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The association between asthma and rhinitis is stable over time despite diverging trends in prevalence

Anders Bjerg^{a,*}, Jonas Eriksson^a, Inga Sif Ólafsdóttir^b,
Roelinde Middelveld^c, Karl Franklin^d, Bertil Forsberg^e,
Kjell Larsson^f, Kjell Torén^g, Sven-Erik Dahlén^c,
Christer Janson^b

^a Krefting Research Centre, Department of Internal Medicine and Clinical Nutrition, University of Gothenburg, Göteborg, Sweden

^b Department of Medical Sciences, Respiratory Medicine and Allergology, Uppsala University, Uppsala, Sweden

^c Experimental Asthma and Allergy Research, The National Institute of Environmental Medicine, Karolinska Institutet, Stockholm, Sweden

^d Department of Surgery, University of Umeå, Umeå, Sweden

^e Environmental and Occupational Medicine, Department of Public Health and Clinical Medicine, Umeå University, Umeå, Sweden

^f Unit of Lung and Allergy Research, The National Institute of Environmental Medicine, Karolinska Institutet, Stockholm, Sweden

^g Department of Public Health and Community Medicine, Sahlgrenska Academy, University of Gothenburg, Göteborg, Sweden

Received 26 October 2014; accepted 13 January 2015

KEYWORDS

Asthma;
Rhinitis;
Wheeze;
Smoking;
Epidemiology;
Adults

Summary

Background: Despite the well-known association between asthma and rhinitis, in Swedish adults the prevalence of rhinitis rose from 22% to 31% between 1990 and 2008 while asthma prevalence was unchanged. We tested whether the association of rhinitis with asthma was stable over time using the same population-based databases.

Methods: Two surveys of adults (20–44 years) living in three regions of Sweden, carried out in 1990 (n = 8982) and 2008 (n = 9156) were compared. Identical questions regarding respiratory symptoms, asthma and rhinitis were used. Asthmatic wheeze: Wheeze with breathlessness

Abbreviations: ECRHS, European Community Respiratory Health Survey; GA2LEN, Global Allergy and Asthma European Network; OR, odds ratio; CI, confidence interval.

* Corresponding author. Krefting Research Centre, Göteborgs Universitet, Box 424, S-405 30 Göteborg, Sweden. Tel.: +46 70 7604459. E-mail address: anders.bjerg@gu.se (A. Bjerg).

<http://dx.doi.org/10.1016/j.rmed.2015.01.002>

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Please cite this article in press as: Bjerg A, et al., The association between asthma and rhinitis is stable over time despite diverging trends in prevalence, Respiratory Medicine (2015), <http://dx.doi.org/10.1016/j.rmed.2015.01.002>

apart from colds. Current asthma: Asthma attacks and/or asthma medication use.

Results: Subjects with rhinitis had level time trends in asthmatic wheeze, current asthma and most nocturnal respiratory symptoms between 1990 and 2008, adjusted for age, sex, area and smoking. Any wheeze however decreased slightly. In never-smokers asthma symptoms were similarly associated with rhinitis in 1990 and 2008: any wheeze OR 4.0 vs. 4.4 ($p = 0.339$); asthmatic wheeze OR 6.0 vs. 5.9 ($p = 0.937$); and current asthma OR 9.6 vs. 7.7 ($p = 0.213$). In the whole population there were decreases in the asthma symptoms most closely associated to smoking, which decreased by half 1990–2008. Conversely current asthma, which was strongly associated with rhinitis and not with smoking, increased ($p < 0.001$).

Conclusions: The association of rhinitis with asthma was stable between 1990 and 2008. The pattern in the time trends of asthma outcomes strongly suggests that decreased smoking counterbalanced the driving effect of increased rhinitis on asthma prevalence. The findings illustrate the public health benefits of decreased smoking.

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Introduction

Asthma and symptoms from the lower airways are closely associated to rhinitis [1]. In westernised countries a majority of adults with asthma also have rhinitis, and it is almost ubiquitous in adult-onset asthma [1–4]. The two diseases also share several pathophysiological features and are both closely related to allergic sensitization, which has led to the concept of a “united airways disease” [2,5,6]. Increases in the prevalence of asthma and rhinitis since the 1960s have rendered them serious public health issues [7].

