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Early View

Original article

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Please cite this article as: Räisänen P, Backman H, Hedman L, *et al*. High but stable incidence of adult-onset asthma in northern Sweden over the last decades. *ERJ Open Res* 2021; in press (https://doi.org/10.1183/23120541.00262-2021).

High but stable incidence of adult-onset asthma in northern Sweden over the last decades.

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Take home message: The incidence of adult-onset asthma adults has been stable in Sweden over the last 30 years, but the relatively high incidence rate in combination with low remission rate in adulthood contributes to the reported increase in asthma prevalence among adults.

Word count: 2985 **Abstract**: 248

Number of tables: 4 + 1 supplemental table **Numbers of figures**: 2

Abstract

Background: The prevalence of asthma has increased both among children and adults during the latter half of the 20th century. The prevalence among adults is affected by the incidence of asthma in childhood but also in adulthood. Time trends in asthma incidence are poorly studied.

Aim: The aim was to study the incidence of adult-onset asthma from 1996-2006 and 2006-2016, and compare the risk factor patterns.

Methods: Within the Obstructive Lung Disease in Northern Sweden (OLIN) studies, two randomly selected population-based samples in ages 20-69 years participated in postal questionnaire surveys about asthma in 1996 (n=7104, 85%) and 2006 (n=6165, 77%), respectively. A 10-year follow-up of the two cohorts with the same validated questionnaire was performed, and n=5709 and n=4552, respectively, responded. Different definitions of population at risk were used in the calculations of asthma incidence. The protocol followed a study performed 1986 to 1996 in the same area.

Results: The crude incidence rate of physician-diagnosed asthma was 4.4/1000/year (men 3.8, women 5.5) from 1996-2006, and 4.8/1000/year (men 3.7, women 6.2) from 2006-2016. When correcting for possible under-diagnosis at study entry, the incidence rate was 2.4/1000/year from 1996-2006 and 2.6/1000/year from 2006-2016. The incidence rates were similar across age groups. Allergic rhino-conjunctivitis was the main risk factor for incident asthma in both observation periods (risk ratios 2.4-2.6).

Conclusions: The incidence of adult-onset asthma has been stable over the last two decades, and on similar level since the 1980s. The high incidence contributes to the increase in asthma prevalence.

Introduction

The prevalence of asthma is frequently studied and a consistent pattern of a worldwide increase during the latter half of the 20th century has been reported, although the increase may have leveled off in some areas [1,2]. The reason for the increase is unclear, but changes in lifestyle, environments, and rapid urbanization may have contributed [1,3-5]. Prevalence is mainly a function of incidence and remission. In adulthood, asthma is regarded as a chronic disease due to low remission [6,7], why the prevalence among adults is a result of the high incidence in childhood and adolescence [8-11] with persistence into adulthood, but also due to the relatively high incidence in adulthood [4,12-24]. However, incidence studies of adult-onset asthma are scarce, particularly longitudinal population-based studies.

Comparing incidence rates of asthma is complex as the results are highly sensitive to the age of the study population and the methods used. Reported incidence estimates vary substantially but are higher among children and teenagers, 10-30/1000/year [8-11,20], than among adults, 0.2-5/1000/year [4,12-24]. Results from retrospective [11,13,22,24,25] and register studies [13] tend to generate lower incidence rates than prospective studies [11-21,25]. The definitions of both the outcome and the population at risk significantly influences the incidence rate [12,15,18,19], which highlights the importance of using the same methods and definitions to enable comparisons of results from different studies and over time. Three studies in Sweden or the neighboring countries, whereof one in the same area as the current study, based on identical methods reported similar incidence rates of physician-diagnosed asthma among adults from the 1980's up until 2006, 2-3/1000/year [15,16,18], but it is unknown if the incidence has changed thereafter. As the prevalence of asthma in adults has increased in Sweden during the last decades [2,26] we hypothesized

that the incidence of adult-onset asthma still is high or even has increased during the same period. Thus, the main aim of the current study was to estimate the incidence of adult-onset asthma during the period 1996 to 2016 by surveys of two cohorts each followed for ten years, one from 1996 to 2006 and the other from 2006 to 2016. A further aim was to identify risk factors for adult-onset asthma.

