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Adult-onset asthma in west Sweden – Incidence, sex differences and impact of occupational exposures

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Received 12 February 2011; accepted 6 June 2011

KEYWORDS

Asthma;
Epidemiology;
Incidence;
Adult;
Age;
Occupation

Summary

The aim was to estimate the incidence rate of adult-onset asthma in relation to age, sex, smoking and occupational exposures.

A random sample of 18,087 subjects aged 16–75 years was investigated using a respiratory questionnaire. Adult-onset asthma was defined as "physician-diagnosed" asthma with onset at or after 16 years of age. The subjects were asked about year of asthma diagnosis and year of starting and stopping smoking. Subjects with onset of asthma before 16 years of age and physician-diagnosed chronic obstructive pulmonary disease were excluded resulting in a study population of 15,761 subjects. Incidence-rates of adult-onset asthma were calculated and relative risks were assessed using Cox-regression models.

During the observation period 1990–2008, 359 new cases of asthma occurred and the cumulative incidence for adult-onset asthma was 2.3%. The crude incidence rate was 1.4/1000 person-years (95% confidence interval 1.3/1000–1.6/1000), with significantly higher incidence rate among women than among men. The incidence rate of asthma during never-smoking years was similar to that during smoking years. The rate of asthma incidence decreased with increasing age. Occupational dust and fume exposure and being female were associated with increased risk of asthma. The attributable fraction for occupational exposure to gas, dust and fumes was 9.4% in the total group, 17.3% among men and 5.1% among women.

The incidence rate of asthma was higher among women than among men, and the rate declined with increasing age. A substantial proportion of the new-onset asthma cases could be attributed to occupational exposures.

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Introduction

During the past two decades a number of epidemiologic studies have been published on incidence of asthma among adults. These incidence rates, i.e. the number of new cases/1000 person-years, have shown a variable pattern with estimates ranging from 1/1000 to 7/1000 person-years.^{1–9} However, the studies with a prospective design all yielded fairly homogenous results, indicating an overall incidence rate around 2/1000 in the age group 20–50 years.^{5–9}

Some aspects remain to be further examined. Women seem to have a higher incidence of asthma, but there are few studies with sex-specific estimates. It is also not clear to what extent the incidence of asthma among adults is age-dependent – though some studies indicate a flat rate in the age groups 20–50 years. Furthermore, there is a lack of knowledge regarding the incidence among elderly people; this group carries the methodological problem of potential misclassification in relation to chronic obstructive pulmonary disease (COPD).

The importance of occupational exposures as a risk factor for adult-onset asthma is well established. There are still conflicting data about the absolute importance of occupational exposures, i.e. the number of cases that occur due to the occupational exposures.¹⁰ One way to assess this is by means of the population attributable fraction, for which a recent review found a weighted estimate of 18%.¹¹ The population attributable fraction is defined as the fraction of all cases (exposed and unexposed) that would not have occurred if the exposure had not occurred.¹² However, the population attributable fraction in the individual papers ranged from 8 to 29%. There was also a remarkable lack of sex-specific estimates. Hence, there is a need for further analyses of the population attributable fraction of occupational exposures and onset of asthma in general population samples.

We present a large retrospective study of the incidence rate of asthma among adults from a county in Western Sweden, with the aim of estimating the incidence rate of adult-onset asthma and its relation to gender, smoking, and occupational exposures. The size of the study and the wide age range made it feasible to analyze the incidence among the older age groups after exclusion of subjects with physician-diagnosed COPD.

Methods

In 2008, a questionnaire about respiratory symptoms, smoking and occupational exposures was mailed to a random sample of 30,000 subjects, ages 16–75 years (born 1933–1992) living in the county of Western Sweden.¹³ After one reminder, 18,087 subjects (62%) responded to the questionnaire (9897 women and 8190 men).

Physician-diagnosed asthma was defined as a positive response to the question, “Have you been diagnosed by a physician as having bronchial asthma?”. The subjects were also asked about the year of their diagnosis of asthma. Subjects reporting a diagnosis of asthma from 16 years of age were labeled as having adult-onset asthma.^{14,15}

Chronic obstructive pulmonary disease (COPD) was defined as a positive answer to “Have you been diagnosed

by a physician as having chronic obstructive pulmonary disease (COPD)?”.

Hay fever was defined as a positive answer to “Have you, or have you had hay fever?”. Rhinitis was defined as a positive answer to “Have you after 15 years of age ever suffered from nasal complaints, other than hay fever, blockage and/or sneezings without having a common cold?”.¹⁶

Occupational exposure was defined as an affirmative answer to the single item “Have you ever in your work been exposed to gas, dust or fume?”.