Despite the close clinical, epidemiological, and mechanistic associations between the two conditions, some recent studies have demonstrated isolated increases in rhinitis, while the prevalence of asthma has remained level [8–10]. To date, the most reliable way to study time trends is by applying identical methods to similar, representative samples from the population on two or more occasions [11]. In contrast to in children, there are comparatively fewer such studies in adults [9,10,12,13].

Using two large population-based surveys in the same areas we found a substantial increase in the prevalence of rhinitis from 21.6% to 30.9% ($p < 0.001$) between 1990 and 2008, with no corresponding increase in asthma symptoms [8]. These observations could indicate that the association between asthma and rhinitis changed during the time period. To our best knowledge the stability of the association between asthma and rhinitis has not been studied over time using repeated population surveys. The aim of the present study was to describe in detail the association between asthma symptoms and rhinitis and to test its stability over time.

Material and methods

Study design and study population

The design, methodology and population of this study have been described in detail previously [8,14]. In brief, we analysed data from two large population-based surveys: In 1990, Sweden participated in the European Respiratory

Health Survey (ECRHS) by inviting 10,800 adults aged 20–44 years in three centres, of which 86% participated [15]. In 2008, the four Swedish centres in the Global Allergy and Asthma European Network (GA²LEN) invited 45,000 adults aged 16–75 years, with 60% participation [16].

The age intervals (20–44 years) and study areas (Göteborg, Uppsala and Umeå) that were surveyed both years were included in the present analysis. After elimination of incomplete questionnaires, data from 8982 (52% female) subjects in 1990 and 9156 (57% female) subjects in 2008 remained. The same core questions on respiratory symptoms, asthma and rhinitis were used both years. In 1990, the three local Ethics Committees and the Swedish Data Protection Board approved of the study. The 2008 study and the present comparison study were approved of by the Regional Ethical Review Board in Uppsala.

Definitions and statistical analyses

The ECRHS definitions and validations against objective measures have been thoroughly described previously [15,17]. All definitions used in the comparison study have been published [8] and only those of special relevance are listed below. Prevalence was defined as presence in the last 12 months.

“Any wheeze”: Wheeze or whistling in the chest.

“Asthmatic wheeze”: Positive answers to the three questions “Any wheeze”, “Wheeze with breathlessness” and “Wheeze without a cold” [8].

“Current asthma”: A positive answer to the question “Do you have asthma?” and to either or both of “Asthma attack” and “Use of asthma medications” [8].

“Asthma symptoms” and “Asthma symptom score”: An arbitrary score for asthma symptoms was calculated by adding one point (total 0–8) for each of the following asthma symptom items [8]: Any of “Any wheeze” or “Wheeze with breathlessness” or “Wheeze without a cold” (1 point); “Asthmatic wheeze” (1 point); “Asthma attack” (1 point); “Use of asthma medications” (1 point); “Current asthma” (1 point); “Nocturnal chest

tightness" (1 point); "Nocturnal breathlessness" (1 point); "Nocturnal cough" (1 point).

"Rhinitis": Nasal allergies including hay fever.

The following analyses were performed to describe the relationship between asthma and rhinitis over time: prevalence of asthma symptoms both years was investigated in subjects with and without rhinitis respectively; the associations of rhinitis with different asthma indices was tested with adjustment for basic demographics, with additional adjustment for smoking and finally in never-smokers, to account for the considerable decrease in smoking prevalence from 1990 to 2008 [8]; and the prevalence of rhinitis was also analysed in subjects with different asthma symptoms. Comparisons of prevalence (%) used the two-sided χ^2 test for statistical significance. Binary logistic regression was used to calculate adjusted odds ratios (OR) and their 95% confidence intervals (CI). Interactions were tested by inclusion of interaction terms (e.g. study year*rhinitis) in the logistic regression models. P values < 0.05 were considered as statistically significant. All analyses were performed using PASW Statistics 18.0 (IBM Corp, New York, USA).