Material and Methods

Study population

The study was performed within the Obstructive Lung Disease in Northern Sweden (OLIN) Studies. All surveys were approved by the Regional Ethical Review Board at Umeå University.

The present paper is based on two random population samples, each followed for ten years. The first sample consists of participants from a postal questionnaire survey of a general population sample in ages 20-69 years, performed in 1996 (n=7104, 85% response rate) [2]. This cohort was followed up with the same questionnaire in 2006, when 5709 individuals participated (80% response rate). The second sample was recruited in 2006 with identical methods (n=6165, 77% response rate) [2], and followed up in 2016 (n=4552, 74% response rate). Individuals from these two cohorts that participated both at baseline and at the follow-up constitute the study populations in the current paper, n=5709 from cohort recruited in 1996 and n=4552 from the cohort recruited in 2006 (Table 1). The surveys were all performed during the same time period of the year, January to May. We have previously published incidence rates of adult-onset asthma based on a cohort recruited in 1986 in similar ages and in the same area, which was followed-up in 1992 [12] and 1996 [15]. The

calculations of incidence in the current paper followed the same protocol as in these previous studies.

Questionnaire

The OLIN questionnaire was used in all surveys. It was originally developed from the British Medical Research Council questionnaire and has been validated against physiological variables [27]. It has been used within the OLIN since 1986 and frequently in other studies of asthma and respiratory diseases in Sweden and other countries [18,19,24,26].

Definitions

The main outcome was physician-diagnosed asthma. The definitions for asthma and respiratory symptoms were based on the following questions:

Physician-diagnosed asthma: ''Have you been diagnosed as having asthma by a physician?''

Ever asthma: ''Have you ever had asthma?''

Asthma medication use: ''Do you currently use asthma medicines (on a regular basis or as needed)?''

Family history of asthma: "Have any of your parents or siblings asthma, or have they had asthma?"

Recurrent wheeze: ''Do you usually have wheezing or whistling in your chest when breathing?''

Attacks of shortness of breath (SOB): Affirmative answer to both ''Do you presently have, or have had in the last 10 years, asthma symptoms (intermittent breathlessness or attacks of shortness of breath; the symptoms may exist simultaneously with or without cough or wheezing)'' and ''Have you had these problems within the last year?''

Allergic rhino-conjunctivitis (ARC) "Do you have or have you had allergic nose or eye problems (hayfever)?"

Smoking habits: Smoking habits were divided into non-smokers, ex-smokers (quit smoking at least 12 months prior to the survey) and smokers (smoked during the 12 months preceding the survey)

Classification of socioeconomic status was based on main occupation and categorized into three groups; professionals, non-manual workers, and manual workers according to classifications by Statistics Sweden.

Statistical analyses

The analyses were performed using the software IBM SPSS Statistics for Windows, v26, Armonk, New York, USA. Internal missing on specific questions was low in all surveys, <5 %. Internal missing about asthma and respiratory symptoms was treated as a negative response while internal missing about exposures was treated as missing. The chi-square test was used to test for differences in proportions and the Students t-test for differences in means. Poisson regression analysis with physician-diagnosed asthma as outcome was utilized to estimate risk ratios (RR) with 95% CI. The models were analyzed both unadjusted and adjusted with age, sex, allergic rhino-conjunctivitis, family history of asthma, smoking habits and socioeconomic status included as covariates.

The cumulative incidence of physician-diagnosed asthma was estimated from two models of defining the population at risk. In model A, individuals with any of the following variables at baseline were excluded from the population at risk: physician-diagnosed asthma, ever having had asthma, asthma medication use, recurrent wheeze or attacks of SOB last 12 months. In model B, individuals were excluded from the population at risk if reporting having

physician-diagnosed asthma at baseline. The cumulative incidence of asthma medication use and recurrent wheeze was also estimated by model A and B, and additionally by a third model C, where the population at risk excluded those reporting asthma medication use at baseline when asthma medication use was analyzed as the outcome variable, and where the population at risk excluded those reporting recurrent wheeze at baseline when recurrent wheeze was the outcome. As we did not have complete data on person-years we used the cumulative incidence over the ten years observation period in each cohort to estimate annual incidence rate by assuming the incidence to be constant. The estimated annual incidence rate was calculated as $Incidence\ rate = \frac{a}{(10\times(b-\left(\frac{a}{2}\right))}$ where a is the number of incident cases and b the number of subjects in the population at risk at the start of the study, as also estimated in other studies [15,18,19].