For the purposes of this study the following subjects were excluded: subjects with incomplete data on age ($n = 20$), subjects with onset of physician-diagnosed asthma before the age of 16 years ($n = 235$), subjects with physician-diagnosed COPD ($n = 468$) and subjects with incomplete data on smoking ($n = 1603$); this resulted in a study population of 15,761 subjects. Most of the subjects with incomplete data on smoking were those who reported a stopped-smoking date prior to their started-smoking date ($n = 1524$).

Statistical analysis

Statistical analyses were performed with version 9.2 of the SAS statistical package (SAS Inst., NC, US). Incidence rates were calculated as the numbers of new cases of physician-diagnosed asthma divided by the person-years at risk during the observation period 1990–2008. Thus, neither person-years nor asthma cases occurring before 1990 were used in the analysis. When asthma occurred during the observation period, the subject ceased to contribute person-years. Incidence rates were calculated, and 95% confidence intervals (CI) were outlined assuming a Poisson distribution. Incidence rate ratios (IRR) and 95% CI were also calculated. P -values were based on a χ^2 -test for categorical variables and on a t -test for continuous variables.

The incidence rate calculations were also stratified according to smoking, that is, we calculated the incidence rates among never-smokers using the never-smoking person years. The incidence rates among ex-smokers were based on the person-years occurring after the stopping smoking. Person-years (among ex-smokers) occurring before stopping smoking were treated as smoking person-years. Incidence rates among current smokers were based on person-years occurring after starting smoking.

Cox regression analyses (PROC PHREG) were performed with person-years under observation as the dependent variable and physician-diagnosed asthma as an event. Hazard ratios (HR) were calculated for explanatory variables, age, gender, rhinitis and occupational exposures, included simultaneously in the model. The Cox regression analyses were also performed on separate strata for males and females. Smoking was handled as a time-dependent variable.

The population attributable fraction (AF) was calculated as $AF = [(OR-1)/OR]^P$, where P is the prevalence of exposure among the cases.¹⁰ Exposure was defined as an affirmative answer to the item about ever exposed to gas, dust or fumes. This formula is for adjusted data, where it is supposed that confounding has been removed.¹² The estimates of population attributable proportion was stratified for sex.

Results

The mean age of the population was 43.5 years and the prevalence of never-smokers were 62.2% with small variations between men and women (Table 1). During the observation period 1990 to 2008 it occurred 359 new cases of asthma and the cumulative incidence for physician-diagnosed asthma was 2.3%. The crude incidence rate was 1.4/1000 person-years (95% CI 1.3/1000–1.6/1000), with significantly higher incidence rate among women compared to men (Table 2). Smoking seemed to have a marginal influence on the incidence of asthma as the incidence rates during the never-smoking years were the same as during the smoking years (Table 2).

There was a significantly decreasing incidence rate of asthma incidence with increasing age (Table 3). The age-dependent decrease of the incidence of asthma was present among both men and women. Among the men, the incidence decreased quite steeply from 1.5/1000 person-years to 0.6/1000 person-years ($p = 0.001$). Among the women the decrease was less pronounced and without formal statistical significance ($p = 0.08$). There were similar findings when the analysis was restricted to never-smokers (Table 3).

The Cox regression model, comprising gender, rhinitis and occupational dust and fume exposure in the same model, showed an increased relative risk for asthma among women (HR 2.1, 95% CI 1.7–2.7) compared to men. Occupational dust and fume exposure was associated with an increased risk for asthma (HR 1.8, 95% CI 1.4–2.3), with higher risk among men (HR 2.3, 95% CI 1.5–3.3) as was observed among women (HR 1.6, 95% CI 1.2–2.1). We also performed separate, modeling for ever-smokers and never-smokers showing the highest risk among ever-smoking men (HR 3.4, 95% CI 1.8–6.7) (Table 4).

The population attributable fraction for occupational exposure to gas, dust or fumes for incident asthma was 9.4%. Among men the population attributable fraction was 17.3% and among women it was 5.1%.

Discussion

The main finding of this study was a decreasing incidence of asthma with increasing age, which to some extent is contrary to other studies. The previously well-described difference between males and females were also observed in this analysis. Finally, the study also provided more data supporting the strong relation between occupational exposures and adult-onset asthma.

Our study has several strengths. Since this study was analyzed with a longitudinal approach and was carried out within a large random general population-sample aged 16–75 years with the observation period from 1990 to 2008, our results could be valid also for other similar populations. We also provide age- and sex-specific incidence rates of asthma, which can contribute to an improved understanding of the epidemiology of adult asthma.