Results

Both 1990 and 2008 subjects with rhinitis had higher prevalence of asthma symptoms compared to subjects without rhinitis, the most common being any wheeze and nocturnal cough (Table 1). Moreover, regardless of study year the prevalence of rhinitis increased linearly with increasing number of asthma symptoms (1–8), and in subjects with all eight asthma symptoms the prevalence of rhinitis was above 70% both years (Fig. 1). In each asthma

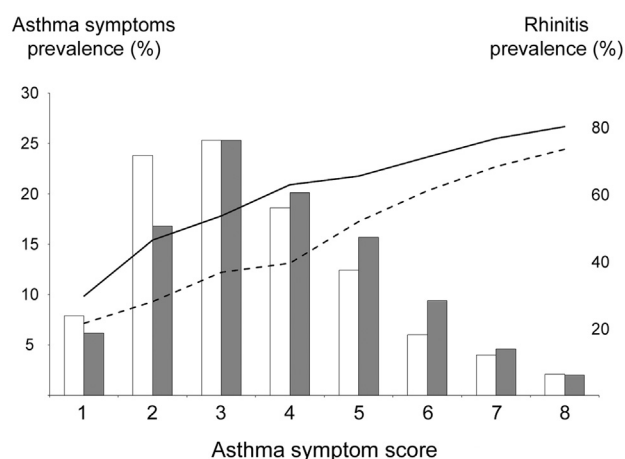


Figure 1 Prevalence of rhinitis by asthma symptom score. Lines: Prevalence (%; right column) of rhinitis by asthma symptom score. Bars: Prevalence (%; left column) of each asthma symptom score among subjects with rhinitis. 1990: white bars, dashed line. 2008: grey bars, solid line.

symptom score stratum the prevalence of rhinitis was higher in the second survey. From 1990 to 2008 there was a shift towards higher prevalence of having four or more asthma symptoms in subjects with rhinitis, from 43.1% to 51.8% ($p < 0.001$), indicating an increasing symptom burden.

From 1990 to 2008 the prevalence of any wheeze decreased in subjects with and without rhinitis, from 35.8% to 30.2% and from 16.0% to 9.8% respectively (both $p < 0.001$) (Table 1). Most asthma symptoms, except asthma attacks, decreased in prevalence independently of the presence of rhinitis. In subjects with rhinitis the largest decreases in any wheeze, asthmatic wheeze and any nocturnal symptom were seen in the oldest age group, 36–44 years (Table 2). Compared to females, males had larger decreases in any wheeze and asthmatic wheeze, from 36.2% to 28.9% ($p < 0.001$) and from 17.3% to 14.0% ($p = 0.031$).

The decreases over time in asthma symptoms among subjects with rhinitis were seen also after adjustment for basic demographics, as indicated by ORs below 1 for study year 2008 vs. 1990 (Table 3, Model I). However, further adjustment for ever having smoked dissipated these negative time trends for almost all asthma symptoms. Any wheeze was an exception, with OR 0.86 (95% CI 0.76–0.98). The prevalence of current asthma was stable regardless of ever-smoking, OR 1.02 (0.88–1.19) and 1.05 (0.91–1.23) in models I and II, respectively.

The absolute increase from 21.6% to 30.9% ($p < 0.001$) in the prevalence of rhinitis corresponded to a relative change of +43% (data not in table). The corresponding relative changes among subjects with any wheeze, asthmatic wheeze and any nocturnal symptom were +52%, +33% and +37% respectively (all $p < 0.001$). Among lifelong never-smokers the corresponding relative changes were substantially smaller: +23%, +12% and +16%. The relative change in rhinitis in subjects with current asthma was only +7% ($p = 0.045$), and not statistically significant in those who had never smoked ($p = 0.436$).

Table 1 Prevalence (%) of asthma symptoms among subjects with and without rhinitis, respectively. P-values for study year 2008 vs. 1990, statistically significant changes in boldface.

