



The increase of asthma prevalence has levelled off and symptoms decreased in adults during 20 years from 1996 to 2016 in Helsinki, Finland



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ARTICLE INFO

Keywords:

Asthma
Asthma prevalence
Physician diagnosed asthma
Respiratory symptoms
Rhinoconjunctivitis

ABSTRACT

Background: Mortality and hospitalization due to asthma have decreased in many European countries, but asthma symptoms still cause a lot of morbidity and costs.

Objectives: We evaluated prevalence trends of asthma, asthma symptoms and allergic rhinoconjunctivitis in adults aged 20–69 years during a 20-year period from 1996 to 2016 in the city of Helsinki, the capital of Finland.

Methods: Three cross-sectional postal surveys were conducted in random population samples 10 years apart. In 1996, 2006 and 2016, a total of 6062 (response rate 75.9%), 2449 (61.9%) and 4026 subjects (50.3%) took part, respectively.

Results: In all responders, the prevalence of physician-diagnosed asthma was 6.6% in 1996, 10% in 2006 and 10.9% in 2016. The prevalence increased from 1996 to 2006, but stabilized from 2006 to 2016, both in men and women and in smokers and non-smokers. The prevalence of current asthma (8.5% in 2006 and 8.8% in 2016) and of asthma with rhinoconjunctivitis (7.6% in 2006 and 7.5% in 2016) remained also at the same level. Allergic rhinoconjunctivitis decreased significantly from 2006 (42.7%) to 2016 (39.0%, $p = 0.004$). Those with physician diagnosed asthma reported significantly less symptoms in 2016 compared to 2006 and 1996, although there was no change in smoking habits or medication use. Young asthmatics (20–29 years) without rhinoconjunctivitis reported least symptoms.

Conclusion: Previously observed increase of physician-diagnosed asthma prevalence in adults seems to be levelling off in Helsinki, and patients have fewer symptoms than 20 years ago. In addition, allergic rhinoconjunctivitis is less frequent than 10 years earlier. (247 words).

1. Introduction

Over the last decades, the prevalence of asthma has been increasing worldwide, but improved management and understanding of the disease have reduced morbidity and mortality [1]. However, asthma remains a major public health concern with high costs both to the patients and society. The reasons for asthma increase after the Second World War have been debated. Currently, there is growing evidence that reduced contact with natural environments and immune regulating microbes may play a role in the pathogenesis of allergic disease, including asthma [2,3].

Asthma has different phenotypes, symptoms and severity [4–6].

Allergic rhinitis, smoking and obesity are recognised risk factors to asthma and poor asthma control [7–9]. Symptoms vary from mild coughing and sputum production to breathlessness caused by airway obstruction, to severe exacerbations, and even to death. Effective preventive measures have not been established, but proactive management of symptoms and prevention of exacerbations with guided self-management have considerably improved patients' ability to live normal life [10,11].

In Finland, specific programmes have been implemented to reduce the burden of these conditions. The Asthma Programme (1994–2004) changed the first line treatment from inhaled bronchodilators to corticosteroids and educated health care professionals and patients to stop

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exacerbations effectively. The Programme reduced the number of hospital days due to asthma by 54% [11]. The recent Allergy Programme (2008–2018) aimed to improve immunological tolerance, endorse allergy health and cut down costs. The mid-term results indicate that asthma burden continues to decrease in Finland [12].

We have followed asthma and rhinitis prevalence, symptoms and medication in the city of Helsinki in 1996, 2006 and 2016. In the present study, we report the results of the 2016 survey and give an overview of the 20-year trends.

2. Population and methods

2.1. Study population

Three cross-sectional postal surveys were mailed in 1996, 2006 and 2016 to randomly selected adult population, aged 20–69 years, in the city of Helsinki. The genders were randomized separately in 10 years age cohorts taking into account the overall gender distribution in the population. Each survey was conducted in early spring, before the pollen season. In 1996, 6062 individuals responded, 2449 in 2006 and 4026 in 2016 (response rates 75.9%, 61.7% and 50.3%, respectively). The population samples were obtained from the Finnish National Population Registry.

The invited individuals were given the opportunity to respond by mail in 1996 and 2006, and by mail or via internet in 2016. Reminders were sent twice each study year.

In 2016, of the 8000 invited subjects 17 refused to participate, 7 mailed an empty questionnaire and one had died. Of the remaining 7975 subjects 4026 (50.3%) responded. Twenty-eight questionnaires were excluded because they were not adequately fulfilled. Thus, the sample consisted of 3998 responders.

The study was approved by the Coordinating Ethics Committee of Helsinki and Uusimaa Hospital District (200/13/03/00/2015).

2.2. Questionnaire

The Finnish version of the FinEsS (FinlandEstoniaSweden) postal survey has been published previously [13]. The questions focus on respiratory symptoms, asthma and risk factors like smoking habits.

2.3. Questions and definitions

Self-reported allergic rhinoconjunctivitis. Do you have now or have you previously had allergic rhinitis (e.g. hay fever) or allergic eye symptoms?

Physician-diagnosed asthma. Have you been diagnosed by a doctor as having asthma?

Asthma with rhinoconjunctivitis. Positive answers to (1) physician-diagnosed asthma, and (2) self-reported allergic rhinoconjunctivitis.

Asthma without rhinoconjunctivitis. A positive answer to (1) physician-diagnosed asthma, and (2) a negative answer to

rhinoconjunctivitis.

Current asthma. Physician diagnosed asthma in combination with a positive answer to at least one of the following questions: (1) have you had shortness of breath during the last 12 months, (2) have you had any wheeze during the last 12 months, or (3) do you currently use asthma medication?