The present study design has also a number of limitations. The most obvious is the retrospective design and that the outcome is based on physician-diagnosed asthma. However, this has been shown to have a high specificity and a low sensitivity.¹⁴ Hence, the use of physician-diagnosed asthma in epidemiological studies will cause an under detection of subjects with asthma. It is also reasonable to assume that the false negatives are subjects with mild asthma.¹⁵ In addition to the underreporting by the subjects themselves, there is probably under-diagnosis by the physicians. Taken together this implicates that the observed incidence rates in the current study probably are an underestimation of the true incidence rates of asthma.

The reported year of onset for asthma is sensitive to misclassification, meaning that a subject may report an incorrect year. There are two studies validating the self-reported year of diagnosis or disease onset among subjects with asthma,^{15,17} showing that almost all subjects with asthma reported accurate years-of-onset (± 2 years).

The use of physician-diagnosed asthma, i.e. self-reported asthma, may introduce misclassification in relation to chronic obstructive pulmonary disease (COPD). This misclassification is age dependent, because COPD mainly occurs after 50 years of age. The age of the present population was between 16 and 75 years, which to some extent minimizes the misclassification in relation to COPD. We have tried to diminish this bias by excluding subjects with physician-diagnosed COPD.

In this study the average response rate was 62% and this might introduce bias. In a recent editorial it has been stated that epidemiological studies should include analysis of the non-response bias.¹⁸ In the present study there was no difference regarding the prevalence of asthma, cough or wheeze between responders and non-responders.¹⁹ However, smokers and unemployed people were overrepresented among the non-responders.¹⁹ It has been showed that late responders are predominantly of male sex, younger and are more likely to live in urban areas,^{20,21} as well as predominantly students or unemployed.²²

In the assessment of non-response bias it is also important to focus on the non-response effect on the exposure-disease

Table 1 Age, sex, smoking habits, and cumulative incidence of asthma at follow-up in a retrospective study of asthma incidence from 1990 to 2008 of 15,761 adult subjects from Western Sweden (SD = standard deviation).

	All subjects ($n = 15,761$)	Males ($n = 7097$)	Females ($n = 8664$)
Mean age (SD)	43.5 (16.0)	43.9 (15.9)	43.2 (16.1)
Never smokers	62.2% ($n = 9808$)	63.1% ($n = 4478$)	61.5% ($n = 5330$)
Ex-smokers	16.4% ($n = 2582$)	16.1% ($n = 1144$)	16.6% ($n = 1438$)
Current smokers	21.4% ($n = 3371$)	20.8% ($n = 1475$)	21.9% ($n = 1896$)
Exposure to gas, dust and fumes	23.3% ($n = 3308$)	30.7% ($n = 2150$)	13.6% ($n = 1158$)
New-onset asthma	2.3% ($n = 359$)	1.5% ($n = 108$)	2.9% ($n = 251$)

Table 2 Incidence rates and relative risks of adult-onset asthma (cases/1000 person-years) in relation to smoking habits, observation period 1990–2008. 95% confidence intervals and number of adult-onset asthma cases in brackets. Subjects with incomplete smoking data are excluded.

Smoking habitis	All	Females	Males	Incidence rate ratios (Females/males)
All	1.4 (1.3–1.6) <i>N</i> = 359	1.8 (1.6–2.1) <i>N</i> = 251	0.9 (0.8–1.1) <i>N</i> = 108	1.9 (1.6–2.4)
Never smokers	1.4 (1.2–1.6) <i>n</i> = 217	1.8 (1.5–2.1) <i>n</i> = 149	1.0 (0.8–1.2) <i>n</i> = 68	1.8 (1.4–2.5)
Ex-smokers	1.1 (0.7–1.7) <i>n</i> = 24	1.3 (0.7–2.1) <i>n</i> = 15	0.9 (0.4–1.7) <i>n</i> = 9	1.4 (0.56–3.3)
Current smokers	1.4 (1.2–1.7) <i>n</i> = 118	1.9 (1.5–2.4) <i>n</i> = 87	0.9 (0.6–1.2) <i>n</i> = 31	2.3 (1.5–3.4)
Incidence rate ratios smokers/never-smokers	1.0 (0.8–1.3)	1.1 (0.8–1.4)	0.9 (0.6–1.3)	N.a.

