this field.

In South Australia, the prevalence of asthma increased from 1990 (7.5%) to 1997 (12.3%), but thereafter it remained stable until 2003 (12.2%).[11] In Busselton, Western Australia, the prevalence of physician-diagnosed asthma in ages 18-54 years increased from 1990 to 2005-2007, while recent wheeze tended to decrease and combinations of physician-diagnosed asthma, wheeze and hyperresponsiveness were on level.[12] At the same time, the prevalence of atopy, however only among men, and obesity increased. The authors concluded that the increase in asthma since the 1980s partly was explained by increased symptoms and atopy, and partly by diagnostic transfer and increased awareness of asthma.[12] In contrast, the authors of a study in the UK among adults aged 20-44 years concluded that the entire increase in physician-diagnosed asthma, asthma medicine use and respiratory symptoms they observed from

TABLE 5 Prevalence (%) of current asthma, asthma medicine use, respiratory symptoms and smoking among subjects with and without allergic rhino-conjunctivitis (ARC) and among subjects with physician-diagnosed asthma

		ARC		With physician-diagnosed asthma
	Year	Without	With	
Current asthma	1996	4.5%	21.4%	90.0%
	2006	5.2%	24.1%	86.0%
	2016	5.2%	25.5%	83.1%
	P-value*	.125	.006	<.001
Allergic asthma	1996	N/A	21.4%	52.7%
	2006		24.1%	52.1%
	2016		25.5%	54.5%
	P-value*		.006	.501
Non-allergic asthma	1996	4.5%	N/A	37.3%
	2006	5.2%		33.9%
	2016	5.2%		28.7%
	P-value*	.125		.001
Asthma medicine use	1996	6.1%	27.1%	80.2%
	2006	6.8%	29.3%	75.5%
	2016	6.9%	30.6%	74.6%
	P-value*	.104	.029	.014
Any wheeze last 12 months	1996	13.5%	35.4%	72.1%
	2006	13.2%	35.0%	63.7%
	2016	12.1%	33.7%	61.8%
	P-value*	.043	.316	<.001
Attacks of SOB last 12 months	1996	8.9%	32.9%	73.9%
	2006	7.9%	30.0%	66.0%
	2016	6.9%	29.4%	61.4%
	P-value*	<.001	.033	<.001
Current smoking	1996	28.3%	24.4%	24.7%
	2006	20.2%	16.7%	19.9%
	2016	13.3%	10.0%	11.1%
	P-value*	<.001	<.001	<.001
Non-smoking	1996	49.8%	55.5%	49.8%
	2006	56.8%	62.1%	53.9%
	2016	63.3%	70.3%	67.3%
	P-value*	<.001	<.001	<.001

ARC, Allergic rhino-conjunctivitis; SOB, shortness of breath.
**P*-value, Mantel-Haenszel test for trend over the 3 y.

1992-1993 to 1998-1999 resulted from increased awareness about asthma and diagnostic practices and not from a true increase in prevalence.[9] Thus, the prevalence trends among adults differ in different parts of the world, which also has been clearly demonstrated among both children and teenagers,[16] and the interpretations of study results also differ. However, recent review papers analysing asthma prevalence trends have concluded that the observed increase partly, but not entirely, is related to increased awareness and diagnostic practices. They further conclude that results after 1990 are conflicting, but that the prevalence among adults now may be stabilizing or even decreasing especially in some high-prevalence Westernized areas.[19,21,23] Our results indicate increasing diagnostic practices including milder disease, as observed in children in the same area,[49] but also a real increase in allergic asthma as both the prevalence of ARC increased and the prevalence of current asthma increased among subjects with ARC. The parallel increase in allergic rhinitis in Sweden[26] and Finland,[24] the increase in allergic asthma symptoms in Denmark[22] and the increase in allergic sensitization in Sweden among both children and adults[28-30] (an objective measure not affected by increased awareness in the society) support a real increase in allergic asthma.