	Subjects with rhinitis			Subjects without rhinitis		
	1990	2008	P	1990	2008	p
Wheeze						
Any	35.8	30.2	<0.001	16.0	9.8	<0.001
with	21.7	19.9	0.127	8.2	5.8	<0.001
breathlessness						
without a cold	25.1	21.2	0.002	8.6	5.3	<0.001
Asthmatic	16.7	14.8	0.084	4.6	3.4	<0.001
wheeze						
Nocturnal symptoms						
Any	45.1	40.4	0.001	29.4	26.4	<0.001
Chest tightness	20.9	17.8	0.008	8.5	7.7	0.099
Breathlessness	10.4	7.6	0.001	3.9	3.7	0.597
Cough	34.7	31.3	0.014	24.4	21.7	<0.001
Asthma attack	10.1	10.9	0.372	1.3	1.6	0.159
Asthma	17.3	16.8	0.684	1.8	2.4	0.025
medications						
Current asthma	19.5	19.2	0.851	2.3	2.9	0.035

Table 2 Prevalence (%) of four asthma symptoms among subjects with rhinitis by basic demographic characteristics. P-values for study year 2008 vs. 1990, statistically significant changes in boldface.

	Any wheeze			Asthmatic wheeze			Current asthma			Any nocturnal symptom		
	1990	2008	p	1990	2008	P	1990	2008	p	1990	2008	p
All	35.8	30.2	<0.001	16.7	14.8	0.084	19.5	19.2	0.851	45.1	40.4	0.001
Sex												
Male	36.2	28.9	<0.001	17.3	14.0	0.031	17.9	17.7	0.910	38.6	33.6	0.016
Female	35.5	31.2	0.030	16.0	15.5	0.715	21.0	20.5	0.744	51.5	45.8	0.005
Age												
20–27	36.2	30.1	0.010	18.8	16.7	0.280	21.7	21.7	0.975	43.2	41.3	0.457
28–35	32.6	29.4	0.156	13.0	14.6	0.340	16.7	19.0	0.222	44.4	40.1	0.068
36–44	39.0	31.3	0.003	18.5	13.8	0.006	20.1	17.1	0.148	48.2	40.0	0.002
Centre												
Göteborg	36.2	28.6	0.001	14.3	12.9	0.409	16.0	16.2	0.910	48.0	35.5	<0.001
Uppsala	33.1	28.0	0.035	16.8	14.3	0.182	19.1	19.7	0.768	43.6	42.2	0.506
Umeå	38.0	34.8	0.194	18.6	18.2	0.874	22.8	23.3	0.820	44.2	45.9	0.593

Due to the large decreases in ever- and current smoking (from 50% to 26% and from 35% to 12% respectively) between 1990 and 2008 the associations of rhinitis with asthma symptoms were tested in never-smokers with adjustment for basic demographics (age, sex, study centre) (Fig. 2). For each outcome the highly similar adjusted odds ratios both years and largely overlapping confidence intervals reveal that the associations did not change

statistically significantly from 1990 to 2008: Any wheeze from OR 3.99 (3.36–4.76) to OR 4.43 (3.84–5.11) ($p = 0.339$); asthmatic wheeze from OR 5.98 (4.60–7.79) to 5.88 (4.75–7.29) ($p = 0.937$); and current asthma from OR 9.64 (7.37–12.6) to 7.70 (6.30–9.43) ($p = 0.213$). Rhinitis was more strongly associated with current asthma than with any wheeze in both surveys.

Discussion

This study is the first to test the stability over time of the association between asthma and rhinitis using large, population-based samples of adults. Following our previous findings of diverging time trends in asthma and rhinitis [8], we tested whether the association of rhinitis with asthma symptoms had changed between 1990 and 2008. Following the present in-depth analysis this was found not to be the case, based on three major observations: a) The adjusted odds ratios of rhinitis for asthma symptoms were largely unchanged from 1990 to 2008 when measured in never-smokers; b) Adjusted for demographic factors and smoking, no statistically significant time trends in the majority of asthma symptoms were seen among subjects with rhinitis; c) The increase in prevalence of rhinitis was seen similarly in subjects with and without asthma symptoms.