Asthma medication use. Do you currently use asthma drugs (regularly or as needed)?

Asthma symptoms. Do you have now, or have you had asthma symptoms during the last 12 months (breathlessness with or without cough or wheezing)?

Longstanding cough. Have you had longstanding cough during the last 12 months?

Sputum production. Have you brought up phlegm on most days for at least three months yearly during the last two years?

Wheeze. Is it usual that you have wheezing, whistling or noisy sounds in your chest when breathing?

Past year wheeze. Have you had wheezing or whistling in your chest at any time in the last 12 months?

Dyspnoea with wheeze. Have you been breathless when the wheezing sound has been present?

Wheeze without cold. Have you had wheezing or whistling when you did not have a cold?

Asthmatic wheeze. A positive answer to wheeze, breathless with wheeze, and wheeze without cold during the last year.

Morning dyspnoea. Have you waked up with a feeling of tightness in your chest at any time during the last year?

Smoker. Current smoker or having stopped smoking during the last year.

Ex-smoker. Stopped smoking more than a year prior to the study.

Non-smoker. Neither current smoker nor ex-smoker.

2.4. Statistical analyses

All analyses were performed using IBM SPSS version 23.0. Descriptive statistics i.e. frequencies and percentages were used to describe the study populations. Chi-square test was used to analyse differences between groups. $p < 0.05$ was regarded as statistically significant. Odds ratios (OR) for physician diagnosed asthma were estimated with logistic regression model adjusted for year, age and sex.

3. Results

The characteristics of the study population each study year, divided to men and women and in 10 years age cohorts are shown in Table 1.

The development of the asthma prevalence is given in Table 2 and Fig. 1. The prevalence of physician diagnosed asthma, current asthma and asthma with rhinoconjunctivitis increased significantly during the first 10 years of the observation period but remained at the same level during the latter period from 2006 to 2016. The prevalence of physician diagnosed asthma was 6,6% in 1996, 10,0% in 2006, and 10,9% in

Table 1

Age, gender and smoking of the study population in the three FinEsS questionnaire surveys in 1996, 2006 and 2016 in the city of Helsinki.

	Men 1996	Men 2006	Men 2016	Women 1996	Women 2006	Women 2016
N (%)	2598 (42.9%)	1084 (44.3%)	1693 (42.3%)	3460 (57.1%)	1365 (55.7%)	2305 (57.7%)
Mean (SD) age, years	42.3 (13.1)	45.0 (13.9)	45.5 (14.4)	42.2 (13.3)	45.4 (14.1)	45.2 (15.0)
Age 20–29	506 (19.5%)	200 (18.5%)	290 (17.1%)	758 (21.9%)	277 (20.3%)	457 (19.8%)
30–39	656 (25.3%)	224 (20.7%)	392 (23.2%)	831 (24.0%)	254 (18.6%)	481 (20.9%)
40–49	599 (23.1%)	236 (21.8%)	283 (16.7%)	787 (22.7%)	240 (17.6%)	373 (16.2%)
50–59	490 (18.9%)	219 (20.2%)	356 (21.0%)	647 (18.7%)	323 (23.7%)	469 (20.3%)
60–69	347 (13.4%)	205 (18.9%)	363 (21.4%)	437 (12.6%)	271 (19.9%)	509 (22.1%)
Smokers	1013 (39.0%)	357 (32.9%)	493 (29.1%)	1063 (30.7%)	330 (24.2%)	493 (21.4%)
Ex-smokers	570 (21.9%)	265 (24.4%)	414 (24.5%)	504 (14.6%)	284 (20.8%)	469 (20.3%)
Non-smokers	1013 (39.0%)	463 (42.7%)	808 (47.7%)	1897 (54.8%)	751 (55.0%)	1368 (59.3%)

Table 2

All responders. Prevalence of asthma and asthma related symptoms from 1996 to 2016. *Current asthma* = physician-diagnosed asthma AND wheeze OR dyspnoea OR use of asthma medication during the last 12 months. *Asthmatic wheeze* = wheeze during the last 12 months AND dyspnea with wheeze AND wheeze without cold.

Symptom	1996	2006	2016	p-value 1996 vs 2016	p-value 2006 vs 2016
Physician-dg asthma	398 (6.6%)	245 (10.0%)	437 (10.9%)	0.000	0.240
Current asthma	352 (5.8%)	208 (8.5%)	351 (8.8%)	0.000	0.692
Asthma with rhinoconjunctivitis	286 (4.7%)	186 (7.6%)	300 (7.5%)	0.000	0.893
Asthma without rhinoconjunctivitis	112 (1.8%)	59 (2.4%)	137 (3.4%)	0.000	0.021
Asthma medication	363 (6.0%)	229 (9.4%)	464 (11.6%)	0.000	0.005
Asthma symptoms	784 (12.9%)	371 (15.1%)	574 (14.4%)	0.014	0.383
Prolonged cough	1207 (19.9%)	463 (18.9%)	720 (18.0%)	0.055	0.377
Sputum production	734 (12.1%)	271 (11.1%)	328 (8.2%)	0.000	0.000
Wheeze	440 (7.3%)	177 (7.2%)	279 (7.0%)	0.856	0.705
Past year wheeze	1210 (20.0%)	542 (22.1%)	756 (18.9%)	0.007	0.002
Dyspnoea with wheeze	627 (10.3%)	268 (10.9%)	313 (7.8%)	0.000	0.000
Wheeze without cold	788 (13.0%)	339 (13.8%)	423 (10.6%)	0.000	0.000
Morning dyspnoea	1512 (25.0%)	592 (24.2%)	854 (21.4%)	0.000	0.009
Asthmatic wheeze	444 (7.3%)	189 (7.7%)	213 (5.3%)	0.000	0.000
Rhinoconjunctivitis	2234 (36.9%)	1045 (42.7%)	1561 (39.0%)	0.000	0.000

2016, of current asthma 5.8%, 8.5%, and 8.8%, and of asthma with rhinoconjunctivitis 4.7%, 7.6% and 7.5%, respectively. Asthma without rhinoconjunctivitis still increased slightly from 2006 to 2016, both in men and women and in smokers and non-smokers.