4.1 | Strengths and limitations

A limitation of the study is the marked decrease in participation rates by time, which may have biased the prevalence estimates, especially among the youngest subjects where the decreasing participation was most pronounced. This is a general problem in several areas. For instance, participation rates decreased from 84% in 1976-1989 to 55% in 2001-2004 in Denmark[45] and from 86% in 1991-1993 to 57% in 2007-2010 in Italy.[14] However, our efforts to control for differences in participation rates between surveys confirmed the main findings. COPD is an under-diagnosed disease and it is likely that misclassification of COPD as asthma among the elderly occurred less frequently in 2016 than in the earlier surveys.[15] This may explain why no increase in asthma was found in recent years in these ages. On the other hand, as the prevalence of ARC increased significantly among the elderly also an increase in asthma could have been expected. More clinical studies about asthma and rhinitis among elderly are warranted. Furthermore, studies on asthma incidence among adults are scarce, but previous studies in northern Sweden revealed a high incidence during the late 20th century,[50]

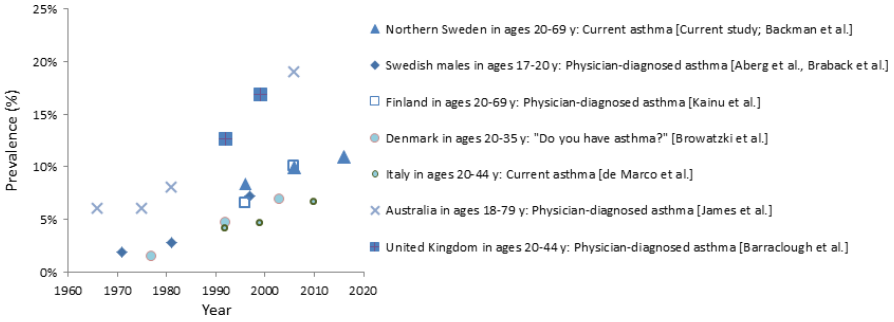

FIGURE 3 Repeated surveys of asthma prevalence among adults in the general population, with the same methods within the same age-span and area

results in line with a higher prevalence some years later. Increased diagnostic practices and awareness of asthma in the society may affect the prevalence of physician-diagnosed asthma, which in turn may also include remittent asthma. To avoid these biases, current asthma and current asthma symptoms were used. Our study merits from the random sampling of three large cross-sectional samples 10 years apart within the same age-span and geographical area and from the use of the same validated questionnaire in all three surveys. The increase in objectively measured allergic sensitization in the same area[28-30] further supports the finding of an increased prevalence of allergic asthma.

5 | CONCLUSION

In summary, the prevalence of current asthma increased from 1996 to 2016, mainly among the middle-aged and women. The increase was explained by a continuing increase in allergic asthma from 1996 to 2006 and then further from 2006 to 2016, while the prevalence of non-allergic asthma remained stable in all three surveys.

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CONFLICTS OF INTERESTS

The authors have the following conflict of interests to declare: Dr. Backman reports personal fees from Boehringer Ingelheim outside the submitted work; Mr. Räisänen, Dr. Hedman, Dr. Stridsman and Dr. Andersson have nothing to disclose; Dr. Lindberg reports personal fees from AstraZeneca, personal fees from Novartis, personal fees from ActiveCare and personal fees from Boehringer Ingelheim outside the submitted work; Dr. Lundbäck reports grants from AstraZeneca, grants from GSK, personal fees from GSK, personal fees from AstraZeneca and personal fees from Novartis outside the submitted work; Dr. Rönmark reports unconditional grants from The Swedish Heart & Lung Foundation, The Swedish Research Council, ALF—a regional agreement between Umeå University and Norrbotten County Council, Norrbotten County Council, The Swedish Asthma-Allergy Foundation and Visare Norr during the conduct of the study.

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SUPPORTING INFORMATION

Additional Supporting Information may be found online in the supporting information tab for this article.

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