N.a. = not applicable.

relationship.¹⁸ We found in our previous analysis that although the prevalence of the symptoms and predictors (exposures) was affected by the response, the exposure-response relationships were hardly affected.¹⁹ Similar results have been presented by others.²¹ Hence, we conclude that even if certain groups such as smokers and unemployed are over-represented among non-responders this is considered to have marginally influence of the incidence rates, as the non-response seems to affect both asthmatics and non-asthmatics. We also conclude that the observed exposure-response relationships are marginally affected by the present non-response bias as supported by our previous study and by others.^{19,21}

During the observation period the current study had 359 new cases of asthma occurred giving an overall incidence rate of 1.4 cases/1000 person years. This is in accordance with several other studies. Studies investigating incidence of asthma among adults have been reviewed in two papers.^{3,23} Our own review from 1999 concluded that the incidence of adult asthma ranged between 1 and 2 cases/1000 person-years. The review by Eagan and colleagues also found incidences of asthma varying between 1 and 2 cases/1000 person-years, but they observed that prospective studies in general produced higher and more variable estimates of the incidence rates. The incidence rates ranged from 1.1/1000 person-years to 14.5/1000 person-years with a crude mean incidence around 5/100 person-years. However, in prospective studies inclusion at baseline of

subjects with asthma or asthma symptoms may heavily influence the outcomes as earlier described.⁶ The incidence rate from the present study, 1.4/1000 person-years, is probably falsely decreased because our definition of new-onset asthma is based on an operational definition with low sensitivity, i.e., the observed incidence is an underestimation of the true underlying process of asthma onset. This incidence range is similar to that in other studies, as described above. As in most other studies we also found a higher incidence rate for women (1.8/1000 person-years) compared with men (0.9/1000 person-years). Different factors such as airway size, hormonal factor status, and occupational exposures may be of importance.

The most novel finding in our study is the decreasing incidence rate by age. As summarized in previous reviews the incidence rate of asthma seems to increase with increasing age, even if there are surprisingly few studies presenting age stratified incidence estimates. We have identified six prospective general-population studies with sex-specific age-separated estimates of the incidence rates (Table 5). In most of them there was an age-dependent increase of the incidence. In one of them, a study from US investigating the incidence rate of asthma among older people observed a lower incidence among those over 85 yrs compared to those aged 65–74 yrs.²⁶ That study was the only one that excluded subjects with COPD.

We think that the exclusion of subjects reporting physician-diagnosed COPD will diminish the misclassification

Table 3 Incidence rates (cases/1000 person-years) with 95% CI of adult-onset asthma in a random sample of 15,761 subjects according to sex and age group.

Age interval	All		Females		Males	
	All	Never-smokers	All	Never-smokers	All	Never-smokers
16–35 yrs	1.9 (1.5–2.2) <i>n</i> = 112	1.7 (1.4–2.2) <i>n</i> = 73	2.2 (1.7–2.7) <i>n</i> = 74	1.9 (1.4–2.6) <i>n</i> = 44	1.5 (1.0–2.0) <i>n</i> = 38	1.5 (1.0–2.2) <i>N</i> = 29
36–55 yrs	1.4 (1.2–1.6) <i>n</i> = 151	1.4 (1.1–1.7) <i>n</i> = 89	1.8 (1.5–2.1) <i>n</i> = 104	1.8 (1.4–2.4) <i>n</i> = 60	0.9 (0.7–1.2) <i>n</i> = 47	0.9 (0.6–1.3) <i>n</i> = 29
56–75 yrs	1.1 (0.9–1.4) <i>n</i> = 96	1.2 (0.9–1.5) <i>n</i> = 55	1.6 (1.3–2.0) <i>n</i> = 73	1.7 (1.2–2.2) <i>n</i> = 65	0.6 (0.4–0.9) <i>n</i> = 23	0.5 (0.2–0.9) <i>N</i> = 10
All	1.4 (1.3–1.6) <i>n</i> = 359	1.4 (1.2–1.6) <i>n</i> = 217	1.8 (1.6–2.1) <i>N</i> = 251	1.8 (1.5–2.1) <i>N</i> = 149	0.9 (0.8–1.1) <i>N</i> = 108	1.0 (0.8–1.2) <i>N</i> = 68

Table 4 Hazard Ratio (HR) and 95% confidence intervals (95% CI) for physician-diagnosed asthma in a retrospective general population-based study.