Young men aged 20–29 years were exceptions as physician-diagnosed asthma increased among them from 2006 to 2016 (Table 3). Alarming 40% of them reported smoking, when the figure was 18.8% ten years earlier. Asthma prevalence increase is seen also among 40–49 years, but the increase is not significant among men or women separately. In women, the prevalence of physician diagnosed asthma was stable from 2006 to 2016 both among non-smokers (9.7% vs 9.1%) and smokers (12.4% vs 12.8%).

In 20 years, a remarkable decrease was observed in asthma symptoms in those subjects with physician-diagnosed disease regardless whether they were smoking or not (Fig. 2). In 1996, 62.6% of the non-smoking asthmatics reported wheezing during the past year, while the figure was 45.3% in 2016 (p = 0.002). In smokers the respective figures were 80.2% and 66.9% (p = 0.040). Young asthmatic subjects, aged 20–29 years and without rhinoconjunctivitis reported the lowest occurrence of asthma symptoms. For example, not more than 8.3% of them reported asthmatic wheeze (compared to 25.2% in all asthmatics). The asthmatics also reported somewhat less rhinoconjunctivitis in 2006 compared with 2016 (75.9% vs 68.6%, p = 0.044).

Altogether, the prevalence of self-reported allergic rhinoconjunctivitis decreased significantly from 2006 to 2016 (42.7% vs 39.0%, p = 0.004) (Table 2). This was observed among non-smokers (42.8% vs

Table 3

All responders. The prevalence of physician diagnosed asthma, and in men and women by age group from 1996 to 2016.

	1996	2006	2016	P-VALUE	P-VALUE
ALL					
AGE GROUP				1996 vs 2016	2006 vs 2016
20–29	80 (6.3%)	46 (9.6%)	104 (13.9%)	0.000	0.026
30–39	81 (5.4%)	54 (11.3%)	88 (10.1%)	0.000	0.486
40–49	81 (5.8%)	37 (7.8%)	76 (11.6%)	0.000	0.035
50–59	66 (5.8%)	60 (11.1%)	87 (10.5%)	0.000	0.759
60–69	90 (11.5%)	48 (10.1%)	82 (9.1%)	0.286	0.570
MEN					
20–29	31 (6.1%)	16 (8.0%)	50 (17.2%)	0.000	0.003
30–39	23 (3.5%)	20 (8.9%)	51 (13.0%)	0.000	0.127
40–49	34 (5.7%)	18 (7.6%)	32 (11.3%)	0.012	0.157
50–59	20 (4.1%)	23 (10.5%)	34 (9.6%)	0.001	0.711
60–69	37 (10.7%)	23 (11.2%)	25 (6.7%)	0.099	0.061
WOMEN					
20–29	49 (6.5%)	30 (10.8%)	54 (11.8%)	0.003	0.684
30–39	58 (7.0%)	34 (13.4%)	37 (7.7%)	0.004	0.013
40–49	47 (6.0%)	19 (7.9%)	44 (11.8%)	0.003	0.123
50–59	46 (7.1%)	37 (11.5%)	53 (11.3%)	0.023	0.946
60–69	53 (12.1%)	25 (9.2%)	57 (10.9%)	0.483	0.473

39.2%, p = 0.039) and in women (45.9% vs 41.3%, p = 0.006). The prevalence decreased also among men, but not significantly (38.7% vs 36.0%, p = 0.16).

Among all responders, smoking decreased and the use of asthma medication increased in 20 years (Tables 1 and 2). In asthmatics,

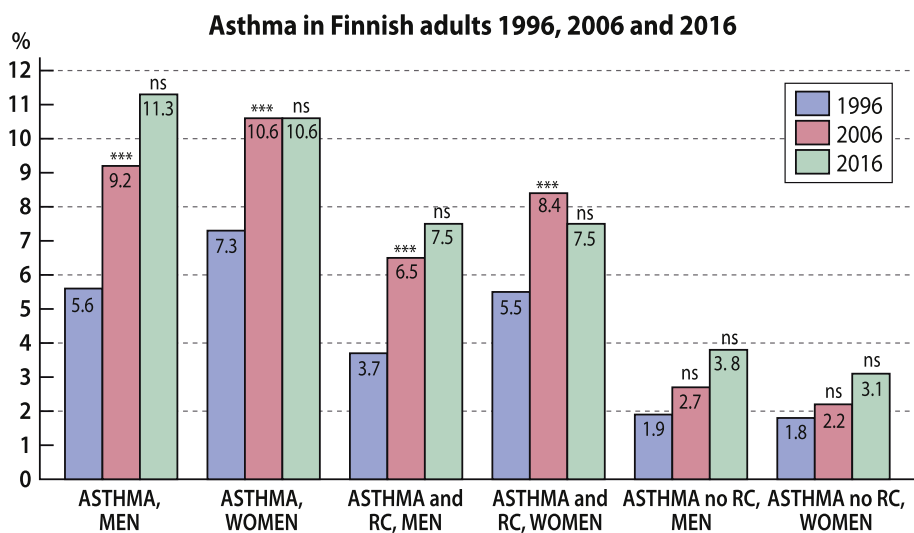


Fig. 1. Prevalence (%) of physician-diagnosed asthma and asthma with and without rhinoconjunctivitis by gender from 1996 to 2016. Statistical comparison between 1996 and 2006 and between 2006 and 2016 (*p < 0.05, **p < 0.01, ***p < 0.001, ns = non significant). For all subjects, asthma prevalence, with or without rhinoconjunctivitis, did not increase between 2006 and 2016. RC = rhinoconjunctivitis.