Results

Baseline characteristics of the cohorts

In both cohorts the response rate was higher among women both at baseline and at the follow-ups (Table 1). The mean age of the individuals was 44.6 years in the cohort recruited in 1996 and 47.7 years in the cohort recruited in 2006. Smoking was more common in 1996 than 2006 (27.4% vs. 19.3%). Women reported significantly higher prevalence of attacks of SOB, allergic rhino-conjunctivitis and use of asthma medication than men in both cohorts (Table 2).

Incidence rates

According to model A, the incidence rate of physician-diagnosed asthma for the period 1996 to 2006 was 2.4/1000/year (in total 108 new cases during the ten year follow up) with minor differences between sex and age groups. Incidence of asthma medication use was higher among women than men (4.7/1000/year vs 3.4/1000/year, p=0.028). The incidence rate of asthma for the period 2006 to 2016 was 2.6/1000/year (in total 93 new cases), and higher among women than men (3.5/1000/year vs 1.7/1000/year, p=0.001). The incidence of asthma medication use was also higher among women than men (5.7/1000/year vs 3.3/1000/year, p=0.001) (Table 3).

According to model B, the incidence of physician-diagnosed asthma for the period 1996 to 2006 was 4.4/1000/year (in total 225 new cases) and the incidence of asthma medication use was 7.4/1000/year. For the period 2006 to 2016 the corresponding incidence rates were 4.8/1000/year (in total 188 new cases) and 8.3/1000/year, respectively. These incidence estimates were all significantly higher among women (Table 3).

According to model C, where the population at risk only excluded those reporting the outcome variable at baseline, the incidence rates of asthma medication use and recurrent wheeze were in between the estimations from models A and B. The incidence of recurrent wheeze did not differ by sex in any model or observation period (Table 3).

Risk factors and respiratory symptoms of incident asthma

In an adjusted Poisson regression analysis, allergic rhino-conjunctivitis was a significant risk factor for incident physician-diagnosed asthma, defined by model A, in both observation

periods, with RR 2.62 (1.69-4.07) and RR 2.39 (1.48-3.87), respectively (Table 4). Female sex was a significant risk factor in the observation period 2006 to 2016, RR 1.99 (1.22-3.25) but not from 1996 to 2006. Family history of asthma was a borderline risk factor for the period 1996 to 2006, RR 1.50 (0.93-2.43), but significant from 2006 to 2016, RR 1.75 (1.05-2.90). Ex-smoking was a borderline risk factor from 1996 to 2006.

The same analysis as above yielded a closely similar pattern also according to model B with family history of asthma, allergic rhino-conjunctivitis, female sex and ex-smoking as significant risk factors for incident physician-diagnosed asthma during the period 1996 to 2006. The same risk factors, except ex-smoking, were found for the period 2006 to 2016 (Supplemental Table 1).

Among individuals with adult-onset asthma in the cohort observed from 1996 to 2006, 70% reported attacks of SOB last 12 months, 43% allergic rhino-conjunctivitis, and 83% used asthma medication at the follow up in 2006. The corresponding figures for individuals with adult-onset asthma in the cohort observed from 2006 to 2016 were 65%, 44% and 80%, respectively, and these figures did not differ significantly between incident cases in the two cohorts.

Discussion

The main finding of these prospective population-based cohort studies was that the incidence of adult-onset asthma in Northern Sweden was stable from 1996 to 2016, and at similar level as from 1986 to 1996 [12,15]. Thus, the reported increase in asthma prevalence during the last decades is not explained by an increase in adult-onset asthma incidence, but by the stable and relatively high incidence, 2-3/1000/year. The incidence was consistently higher among women than men. In analyzes adjusted for covariates, allergic rhino-conjunctivitis was the main risk factor for adult-onset asthma in both periods.