The fact that the association between asthma and rhinitis was stable over time is not in itself surprising; the interesting thing is that this was obscured in the initial findings. The united airways paradigm is firmly based on epidemiological as well as mechanistic data [1]. The major common pathway is systemic IgE-mediated allergic inflammation in response to inhalant allergens. Endobronchial allergen challenge elicits also an inflammatory response in the nasal mucosa [18] and vice versa [19], with activation and recruitment of eosinophils, mast cells and basophils and release of cysteinyl leukotrienes. Although both asthma and rhinitis are multifactorial diseases, it is unlikely that these common pathophysiological pathways, which are biological systems, should have changed over time.

Table 3 Adjusted risk of asthma symptoms from study year 2008 vs. 1990 among subjects with rhinitis. Adjusted odds ratios (OR) including 95% confidence intervals (CI) of study year 2008 vs. 1990 for respiratory and asthma symptoms, which were each analysed separately, among subjects with rhinitis. An OR above 1 indicates that the prevalence increased from 1990 to 2008 and vice versa. Statistically significant changes in boldface.

	Study year 2008 vs. 1990			
	Model I ^a		Model II ^b	
	OR	95% CI	OR	95% CI
Wheeze				
Any	0.78	0.69–0.89	0.86	0.76–0.98
With breathlessness	0.91	0.79–1.05	0.98	0.85–1.14
Without a cold	0.83	0.72–0.95	0.90	0.78–1.03
Asthmatic wheeze	0.91	0.77–1.06	0.96	0.82–1.13
Nocturnal symptoms				
Any	0.82	0.73–0.92	0.89	0.79–1.00
Chest tightness	0.81	0.70–0.94	0.89	0.76–1.03
Breathlessness	0.69	0.56–0.84	0.73	0.59–0.89
Cough	0.84	0.74–0.95	0.91	0.80–1.04
Asthma attack	1.13	0.93–1.37	1.16	0.96–1.41
Asthma medications	1.01	0.86–1.17	1.04	0.89–1.22
Current asthma	1.02	0.88–1.19	1.05	0.91–1.23

^a Adjusted for sex (male, female), age (20–27, 28–35, 36–44 years) and study centre (Gothenburg, Uppsala, Umeå).

^b Similarly adjusted for sex, age and study centre, and also for ever smoking.

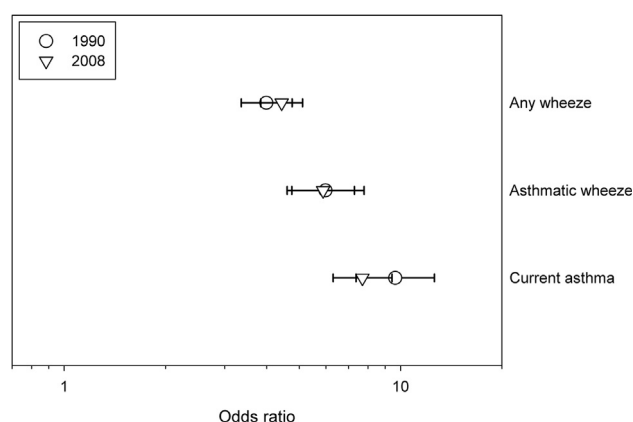


Figure 2 Association of rhinitis with asthma symptoms in never-smokers. The multivariate odds ratios and 95% confidence intervals were adjusted for sex (male, female), age (20–27, 28–35, 36–44 years) and study centre (Gothenburg, Uppsala, Umeå). Note the break 0–0.7 on the y axis.

Trends in asthma symptoms and rhinitis

The majority of previous studies of the prevalence of asthma symptoms and rhinitis have found parallel trends: Increases [12,20–22], slight decreases [23], or the simultaneous levelling of previously upward trends [24]. Isolated increases in rhinitis have also been reported [9,10,22,25], but the majority of these studies were performed in children or teenagers [22–25] or in male conscripts [20,21]. In fact, very little of the present knowledge derives from studies of representative adult populations [1].