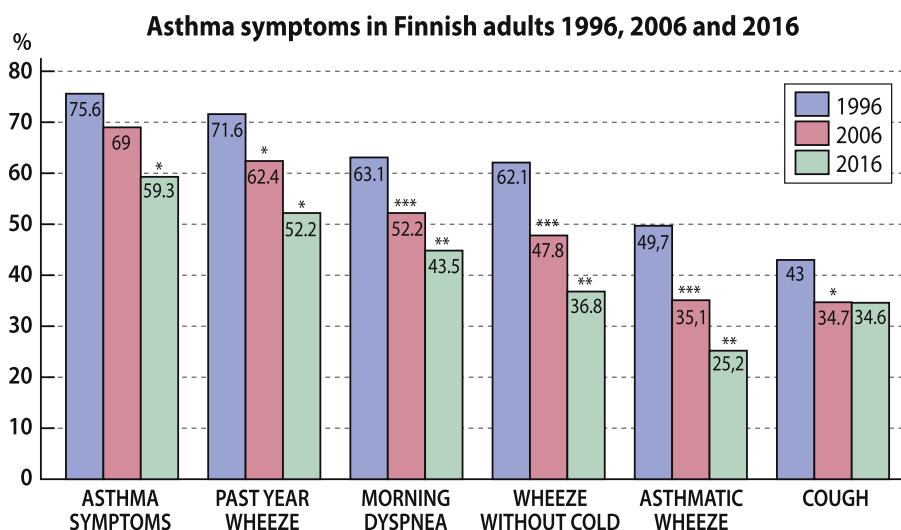


Fig. 2. Prevalence (%) of respiratory symptoms among responders who reported a physician-diagnosed asthma from 1996 to 2016. Statistical comparison between 1996 and 2016 (*p < 0.05, **p < 0.01, ***p < 0.001).

however, asthma medication use from 1996 to 2016 (71.1% vs 70.3%), smoking (33.2% vs 30.6%), and body mass index (BMI, 26.0 vs 26.0) remained the same.

Results of the regression analysis are given in Table 4. The increase of physician diagnosed asthma was evident from 1996 to 2006, but became slower during the last 10 years. Although the overall asthma increase seemed to level off from 2006 to 2016, it was still observed in some subgroups like the youngest (20–29) and the middle-aged (40–49 years) responders.

4. Discussion

The increase of prevalence of physician diagnosed asthma seems to be levelling off in the city of Helsinki. The prevalence of current asthma and asthma with rhinoconjunctivitis increased from 1996 to 2006 but have been stable during the last decade. Asthma symptoms among those with physician diagnosed asthma and the prevalence of rhinoconjunctivitis have decreased significantly. Those subjects with physician diagnosed asthma without rhinoconjunctivitis reported the least symptoms.

The Finnish Asthma Programme 1994–2004 focused on early intervention with anti-inflammatory medication and disease control. Health-care personnel was trained to find the patients at early stage of disease and treat them effectively. Asthmatics were educated to stop

Table 4

All responders. Adjusted Odds ratios (OR) for physician diagnosed asthma in 2006 and 2016, compared with 1996 and 2006 as a reference by age group and gender. Logistic regression with physician-diagnosed asthma as outcome and year of study, age (continuous) and sex as covariates. In separate models for males and females the models are not adjusted for sex. Bold figures indicate statistical significance (P < 0.05).

	Year	(95% CI)	Year	(95% CI)	Year	(95% CI)
	2006		2016		2016	
	vs		vs		vs	
	1996		1996		2006	
20-29	1.586	1.086–2.318	2.365	1.738–3.220	1.525	1.054–2.206
30-39	2.379	1.649–3.433	1.972	1.440–2.702	0.862	0.601–1.236
40-49	1.383	0.922–2.074	2.091	1.506–2.903	1.529	1.011–2.313
50-59	1.929	1.330–2.798	1.890	1.352–2.642	0.964	0.679–1.368
60-69	0.857	0.591–1.242	0.753	0.547–1.038	0.873	0.598–1.275
All	1.550	1.310–1.833	1.742	1.510–2.010	1.104	0.936–1.302
Men	1.669	1.278–2.179	2.213	1.765–2.775	1.266	0.981–1.633
Women	1.480	1.193–1.837	1.479	1.229–1.780	1.001	0.805–1.243

exacerbations proactively by guided self-management. Tobacco legislation was tightened to eradicate smoking in work places and later indoors in public buildings [11]. Public awareness of asthma and allergies was increased by special campaigns. The Programme reduced significantly the asthma burden, e.g. in terms of hospital days [11,14] and costs [15]. In long-term, the decrease of annual costs per patient has been remarkable, even 72% from 1987 to 2013.

Asthma prevalence has increased over the past decades [16–21]. However, it has been discussed if the rise seen in asthma and asthma symptom prevalence would be a consequence of increased disease awareness and better diagnostics [22]. Some studies have also suggested a plateau in prevalence trends [23,24]. In the previous 2006 survey in Helsinki, the prevalence was still rising [25] but has been stable since then. The worldwide prevalence is affected by multiple factors like fast urbanization changing environment and lifestyle [1–3] and economic development [19,26]. Smoking and exposure to tobacco smoke have decreased in several countries in recent years, and may partly explain the decreasing prevalence [27–31]. In the present study, respiratory symptoms decreased both in all responders and in asthmatics. Exposure to tobacco smoke has decreased in Finland, and the Tobacco Act aims to end the use of tobacco products by the year 2030.