To the best of our knowledge we are the first to report about trends in adult-onset asthma incidence over several decades. A review article including incidence studies from 1950s to 1990s indicated an increase in incidence rate by time, however, the methods varied substantially between the included studies [28]. Three longitudinal population-based studies performed in Sweden and neighboring countries during the 1980´s and 1990´s with almost identical methods found incidence rates of 2-3/1000/year [15,16,18]. Our results, 2.4/1000/year from 1996 to 2006 and 2.6/1000/year from 2006 to 2016, are in line with these studies, including the previous study in our region (Figure 1) [15], and indicate a continuing stable trend in incidence rate in Sweden as a whole. However, an incidence rate of 2-3/1000/year in combination with low remission of asthma in adulthood [6,7,18] and similar mortality among adults with asthma as in the general population, means about 1% unit increase in prevalence every ten years and thus contribute to the slowly increasing prevalence of asthma among adults.

Only a limited number of incidence studies of adult-onset asthma are based on prospective longitudinal population-based studies [12-21,23]. These studies show considerable variation in results, 0.7-6/1000/year due to variations in the study design [11,13,14,25], and the definitions of the outcome and the population at risk [12, 14-16,18]. Studies ending up with high incidence rates have often not excluded individuals with symptoms common in asthma from the population at risk. To enable valid comparisons between different studies it is paramount to use identical methods.

Symptoms of asthma may occur several years before a diagnosis of asthma is made and these symptoms may reflect undiagnosed asthma in the population, why the incidence rate may be overestimated. To reduce this bias it is reasonable to also exclude subjects reporting symptoms of asthma from the population at risk. When comparing different populations at risk (model A vs B) we found that the difference in incidence rate of physician-diagnosed asthma between the two models was much smaller in the two current cohorts under study compared with the study from the 1980s which was performed with almost identical methods in the same area (Figure 1). When using model B (not correcting for possible under-diagnosis), the incidence of physician-diagnosed asthma was 4.4-4-8/1000/year in the current cohorts, while it was 8/1000/year in the 1980s cohort [12]. This may reflect a decrease in under-diagnosis of asthma since the 1980s, probably due to changed diagnostic practice and higher awareness of asthma in healthcare and society today [2,26]. However, at the follow-up of our two current cohorts in 2006 and 2016, individuals with incident asthma reported similar prevalence of symptoms of asthma and use of asthma medication. This indicate a similar disease burden among individuals with adult-onset asthma today as ten years ago, which in part contradicts the suggested diagnostic drift regarding asthma in

healthcare. On the other hand, the major change may have occurred before the millennium shift as a consequence of a Swedish national program focusing on asthma during 1995, and perhaps even related to the start of the OLIN-research program in the study area in 1986, resulting in increased awareness of asthma in the society. Still, the higher incidence rate of use of asthma medication compared with asthma diagnosis may indicate some under-diagnosis of asthma also today. Nevertheless, asthma medication is also used in other respiratory diseases, such as bronchitis and COPD, which probably contribute to the high incidence.

In line with previous studies, we found that women had a higher incidence of adult-onset asthma compared with men [12-24,29,30] (Figure 2). This is in contrast to children, where the incidence is higher among boys than girls [8,9,11,22]. The reason for the sex differences is unclear but may be related to hormonal status [29]. The obese-asthma phenotype, often found in adult-onset asthma among women [5,29], may be mediated by interactions between sex hormones and systemic inflammation [31]. Female sex has also been reported to be a predictor for persistent asthma from childhood to adulthood [32,33] why it seems that the increasing prevalence of asthma among adults is mainly driven by women, i.e. by lower remission rate of childhood asthma and higher incidence rate of adult-onset asthma in women than in men.