In a study of 20–44-year-olds by Verlato et al. the prevalence of asthma attacks and wheeze did not change statistically significantly between 1991–1993 and 1998–2000, while nasal allergies increased from 15.4% to 18.3% ($p < 0.001$) [9]. The authors suggested that a non-significant increase in asthma medication use by 0.6% ($p = 0.120$) may have masked an increase in asthma symptoms. This speculation had previously been put forward in the Midspan Family Study, where the prevalence of rhinitis increased 3.4 times between 1972 and 6 and 1996, while that of breathlessness and “asthma and/or wheeze” was unchanged [10]. Yet, in our study, increased medication did not account for the uncoupling of the prevalence trends in asthma symptoms and rhinitis, since in a previous investigation also the outcome “wheeze and/or using asthma medications” in fact decreased in prevalence, $p < 0.001$ [8].

In 1990 the prevalence of rhinitis and asthma symptoms in our study corresponded well with that in large parts of Europe [26], however, there are but few large, high-quality studies for comparison with our 2008 findings. The level prevalence of asthma symptoms are in line with findings in Stockholm, Sweden [8,27]. The study in Stockholm also found around 30% prevalence of rhinitis in subjects aged 20–40 years, similar to our study from larger parts of Sweden [28]. The prevalence of any wheeze, current asthma and asthmatic wheeze in subjects with rhinitis in our study conforms to previous reports of 20–40% prevalence of asthma in this group [1,2].

The risk of rhinitis increased linearly with the number of asthma symptoms present. According to previous studies this could indicate a stronger association of rhinitis with more severe asthma, or the fact that under-treated rhinitis is associated with worse asthma control [1,7]. The fact that our investigation was based on questionnaire responses only, did not include detailed data on treatment of rhinitis and utilised an arbitrary asthma symptom score prevents any firm conclusions regarding asthma severity in relation to rhinitis to be drawn. The decreased prevalence of having only one or two asthma symptoms in subjects with rhinitis in our study however corresponds to a general decrease in unspecific respiratory symptoms such as any wheeze and nocturnal cough in the whole population, which was likely an effect of decreased smoking [8].

Asthma symptoms: the importance of rhinitis, and smoking

Although all asthma symptoms were associated with rhinitis, there were clear differences in the strength of association. In line with previous findings asthma attacks was twice as strongly related to rhinitis compared to any wheeze [4]. A key component of an asthma attack is bronchial hyperresponsiveness, which has been put forward as an important intermediate element in the common inflammatory pathology of rhinitis and asthma [29]. The coexistent inflammation of the upper and lower airways may be related to a systemic circulation of inflammatory mediators released from the upper and/or lower airways [30]. Conversely, e.g. nocturnal cough was common both among subjects with rhinitis and in the general population [8]. This symptom may thus reflect a more diverse respiratory pathology, including non-specific responses to irritants.

Any wheeze takes an intermediate position, as it encompasses both mild and more significant wheeze, and was similarly associated with both rhinitis and current smoking [8,31]. The proportion with any wheeze in subjects with rhinitis compared to those without rhinitis decreased from 1:2 to 1:3 between 1990 and 2008. This large change was not seen for asthma symptoms more strongly associated to rhinitis and/or less associated to smoking.

Smoking is one of the major causes of respiratory disease and symptoms, and the decrease in smoking in our study is in line with previous data from Sweden [32]. [27] Interestingly, a similar decrease was seen in the Midspan Family Study, where also an uncoupling of the time trends in asthma and rhinitis occurred [10]. Could the decrease in smoking have counteracted the driving effect on asthma from an increased prevalence of rhinitis? If so, the asthma symptoms most closely associated with smoking ought to have decreased the most, whereas those more closely related to rhinitis ought to have increased. This theory was investigated as displayed in Fig. 3, which shows the associations of asthma symptoms with rhinitis and smoking, and how the prevalence of smoking, rhinitis and asthma symptoms changed between 1990 and 2008. In fact, the theory predicted quite well the observed outcomes: Current asthma, the asthma symptom most strongly associated with rhinitis but not smoking, increased; any wheeze, which was