Dietary habits are known to affect several diseases such as cardiovascular disease, type 2 diabetes and cancer [32]. Some studies suggest that fruit and vegetable consumption would decrease asthma risk and improve disease control, but the evidence is still modest [33–35]. Processed meat may have a negative effect on asthma control [36]. In a recent French study, Mediterranean like diet was associated with better asthma control even after adjustments for smoking, educational level, and physical activity [37]. Even though we have no data on dietary habits in our study, a recent report from Finland found that the intake of vegetables and fruits was closer to dietary guidelines in women than in men. Younger men consumed less vegetables, fruits and berries than older men [38]. It is possible that the differences in dietary habits could have contributed to the higher asthma risk in young men in the present study.

In all responders, respiratory and asthma symptoms decreased in our study, while they were stable in Norrbotten County, Sweden [16]. In Norrbotten, 18.6% reported wheezing during the last 12 months in 2006 and 18.1% in 2016. In Helsinki, 22.1% of responders reported wheezing during the past year in 2006 and 18.9% in 2016 (p = 0.002). The prevalence of asthmatic wheeze decreased also significantly in Helsinki (7.7% in 2006 vs 5.3% in 2016) but was stable in Sweden (7.4% in 2006 vs 7.2% in 2016) [16]. The asthma prevalence increased

among young men in our study, and the same worrying trend is seen also in Sweden [39]. In a Norwegian study overweight increased the odds of asthma in adolescents [8]. In our study, BMI was the same in 2006 and in 2016 among 20–29 years old men so obesity does not explain the increase in asthma prevalence. In the present study, the response rate was lowest among young men and possible report bias may partly explain the increase in prevalence found in men aged 20–29 years.

In asthmatics, the decrease in symptoms was observed both in our study and in Norrbotten county in 1996–2016 [16]. The smoking habits of responders with physician diagnosed asthma have remained the same in Helsinki, but active smoking has halved among Swedish asthmatics in 20 years (24.7% in 1996 vs 11.1% in 2016). This may partly explain the symptom reduction in Sweden [40]. In the asthma barometer survey carried out in Finnish pharmacies in 2001 and 2010, the self-reported asthma severity has decreased in 10 years in line with the present study results [41]. Air pollution has not been a problem in Finland and it is unlikely that it would explain the decrease in asthma symptoms. According to reports from Helsinki Region Environmental Services Authority the air quality is good and has not changed for decades. It is likely possible that the decrease in asthma symptoms in our study, and Finland in general, is at least in part due to active symptom control measures taken during the Finnish Asthma and Allergy programmes [11,12].

Asthma medication has improved since 1996. Fluticasone-salmeterol combination was launched in Finland in 1996 and budesonide-formoterol in 2001. These medications were already used in 2006 [42]. Overall asthma medication use has been the same during 20 years in our study, but the use of combination products increased by 20% in 2008–2015, according to The Social Insurance Institution of Finland. The symptom reduction is significant both from 1996 to 2006 and from 2006 to 2016. Therefore, it is unlikely that combination products alone would be an essential explanation for the better control.

Self-reported rhinoconjunctivitis has slightly decreased during the last 10 years in our study, but the prevalence is still high, 39.0%. In a Swedish study the prevalence of self-reported rhinoconjunctivitis is somewhat lower but has been rising, from 24.8% in 2006 to 27.8% in 2016 [16]. This fits to another survey from Sweden, where sensitization to common allergens was on rise in schoolchildren [43].

4.1. Strengths and limitations

The present study has several strengths. A large sample size, with a wide age span, reflects general population. The study samples were randomized in 10 years age cohorts taking into account the overall gender and age distribution in the population. The study questions were same in 1996, 2006 and 2016. We present results from three surveys, each 10 years apart from the same area. The three surveys were done with similar methods, so the results would be comparable. Asthma diagnosis is always based on objective lung function measurements in Finland due to the drug reimbursement system making asthma diagnoses reliable. Similar postal questionnaire study is done also in Sweden in 1996, 2006 and 2016. We are working on a joint study project with Swedish Fitness group comparing our results in 1996–2016.

The number of invited subjects in 2006 study was half of that invited in 1996 and 2016, study then performed by Filha [25]. The present results show similar amount of physician diagnosed asthma and asthma with rhinoconjunctivitis in 2006 and in 2016. Also the 95% confidence intervals for prevalence estimates of physician diagnosed asthma and asthma with and without rhinoconjunctivitis overlapped in the 2006 and 2016 cohorts indicating that the difference in cohort size was most probably not relevant.

The response rate declined over the years from 75.9% in 1996 to 61.7% in 2006, and to 50.3% in 2016. Participation rates have decreased by time in epidemiological studies as a general trend. The response rate has been about the same in other epidemiological studies as

in our study, for example 55% in Copenhagen City Heart Study and 53% in a Swedish follow up study on prevalence of asthma [16,44]. The response rate is still moderate considering general decline in response rates during last decades [16,43]. In the present study, a telephone interview of a sample of non-responders was planned but denied by the ethics committee. Therefore, we performed a non-responder-analysis based on information that was available for responders and non-responders. We found that Finnish or Swedish speaking subjects responded more actively compared to those with other native languages. The youngest subjects responded less actively compared to the oldest subjects. To adjust for differences in response rates, we performed analyses for asthma prevalence and smoking habits among respondents to the first, second and third mailing of the questionnaire separately. No significant differences were found in asthma prevalence. Respondents to the first and second mailing were less likely to be smokers than respondents to the third mailing (22.7%, 23.9%, and 30.2%, $p = 0.013$). Earlier, studies have found non-responders being more often young, male and smokers [45,46]. This is in line with our findings. None of the non-responder studies concluded that non-response bias would affect the prevalence of asthma [45,46]. However, in a previous Finnish non-responder-study [47] symptomatic individuals were more likely to respond than individuals without symptoms. Therefore, some non-responder cannot be excluded in the present study in the youngest age groups.