Allergic rhino-conjunctivitis is a well-known risk factor for asthma [4,17,19,21] and is a reasonable proxy for allergic sensitization, at least among younger and middle-aged [21]. In the current study it was the strongest and most stable risk factor for asthma which further strengthen the causality of the association. Several previous studies have found smoking or

ex-smoking associated with incidence of asthma [4,10,12,15,19,23]. In the current study we found that, from 2006, neither smoking nor ex-smoking remained as risk factors for incident asthma among adults. This change is probably a result of the considerable decrease in smoking that have occurred during the last decades in Sweden [2,26]. Not only the prevalence of smoking has decreased but, also the number of cigarettes smoked per day has been reduced [2]. In contrast to previous studies which have reported several markers for low socioeconomic status to be associated with incident asthma [34-36], we did not find any consistent associations with socioeconomic status based on occupation. However, though not significant, the risk ratio for manual work was 1.75 in the 1996 cohort while the RR was close to 1 in the most recent cohort. This may be due to improvement of the working environment, but also due to lack of power in our study, not allowing more detailed occupational classifications.

Several strengths support the validity of the results. First, we used two large population-based cohorts within the same age-span and geographical area and both cohorts were followed for ten years. Second, the response rate was high in both cohorts, both at recruitment and follow-up. Third, for high comparability with previous studies [12,15,18] we used identical methods in the calculations of incidence, and these were based on the same validated questionnaire [27]. Furthermore, the prospective design is, compared with retrospective studies, less associated with recall bias [11,25]. Although the internal validity can be regarded as high, the external validity is unclear due to the lack of studies of trends in asthma incidence. A limitation worth noting is that despite the large sample sizes of the cohorts and the relatively long follow-up, the study lacks power for subgroups analyses. The studies were based on questionnaire data which may have introduced some bias, why we

cannot exclude that some of those diagnosed as having asthma in reality had COPD. However, the incidence were similar across all age groups. Another weakness is the limited information about risk factors, such as body mass index and education level, factors that have been associated with adult-onset asthma [4,5,29,34].

Conclusion

Based on identical methods, the incidence of adult-onset asthma was stable from 1996 to 2016 and at almost identical level since the 1980s. The observed high incidence in parallel with low remission in adulthood contribute to the ongoing increase in prevalence of asthma among adults. As previously found, the incidence was higher among women than men and allergic rhino-conjunctivitis was the main risk factor.

Acknowledgments

The research staff within the OLIN-studies is acknowledged for excellent data collection throughout the years. The study was funded by grants from The Swedish Heart and Lung Foundation, ALF-a regional agreement between Umeå University and Västerbotten and Norrbotten County Council, The Swedish Asthma-Allergy Foundation, Visare Norr, and Norrbotten County Council.

Figure legends

Figure 1.

Incidence rate of physician-diagnosed asthma over three decades, from 1986 to 2016, estimated by two different models of defining population at risk.

Footnote:

Model A: Excluded from population at risk were those who at baseline reported physician-diagnosed asthma, ever asthma, current use of asthma medicine and recurrent wheeze.

Model B: Excluded from population at risk were those who reported physician-diagnosed asthma at baseline.

*Rönmark et al. Allergy 1997 [12]

Figure 2.

Incidence rate of physician-diagnosed asthma by sex during three decades, from 1986 to 2016 by sex.

Footnote:

Incident cases were defined by model A in all cohorts.

Model A: Excluded from population at risk were those who at baseline reported physician-diagnosed asthma, ever asthma, current use of asthma medicine and recurrent wheeze.

*Lundbäck et al. Resp Med 2001 [15]

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Table 1. Study population, invited and participants by age and sex in the two cohorts followed over 10 years, by sex and among all.

	Cohort recruited in 1996				Cohort recruited in 2006		
	Women	Men	All		Women	Men	All
Invited 1996, n	3982	4351	8333	Invited 2006, n	3843	4154	7997
Participated (%)	(87.2)	(83.5)	(85.3)	Participated (%)	(81.6)	(72.9)	(77.1)
Participated, n	3471	3633	7104	Participated, n	3135	3030	6165
Invited to follow-up in 2006, n	3336	3438	6774	Invited to follow-up in 2016, n	3001	2817	5818
Participated both 1996 and 2006, n	2876	2833	5709	Participated both 2006 and 2016, n	2389	2163	4552
(%) of participants in 1996	(82.9)	(78.8)	(80.4)	(%) of participants in 2006	(76.2)	(71.4)	(73.8)

Table 2. Characteristics at recruitment; mean age and prevalence of asthma and respiratory symptoms, smoking habits and socio-economic group in the two cohorts, by sex and among all.