Predictor	All		Females		Males	
	HR ^a	(95%CI)	HR ^a	(95%CI)	HR ^a	(95%CI)
Female sex	2.1	1.7–2.7	N.a.	N.a.	N.a.	N.a.
Rhinitis	3.6	3.0–4.5	3.4	2.7–4.4	4.3	2.9–6.4
Occupational exposure to dust or fumes	1.8	1.4–2.3	1.6	1.2–2.1	2.3	1.5–3.3
Smoking	1.0	0.8–1.3	1.0	0.7–1.2	1.1	0.7–1.6
Never-smokers						
Female sex	2.1	1.6–2.8	N.a.	N.a.	N.a.	N.a.
Rhinitis	3.3	2.5–4.3	2.0	1.3–2.9	3.8	2.3–6.2
Occupational exposure to dust or fumes	1.9	1.4–2.6	2.0	1.3–2.9	1.8	1.1–3.0
Smokers						
Female sex	2.2	1.5–3.2	N.a.	N.a.	N.a.	N.a.
Rhinitis	4.4	3.2–6.1	4.2	2.8–6.2	5.5	2.9–10.4
Occupational exposure to dust or fumes	1.7	1.2–2.4	1.2	0.7–1.9	3.4	1.8–6.7

^a Mutual adjustment for age and the presented predictors.

between asthma and COPD among the older (>50 years) part of the population. In the current study we excluded 468 subjects with COPD of whom 60 also reported physician-diagnosed asthma. COPD occurs in the older ages and if they would have been included, the incidence rate in the older group would have been higher, almost doubled. This kind of misclassification was described already in the Tucson study as they described a tendency among physicians to diagnose an asthma-like disorder as asthma in women and as COPD in males.²⁵

An alternative explanation to the decreasing incidence rate by age is the presence of recall bias. In the present study the incidence decreased with age significantly among males, from 1.5 to 0.6, compared to females, from 2.2 to 1.6. As males are more prone to be non-responders, this may indicate the presence of recall bias as possible explanation for the age-dependent decrease of the asthma incidence.

A third explanation to the observation of a decreasing asthma incidence with increasing age is a birth-cohort effect, i. e. subjects from more recent generations have an higher incidence. This has previously been discussed.²⁹ The reason for this is to large extent unknown, even if changes in susceptibility to environmental stimuli leading to asthma as well as changes in exposure to occupational and environmental factors could have contributed to this increase.⁷

We did not observe an increased risk of asthma during smoking person-years, as in previous studies.⁶ In contrast to some other studies^{27,30} current smoking was not at all associated with increased asthma risk. The importance of tobacco smoking for asthma onset among adults is still controversial. Several studies have found an increased risk but there are also several prospective studies failing to find an increased risk for asthma in relation to smoking.^{1,4,6} To some extent the negative studies can be explained by the "healthy smoker effect," which is more manifest if subjects are only followed for part of their potential smoking time.³¹

Negative studies may also be biased, because there is a tendency to label asthma like disorders as asthma in non-smokers but not in smokers.³²

Occupational exposure to vapors, gas, dust or fume is an important risk factor for adult-onset asthma, and in several studies the population attributable fraction have been between 15 and 20%.^{10,11,33} This indicates that one fifth of every new case of adult asthma is caused by occupational exposures. This means that occupational exposure is one of

Table 5 Prospective epidemiological studies from the general population estimating age and gender specific incidence rates of asthma.

Author, year	Country	Age-strata	Incidence rates	
			Males	Females
²⁴	US	16–24	0	2.0
		25–34	1.0	3.0
		35–44	3.0	2.0
		45–54	2.0	N.a.
		55–64	N.a.	3.0
²⁵	US	20–29	2.0	4.0
		30–39	—	4.0
		40–49	—	4.0
		50–59	—	5.0
		60–69	3.0	8.0
²⁶	US	65–74	1.4	0.8
		75–84	1.2	0.7
		≥85	0.6	0.5
²⁷	Sweden	35–36	2.3	4.7
		50–51	3.2	5.0
		65–66	4.9	3.9
⁸	Denmark	20–21	5	5
		40–41	4	3
²⁸	US	<40	N.a.	2.2
		≥40	N.a.	3.0

the leading environmental factors causing adult asthma. These observations were also confirmed in this study as the population attributable fraction for occupational exposure to gas, dust and fumes for adult-onset asthma was 9.4%. We also observed a higher attributable fraction among men, 17.3%, compared to women, 5.1%. There are few studies with gender-specific estimates of population attributable fraction. In the review from 2009, five papers were identified and in those there was a slightly higher population attributable fraction for females compared to males.¹¹

In conclusion, the incidence rate of asthma was higher among women compared to men, and the rate declined with increasing age. A substantial proportion of the new-onset asthma cases could be attributed to occupational exposures.

Role of funding source

The Swedish Council for Worklife Research and Social Science (FAS); Herman Kreftings Fund for Asthma Research; the Swedish Heart and Lung Foundation; the Norwegian Asthma and Allergy Research Fund; and the Icelandic Research Council supported this study.

Conflict of interest

The authors declare no conflicts of interest.

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