Study limitations also included that no objective measurement of lung function was performed. In Finland, asthma is confirmed with lung function testing, which is a prerequisite for a special reimbursement for asthma medication costs. Therefore, physician diagnosed asthma is an accurate measure to follow asthma trends in Finland.

5. Conclusions

The increase of prevalence of asthma seems to be levelling off in Helsinki. In general, asthmatics had fewer symptoms in 2016 than 2006. At the same time, prevalence of self-reported rhinoconjunctivitis has decreased significantly. Changes in prevalence are small but significant in a large population. The effectively implemented national Asthma Programme (1994–2004) and Allergy Programme (2008–2018) changed management and increased public awareness. They may have reduced symptoms and their severity. Our results encourage systematic work to diagnose and treat asthma and respiratory symptoms effectively for better public health.

Declaration of interests

Hanna Hisinger-Mölkänen works for GlaxoSmithKline as Medical Advisor (since June 2018). This study was mostly done prior to this employment. Our study does not involve data on medication and thus this employment is not considered as competing interest for this epidemiological work.

Other authors have no competing interests.

Funding

This study was supported by a special governmental subsidy for health sciences research (Helsinki University Central Hospital project grants TYH 2013354 and Y2017SK004), Nummela Sanatorium Foundation, Research Foundation for Pulmonary Diseases (Heli), Väinö and Laina Kivi Foundation, and Ida Montin Foundation, the Foundation of the Finnish Anti-Tuberculosis and the Nordic Council of Ministers: NordForsk (Nordic Epilung Study).

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.rmed.2019.07.014>.