	Cohort recruited in 1996 (n=5709)				Cohort recruited in 2006 (n=4552)			
	Women	Men	All	p value[1]	Women	Men	All	p value[1]
Age, mean (SD)	44.8 (13.5)	44.4 (13.2)	44.6 (13.3)	0.249	47.7(13.2)	47.6 (13.1)	47.7 (13.1)	0.731
Smoking habits, %								
Smoker	27.7	23.9	25.8	**<0.001**	20.5	14.2	17.5	**<0.001**
Ex-smoker	19.0	25.0	22.0		23.4	23.9	23.6	
Non-smoker	53.3	51.1	52.2		56.1	62.0	58.9	
Physician-diagnosed asthma, %	8.6	9.1	8.8	0.461	12.1	9.9	11.1	**0.016**
Asthma medication, %	11.3	9.6	10.5	**0.029**	13.5	10.8	12.2	**0.005**
Recurrent wheeze, %	13.2	12.2	12.7	0.274	11.1	11.7	11.4	0.584
Attacks of shortness of breath, %	15.4	12.5	13.9	**0.002**	14.1	11.9	14.3	**0.026**
Allergic rhino-conjunctivitis, %	24.7	22.2	23.4	**0.029**	27.4	22.8	25.2	**<0.001**
Family history of asthma, %	24.6	18.6	21.6	**<0.001**	25.5	19.8	22.8	**<0.001**
Socioeconomic group, %								
Professionals	2.8	7.6	5.3	**<0.001**	5.5	7.7	6.6	**<0.001**
Non-manual workers	43.7	27.8	35.6		47.4	30.1	39.1	
Manual workers	53.5	64.6	59.1		47.1	62.1	54.3	

[1] p-value for differences by sex

SD=Standard deviation

Table 3. Incidence rate, n/1000/year, of different asthma variables by age group, sex and all, by use of different definitions of population at risk.

		Cohort followed from 1996 to 2006							Cohort followed from 2006 to 2016						
		Incidence rate, n/1000/year							Incidence rate, n/1000/year						
		Age group			Sex			p value[1]	Age group			Sex			p value[1]
	Outcome	20-39y	40-59y	60-69y	W	M	All[2]		20-39y	40-59y	60-69y	W	M	All[2]	
Model A	Physician-diagnosed asthma	2.6	2.4	2.6	2.7	2.2	2.4	0.285	2.8	2.6	2.5	3.5	1.7	2.6	**0.001**
	Asthma medication use	4.4	3.9	3.3	4.7	3.4	4.0	**0.028**	4.8	4.7	3.9	5.7	3.3	4.5	**0.001**
	Recurrent wheeze	4.9	4.6	5.5	4.5	5.1	4.8	0.396	4.5	5.9	4.9	5.3	5.2	5.3	0.874
Model B	Physician-diagnosed asthma	4.4	4.5	4.1	5.2	3.6	4.4	**0.008**	4.8	4.4	5.5	5.8	3.6	4.8	**0.001**
	Asthma medication use	7.6	7.4	6.3	9,0	5.6	7.3	**<0.001**	8.5	8.0	8.6	10.2	6.2	8.3	**<0.001**
	Recurrent wheeze	8.2	8.9	10.5	8.7	9.1	8.9	0.631	8.1	9.0	8.3	8.5	8.7	8.6	0.848
Model C	Asthma medication use	6.2	5.7	5.2	7,0	4.6	5.8	**<0.001**	6.6	6.8	5.9	8.3	4.7	6.5	**<0.001**
	Recurrent wheeze	6.0	6.3	7.9	6.3	6.6	6.5	0.698	7.8	7.1	6.2	7.4	6.8	7.1	0.473

Model A: Excluded from population at risk were those who at baseline reported any of physician diagnosed asthma, ever asthma, current use of asthma medicine and recurrent wheeze

Model B: Excluded from population at risk were those who reported physician diagnosed asthma at baseline

Model C: Excluded from population at risk were those who at baseline reported the outcome variable

[1] p-value for differences in cumulative incidence by sex

[2] No statistical difference by study period of any of the outcome variables were found.