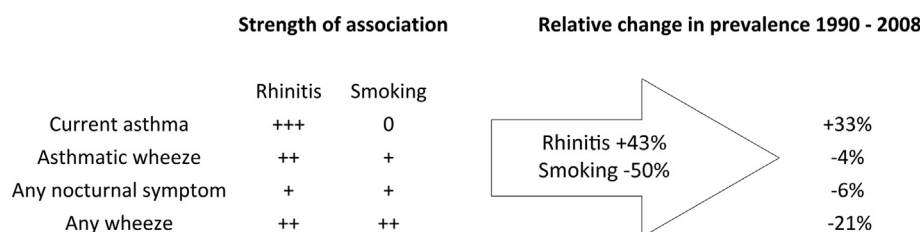


Figure 3 Association of rhinitis and smoking with respiratory outcomes, and changes in prevalence 1990–2008. Left: Semi-quantitative association of rhinitis and smoking with asthma and respiratory symptoms, graded from none (0) to very strong (+++). Right: Relative change in the prevalence of rhinitis and smoking between 1990 and 2008 and the corresponding relative change in prevalence of the respiratory outcomes.

influenced also by smoking, decreased; and nocturnal symptoms, which was not much associated to either risk factor, was largely unchanged. Naturally, this simplified analysis does not account for residual changes in other risk factors. Nonetheless, it outlines how changes in two major risk factors [3,4,33,34] relate to trends in symptoms. And even more importantly, it illustrates the benefits of decreased smoking on the public health level.

Strengths and limitations

A thorough discussion of the methodology has been published previously [8]. The major advantage of the present study was the application of the same, validated questions to two large, representative populations with similar basic demographics at two time points [8,17]. The lower participation in 2008 and the selection of a partly different study area for the Gothenburg sample seemingly did not bias the main results, as supported by the observation that the main trends were similar in all centers and a study of non-response [8,35]. Although causality cannot be directly inferred from associations in a cross-sectional study, the links of asthma symptoms with rhinitis [1–4] and smoking [33,34,36], respectively, have been repeatedly demonstrated.

All questionnaire studies are limited by the lack of objective measures. However, also in clinical practice the diagnosis of asthma relies primarily on the patient's history. To avoid bias from shifts in diagnostic practice and public awareness, symptoms, rather than diagnoses, were surveyed. We studied the associations between rhinitis and several indices of asthma to cover a broad spectrum of respiratory morbidity. The resolution of our study was limited by the use of a single rhinitis question in the ECRHS questionnaire in 1990. It has later been demonstrated that different upper airway symptoms (e.g. nasal blocking, rhinorrhoea) may be differently associated with asthma symptoms [37]. Although testing for allergic sensitisation would have allowed for differentiation between allergic and non-allergic rhinitis, sensitization status is not pivotal since rhinitis symptoms are strongly associated with asthma also in non-sensitized subjects [1,38].

Conclusions

This is the first study to describe simultaneous trends in the prevalence of rhinitis, smoking and a number of symptoms

suggestive of asthma. We conclude that despite the fact that the prevalence of rhinitis increased considerably between 1990 and 2008 while that of most asthma symptoms did not, the strength of their association remained stable. The substantial decrease in smoking is likely to have counteracted the driving effect of increased rhinitis on the prevalence of asthma symptoms. This observation is one important indication of how decreased smoking positively affects respiratory health in the population.

Competing interests

None of the authors have declared any conflict of interest.

Author contributions

RM and CJ coordinated the study. RM, S-ED, BF, KF, KL, JL, KT and CJ took part in study design. ISO, BF and RM were responsible for data collection in the local centers. AB, CJ and JE analysed the data, as presented in this paper, and AB wrote the manuscript. All authors participated in the analysis design, interpretation, review and presentation of the results.

Acknowledgements

Professors Thomas Sandström and Bo Lundbäck are acknowledged for their valuable comments. As a part of the GA²LEN survey, the study was financially supported by the EU Sixth Framework programme for research, contract no. FOOD-CT-2004-506378. The Swedish Heart and Lung Foundation, the Swedish Asthma and Allergy Foundation, the Swedish Heart-Lung Foundation, and The Centre for Allergy Research at Karolinska Institutet also provided financial support. The Gothenburg part was mainly funded by VBG Group Centre for Asthma and Allergy Research.

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