References

- [1] Global Asthma Report, (2018) www.globalasthmareport.org.
- [2] I. Hanski, L. von Hertzen, N. Fyhrquist, K. Koskinen, K. Torppa, T. Laatikainen, P. Karisola, P. Auvinen, L. Paulin, M.J. Mäkelä, E. Vartiainen, T.U. Kosunen, H. Alenius, T. Haahela, Environmental biodiversity, human microbiota, and allergy are interrelated, *Proc. Natl. Acad. Sci. U. S. A.* 109 (2012) 8334–8339, <https://doi.org/10.1073/pnas.1205624109>.
- [3] T. Haahela, T. Laatikainen, H. Alenius, P. Auvinen, N. Fyhrquist, I. Hanski, L. Von Hertzen, P. Jousilahti, T.U. Kosunen, O. Markelova, M.J. Mäkelä, V. Pantelev, M. Uhanov, E. Zilber, E. Vartiainen, Hunt for the origin of allergy - comparing the Finnish and Russian Karelia, *Clin. Exp. Allergy* 45 (2015) 891–901, <https://doi.org/10.1111/cea.12527>.
- [4] P. Ilmarinen, L. Tuomisto, O. Niemela, M. Tommola, J. Haanpaa, H. Kankaanranta, Cluster Analysis on longitudinal data of patients with adult-onset asthma, *J. Allergy Clin. Immunol. Pract.* 5 (2017) 967–978, <https://doi.org/10.1016/j.jaip.2017.01.027>.
- [5] P. Ilmarinen, L.E. Tuomisto, H. Kankaanranta, Phenotypes, risk factors, and mechanisms of adult-onset asthma, *Mediat. Inflamm.* 2015 (2015) 514868, <https://doi.org/10.1155/2015/514868>.
- [6] R. Mincheva, L. Ekerljung, A. Bossio, B. Lundbäck, J. Lötvall, High prevalence of severe asthma in a large random population study, *J. Allergy Clin. Immunol.* 141 (2018) 2256–2264, <https://doi.org/10.1016/j.jaci.2017.07.047>.
- [7] L.E. Tuomisto, P. Ilmarinen, O. Niemela, J. Haanpaa, T. Kankaanranta, H. Kankaanranta, A 12-year prognosis of adult-onset asthma: seinäjoki adult asthma study, *Respir. Med.* 117 (2016) 223–229, <https://doi.org/10.1016/j.rmed.2016.06.017>.
- [8] K.B. Egan, A.S. Ettinger, A.T. DeWan, T.R. Holford, T.L. Holmen, M.B. Bracken, General but not abdominal, overweight increases odds of asthma among Norwegian adolescents: the Young-Hunt study, *Acta Paediatr.* 103 (2014) 1270–1276, <https://doi.org/10.1111/apa.12775>.
- [9] R. Beasley, A. Semprini, E.A. Mitchell, Risk factors for asthma: is prevention possible? *Lancet* 386 (2015) 1075–1085, [https://doi.org/10.1016/S0140-6736\(15\)00156-7](https://doi.org/10.1016/S0140-6736(15)00156-7).
- [10] A. Lahdensuo, T. Haahela, J. Herrala, T. Kava, K. Kiviranta, P. Kuusisto, Randomised comparison of guided self management and traditional treatment of asthma over one year, *BMJ* 312 (1996) 748–752.
- [11] T. Haahela, L.E. Tuomisto, A. Pietinalho, T. Klaukka, M. Erhola, M. Kaila, M.M. Nieminen, E. Kontula, L.A. Laitinen, A 10 year asthma programme in Finland: major change for the better, *Thorax* 61 (2006) 663–670, <https://doi.org/10.1136/thx.2005.055699>.
- [12] T. Haahela, E. Valovirta, J. Bousquet, M. Makela, Allergy programme steering group. The Finnish allergy programme 2008–2018 works, *Eur. Respir. J.* 49 (2017) 1700470, <https://doi.org/10.1183/13993003.00470-2017>.
- [13] P. Pallasaho, B. Lundbäck, S.L. Läspä, E. Jönsson, J. Kotaniemi, A.R. Sovijärvi, L.A. Laitinen, Increasing prevalence of asthma not of chronic bronchitis in Finland? Report from the FinEsS-Helsinki Study, *Respir. Med.* 93 (1999) 798–809.
- [14] P. Kauppi, M. Linna, J. Martikainen, M.J. Makela, T. Haahela, Follow-up of the Finnish Asthma Programme 2000–2010: reduction of hospital burden needs risk group rethinking, *Thorax* 68 (2013) 292–293.
- [15] T. Haahela, F. Herse, J. Karjalainen, T. Klaukka, M. Linna, R.-L. Leskelä, O. Selroos, E. Reissell, The Finnish experience to save asthma costs by improving care in 1987–2013, *J. Allergy Clin. Immunol.* 139 (2017) 408–414, <https://doi.org/10.1016/j.jaci.2016.12.001>.
- [16] H. Backman, P. Raisanen, L. Hedman, C. Stridsman, M. Andersson, A. Lindberg, B. Lundbäck, E. Rönmark, Increased prevalence of allergic asthma from 1996 to 2006 and further to 2016—results from three population surveys, *Clin. Exp. Allergy* 47 (2017) 1426–1435, <https://doi.org/10.1111/cea.12963> Epub 2017 Jul 12.
- [17] W. Eder, M.J. Ege, E. von Mutius, The asthma epidemic, *N. Engl. J. Med.* 355 (2006) 2226–2235, <https://doi.org/10.1056/NEJMra054308>.
- [18] M.I. Asher, S. Montefort, B. Björkstén, C.K. Lai, D.P. Strachan, S.K. Weiland, H. Williams, ISAAC Phase Three Study Group. Worldwide time trends in the prevalence of symptoms of asthma, allergic rhinoconjunctivitis, and eczema in childhood: ISAAC Phases One and Three repeat multicountry cross-sectional surveys, *Lancet* 368 (2006) 733–743.
- [19] T. Laatikainen, L. von Hertzen, J.P. Koskinen, M.J. Makela, P. Jousilahti, T.U. Kosunen, T. Vlasoff, M. Ahström, E. Vartiainen, T. Haahela, Allergy gap between Finnish and Russian Karelia on increase, *Allergy* 66 (2011) 886–892, <https://doi.org/10.1111/j.1398-9995.2010.02533>.
- [20] R. de Marco, V. Cappa, S. Accordini, M. Rava, L. Antonicelli, O. Bortolami, M. Braggioni, M. Bugiani, L. Casali, L. Cazzoletti, I. Cerveri, A.G. Fois, P. Girardi, F. Locatelli, A. Marcon, A. Marinoni, M.G. Panico, P. Pirina, S. Villani, M.E. Zanolin, G. Verlatto, GEIRD Study Group, Trends in the prevalence of asthma and allergic rhinitis in Italy between 1991 and 2010, *Eur. Respir. J.* 39 (2012) 883–892, <https://doi.org/10.1183/09031936.00061611>.
- [21] P. Jousilahti, T. Haahela, T. Laatikainen, M. Makela, E. Vartiainen, Asthma and respiratory allergy prevalence is still increasing among Finnish young adults, *Eur. Respir. J.* 47 (2016) 985–987, <https://doi.org/10.1183/13993003.01702-2015>.
- [22] R. Barraclough, G. Devereux, D.J. Hendrick, S.C. Stenton, Apparent but not real increase in asthma prevalence during the 1990s, *Eur. Respir. J.* 20 (2002) 826–833.