Table 4. Risk factors for incident adult-onset asthma defined by model A: unadjusted and adjusted Risk Ratios with 95% Confidence Intervals (RR, 95%CI) from Poisson regression models.

		Dependent variable: Incident cases of physician-diagnosed asthma defined by model A							
		Cohort followed from 1996 to 2006				Cohort followed from 2006 to 2016			
		Unadjusted		Adjusted		Unadjusted		Adjusted	
Independent variables	Category	RR	(95%CI)	RR	(95%CI)	RR	(95%CI)	RR	(95%CI)
Sex	Men	1		1		1		1	
	Women	1.23	(0.84-1.79)	1.18	(0.77-1.79)	**2.07**	**(1.34-3.21)**	**1.99**	**(1.22-3.25)**
Family history of asthma	No	1		1		1		1	
	Yes	**1.78**	**(1.17-2.72)**	1.50	(0.93-2.43)	**2.10**	**(1.36-3.26)**	**1.75**	**(1.05-2.90)**
Allergic rhino-conjunctivitis	No	1		1		1		1	
	Yes	**2.47**	**(1.65-3.69)**	**2.62**	**(1.69-4.07)**	**2.42**	**(1.58-3.71)**	**2.39**	**(1.48-3.87)**
Smoking habits	Non-smokers	1		1		1		1	
	Ex-smokers	**1.67**	**(1.06-2.62)**	1.62	(0.99-2.67)	0.87	(0.58-1.58)	1.01	(0.59-1.75)
	Smokers	1.42	(0.89-2.26)	1.38	(0.83-2.29)	0.79	(0.42-1.47)	0.89	(0.46-1.69)
Socioeconomic group	Professionals	1		1		1		1	
	Non-manual workers	1.46	(0.45-4.80)	1.32	(0.40-4.37)	0.88	(0.37-2.12)	0.76	(0.31-1.89)
	Manual workers	1.90	(0.60-6.05)	1.75	(0.55-5.60)	0.90	(0.38-2.12)	0.90	(0.38-2.13)

Model A: Excluded from population at risk were those who at baseline reported any of physician diagnosed asthma, ever asthma, current use of asthma medicine and recurrent wheeze

The adjusted regression models included incident physician-diagnosed asthma as outcome, and all variables presented in the table as independent variables.

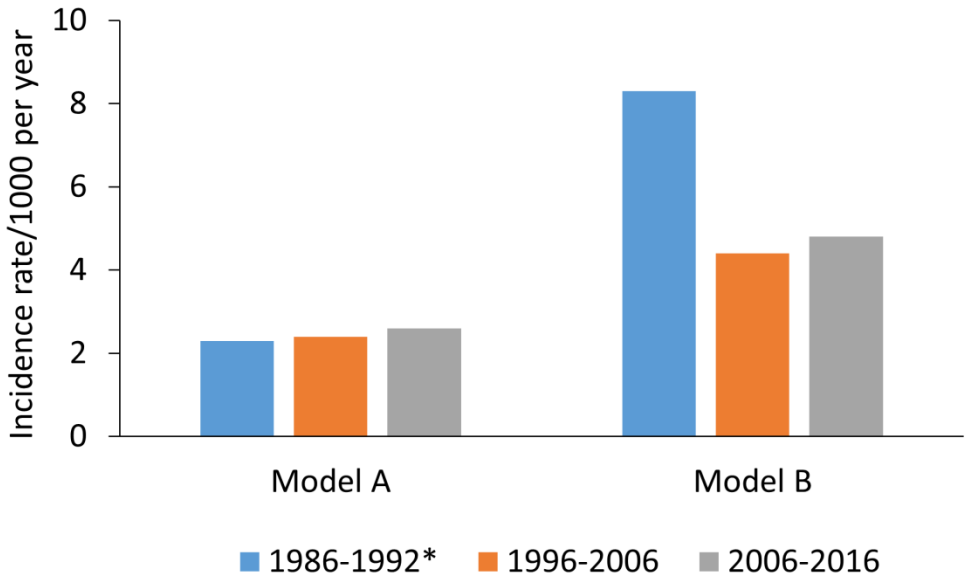
Bold values indicate $p<0.05$.

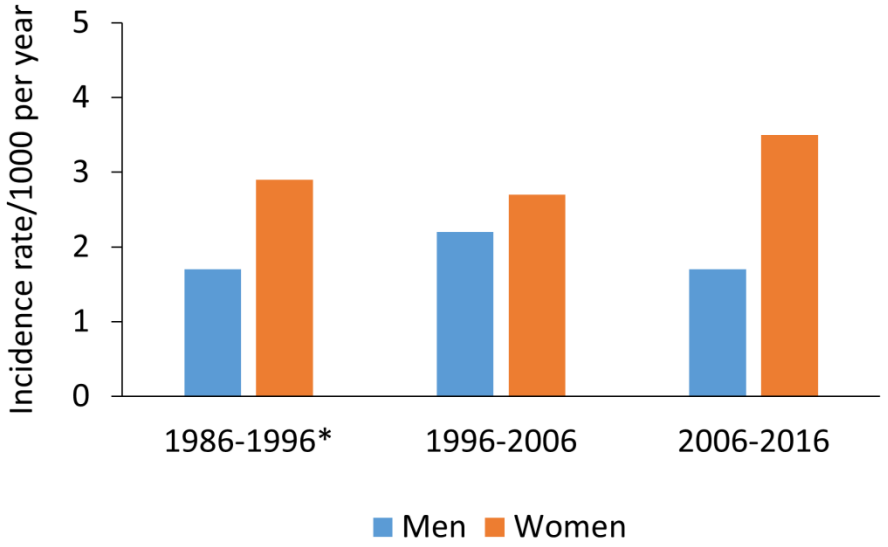
Supplemental Table 1. Risk factors for incident adult-onset asthma, defined by model B: unadjusted and adjusted Risk Ratios with 95%

Confidence Intervals (RR, 95%CI) from Poisson regression models.

		Dependent variable: Incident cases of physician-diagnosed asthma defined by model B							
		Cohort followed from 1996 to 2006				Cohort followed from 2006 to 2016			
		unadjusted		adjusted		unadjusted		adjusted	
Independent variables	Category	RR	(95%CI)	RR	(95%CI)	RR	(95%CI)	RR	(95%CI)
Sex	Men	1		1		1		1	
	Women	**1.42**	**(1.09-1.85)**	**1.35**	**(1.01-1.81)**	**1.60**	**(1.19-2.15)**	**1.55**	**(1.12-2.16)**
Family history of asthma	No	1		1		1		1	
	Yes	**2.07**	**(1.57-2.73)**	**1.93**	**(1.42-2.62)**	**2.22**	**(1.65-2.99)**	**2.13**	**(1.53-2.97)**
Allergic rhino-conjunctivitis	No	1		**1**		1		**1**	
	Yes	**2.79**	**(2.14-3.64)**	**3.00**	**(2.25-4.02)**	**3.07**	**(2.30-4.09)**	**3.11**	**(2.26-4.28)**
Smoking habits	Non-smokers	1		1		1		1	
	Ex-smokers	**1.49**	**(1.08-2.05)**	**1.42**	**(1.01-2.01)**	1.13	(0.79-1.60)	1.14	(0.78-1.67)
	Smokers	1.26	(0.92-1.73)	1.12	(0.80-1.59)	1.14	(0.78-1.68)	1.12	(0.74-1.70)
Socioeconomic group	Professionals	1		1		1		1	
	Non-manual workers	1.76	(0.71-4.38)	1.53	(0.61-3.85)	1.26	(0.60-2.65)	1.12	(0.53-2.35)
	Manual workers	2.29	(0.94-5.60)	2.12	(0.87-5.20)	1.43	(0.69-2.95)	1.38	(0.67-2.85)

Model B: Excluded from population at risk were those who at baseline reported physician diagnosed asthma.
The adjusted regression models included incident physician-diagnosed asthma as outcome, and all variables presented in the table as independent variables.
Bold values indicate $p<0.05$.


Incidence rate/1000 per year
10
8
6
4
2
0
Model A
Model B
1986-1992*
1996-2006
2006-2016


Incidence rate/1000 per year
5
4
3
2
1
0
1986-1996*
1996-2006
2006-2016
Men
Women