- [23] G. Wennergren, L. Ekerljung, B. Alm, J. Eriksson, J. Lotvall, B. Lundback, Asthma in late adolescence—farm childhood is protective and the prevalence increase has levelled off, *Pediatr. Allergy Immunol.* 21 (2010) 806–813, <https://doi.org/10.1111/j.1399-3038.2010.01057>.
- [24] N. Pearce, N. Ait-Khaled, R. Beasley, J. Mallol, U. Keil, E. Mitchell, C. Robertson, ISAAC phase three study group. Worldwide trends in the prevalence of asthma symptoms: phase III of the international study of asthma and allergies in childhood (ISAAC), *Thorax* 62 (2007) 758–766.
- [25] A. Kainu, P. Pallasaho, P. Piirila, A. Lindqvist, A. Sovijärvi, A. Pietinalho, Increase in prevalence of physician-diagnosed asthma in Helsinki during the Finnish Asthma Programme: improved recognition of asthma in primary care? A cross-sectional cohort study, *Prim. Care Respir. J.* 22 (2013) 64–71, <https://doi.org/10.1111/j.1399-3038.2010.01057>.
- [26] A.W. Stewart, E.A. Mitchell, N. Pearce, D.P. Strachan, S.K. Weiland, ISAAC Steering Committee. International Study for Asthma and Allergy in Childhood. The relationship of per capita gross national product to the prevalence of symptoms of asthma and other atopic diseases in children (ISAAC), *Int. J. Epidemiol.* 30 (2001) 173–179.
- [27] X. Zhang, N. Jonhson, G. Carrillo, X. Xu, Decreasing trend in passive tobacco exposure and association with asthma in U.S. children, *Environ. Res.* 166 (2018) 35–41.
- [28] A.M. Neophytou, S.S. Oh, M.J. White, A.J.Y. Mak, D. Hu, S. Huntsman, C. Eng, D. Serebrisky, L.N. Borrell, H.J. Farber, K. Meade, A. Davis, P.C. Avila, S.M. Thyne, W. Rodriguez-Cintron, J.R. Rodriguez-Santana, R. Kumar, E. Brigino-Buenaventura, S. Sen, M.A. Lenoir, L.K. Williams, N.L. Benowitz, J.R. Balmes, E.A. Eisen, E.G. Burchard, Secondhand smoke exposure and asthma outcomes among African-American and Latino children with asthma, *Thorax* 73 (2018) 1041–1048. <https://savutonsuomi.fi/en>.
- [29] V. Siroux, I. Pin, M.P. Oryszczyn, N. Le Moual, F. Kauffmann, Relationships of active smoking to asthma and asthma severity in the EGEA study. Epidemiological study on the genetics and environment of asthma, *Eur. Respir. J.* 15 (2000) 470–477.
- [30] M.G. Belvisi, K. Baker, N. Malloy, K. Raemdonck, B. Dekkak, M. Pieper, A.T. Nials, M.A. Birrel, Modelling the asthma phenotype: impact of cigarette smoke exposure, *Respir. Res.* 19 (2018) 89, <https://doi.org/10.1186/s12931-018-0799-7>.
- [31] C.K. Roberts, R.J. Barnard, Effects of exercise and diet on chronic disease, *J. Appl. Physiol.* 98 (2005) 3–30, <https://doi.org/10.1152/jappphysiol.00852.2004>.
- [32] M. Uddenfeldt, C. Janson, E. Lampa, M. Leander, D. Norback, L. Larsson, A. Rask-Andersen, High BMI is related to higher incidence of asthma, while a fish and fruit diet is related to a lower—Results from a long-term follow-up study of three age groups in Sweden, *Respir. Med.* 104 (2010) 972–980.
- [33] I. Romieu, R. Varraso, V. Avenel, B. Leynaert, F. Kauffmann, F. Clavel-Chapelon, Fruit and vegetable intakes and asthma in the E3N study, *Thorax* 61 (2006) 209–215.
- [34] L.G. Wood, M.L. Garg, J.M. Smart, H.A. Scott, D. Barker, P.G. Gibson, Manipulating antioxidant intake in asthma: a randomized controlled trial, *Am. J. Clin. Nutr.* 96 (2012) 534–543.
- [35] Z. Li, M. Rava, A. Bédard, O. Dumas, J. Garcia-Aymerich, B. Leynaert, C. Pison, N. LeMoual, I. Romieu, V. Siroux, Cured meat intake is associated with worsening asthma symptoms, *Thorax* 72 (2017) 206–212.
- [36] R.M. Andrianasolo, E. Kesse-Guyot, M. Adjibade, S. Hercberg, P. Galan, R. Varraso, Associations between dietary scores with asthma symptoms and asthma control in adults, *Eur. Respir. J.* 52 (2018) 1702572, <https://doi.org/10.1183/13993003.02572-2017>.
- [37] <http://urn.fi/URN:ISBN:978-952-343-238-3>.
- [38] E. Borna, B.I. Nwaru, A. Bjerg, R. Mincheva, M. Rådinger, B. Lundbäck, L. Ekerljung, Changes in prevalence of asthma and respiratory symptoms in western Sweden between 2008 and 2016, *Allergy* 25 (2019), <https://doi.org/10.1111/all.13840>.
- [39] H. Backman, L. Hedman, S.-A. Jansson, A. Lindberg, B. Lundbäck, E. Rönmark, Prevalence trends in respiratory symptoms and asthma in relation to smoking -two cross-sectional studies ten years apart among adults in northern Sweden, *World Allergy Organ. J.* 7 (2014) 1–10, <https://doi.org/10.1186/1939-4551-7-1>.
- [40] P. Kauppi, S. Peura, J. Salimaki, S. Jarvenpaa, M. Linna, T. Haahela, Reduced severity and improved control of self-reported asthma in Finland during 2001–2010, *Asia Pac. Allergy* 5 (2015) 32–39. <http://spc.nam.fi/index/svenska/html/nam/humspc/9/217159.pdf>.
- [41] J. Bunne, H. Moberg, L. Hedman, M. Andersson, A. Bjerg, B. Lundback, E. Rönmark, Increase in allergic sensitization in schoolchildren: two cohorts compared 10 Years apart, *J. Allergy Clin. Immunol. Pract.* 5 (2017) 457–463 e1.
- [42] A. Browatzki, C.R. Ulrik, P. Lange, Prevalence and severity of self-reported asthma in young adults, 1976–2004, *Eur. Respir. J.* 34 (2009) 1046–1051.
- [43] E. Ronmark, L. Ekerljung, J. Lotvall, K. Toren, E. Ronmark, B. Lundback, Large scale questionnaire survey on respiratory health in Sweden: effects of late- and non-response, *Respir. Med.* 103 (2009) 1807–1815.
- [44] M.L. Hazell, J.A. Morris, M.F. Linehan, P.I. Frank, T.L. Frank, Factors influencing the response to postal questionnaire surveys about respiratory symptoms, *Prim. Care Respir. J.* 18 (2009) 165–170.
- [45] J.T. Kotaniemi, J. Hassi, M. Kataja, E. Jönsson, L.A. Laitinen, A.R. Sovijärvi, N. Lundbäck, Does non-responder bias have a significant effect on the results in a postal questionnaire study? *Eur. J. Epidemiol.* 17 (2001) 809–817.