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Prevalence and severity of self-reported asthma in young Danish adults over 3 decades

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Abstract

Aim: To describe prevalence and severity of asthma over three decades in young Danish adults.

Methods: Men and women aged 20-35 yrs were sampled from the population of Copenhagen for the 3 surveys (1976-8, 1991-3, and 2001-4). A total of 3285 (46 % males) subjects answered a questionnaire, and had height, weight, FEV_1, and FVC measured.

Results: The prevalence of self-reported asthma was 1.5%, 4.7% and 6.9 %, respectively ($p < 0.001$). Increasing prevalence of asthma was observed in both males and females, although highest among females. The difference in FEV_1 between asthmatic and non-asthmatic subjects gradually increased, being 2.3 % ($p = 0.56$) and 14.2 % ($p < 0.001$) of predicted value, respectively, in 1976-8 and 2001-4. From the 1991-4 survey, increasing BMI, especially > 30 kg/m^2, was associated with a lower FEV_1 % of predicted value ($p \leq 0.005$), and further analyses suggested an additive effect of asthma and obesity on FEV_1. The proportion of smokers declined from 60 % to 38 % ($p < 0.001$).

Conclusion: Prevalence and severity of asthma has continued to increase over the last three decades among young Danish adults, and the observed increase in severity seems at least partly to be related to the increase in prevalence of obesity.

Introduction

Asthma is a major health problem both with regard to quality of life and morbidity, and may even be potentially life-threatening (1,2,3). Several studies from a number of countries have reported an increase in prevalence of asthma over recent decades (4,5,6,7), and there is clear evidence that this increase cannot be ascribed to an increased awareness of asthma (7). However, very recent studies suggest that the prevalence has reached a plateau in many western countries close to the turn of the century (4,7,8), but presently is it not known if this plateau has been reached in all countries (4,9). Furthermore, it is still not fully understood if the observed changes in prevalence of asthma are related to smoking habits, other life style factors or perhaps unknown environmental factors.

Several cross-sectional and longitudinal studies of adults with asthma have shown that asthmatics, on average, have reduced level of lung function and also a steeper decline over time compared to non-asthmatics (10,11,12,13). However, time trends in severity of asthma have not been extensively studied (6), although this might provide important insight related to the impact of life-style factors and therapy on morbidity.

The Copenhagen City Heart Study comprises a large random sample of the adult general population in central Copenhagen, Denmark, that has been repeatedly examined over three decades, i.e. from 1976 to 2004. Based on this study, the primary aim of the present analysis was to investigate the potential changes over time in prevalence and severity, as judged by the level of lung function, of asthma in young adults aged 20 to 35 years, including the potential impact of smoking and body mass index (BMI).

Methods

Study population and procedures

All subjects included in the present analysis took part in the Copenhagen City Heart Study, a prospective cardiopulmonary study initiated in 1976. Details of the selection procedure and a description of the non-responders, together with the complete examination programme, have been published previously (14,15,16). This prospective epidemiological cardiopulmonary study included a population sample drawn from the Copenhagen Population Register of approximately 90 000 inhabitants aged 20 years and more. The sample was stratified by age with the main emphasis on those aged 35-70 years. However, approximately 5% of the population in the 20-35 year age group was also included. Furthermore, in accordance with the sampling procedure, an additional random sample of young adults, i.e. aged 20 to 35 years, were included at each of the subsequent three surveys. So far, four surveys have been carried out in 1976-78, 1981-84, 1991-94 and 2001-4, respectively. However, because of a substantial overlap of participants in the age group 20 to 35 years in the 1st and 2nd survey due to the short time-span between the two surveys, only data from the 1st, 3rd and 4th survey were included in the present analysis. Furthermore, as the time-span between the 3rd and 4th survey was only 10 years, a number of subjects had to be excluded from the analysis of data from the 4th survey although they fitted into the age criteria at both the 3rd and 4th survey. Each individual participant, therefore, only contributed data to the analysis from his/her first attendance.

Only subjects aged 20 to 35 years at each of the three surveys were included in the present analysis; and a total of 3285 subjects, i.e. 1296, 1277, and 712 individuals, respectively, at each of the three surveys, were included.

All participants at each of the surveys had height and weight measured, and BMI (kg/m^2) calculated; and subjects were classified as normal weight (BMI < 25), over-weight (BMI 25 to 30), or obese (BMI > 30).

Questionnaire

All subjects were asked to fill in a self-administered questionnaire concerning symptoms, smoking status, use of medication, and illnesses. All questionnaires were reviewed by one a member of the technical staff and categorized in the terms of the presence or absence of asthma, based on the response to the question in the questionnaire: "Do you have asthma?" Furthermore participants were defined as having chronic mucus hypersecretion if they responded yes to the question whether they had been bringing up phlegm during at least three months per year for at least two consecutive years.

The questionnaire used differed between the three surveys, and more detailed questions related to respiratory symptoms and therapy were only included in the 1991-3 and the 2001-4 surveys (14,16). At these surveys, the participants were classified according to their responses to the following questions: 'I get short of breath when hurrying on the level or up a slight hill' (comparable to Medical Research Council (MRC) dyspnea score 2 (17); defined as exercise-induced shortness of breath [SOB-E], 'I walk slower than people of my age on the level because of breathlessness or have to stop for breath when walking at my own pace at the level (comparable to MRC 3 (17); defined as shortness of breath [SOB], 'Do you now and then wake up at night due to breathlessness' [SOB at night], 'Do you cough when exercising' (defined as exercise-induced cough [EI-cough], 'Do you cough at night' [cough at night], 'Do you have wheeze' [wheeze], 'Do you have wheeze triggered by exercise' [EI-wheeze], 'Do you take medication for asthma' [asthma medication], and 'Do you have hay fever' [allergic rhinitis].

Subjects reporting daily smoking were classified as current smokers, whereas subjects describing themselves as ex-smoker or non-smoker were classified as non-smokers.

Spirometry

In 1976-78 forced expiratory volume in one second (FEV_1) and forced vital capacity (FVC) were measured with an electronic spirometer (Model N 403, Monaghan, Littleton, Colorado, USA), which was calibrated daily with one litre syringe and weekly against a water sealed Godard spirometer. In 1991-4 and 2001-4 a dry wedge spirometer (Vitalograph, Maidenhead, UK) calibrated weekly against a one litre syringe was used instead, as the electronic spirometer used previously stopped working effectively (6,11).

After at least one trial blow, each subject performed three technically acceptable forced expiratory manoeuvres. At least two measurements of FEV_1 and FVC differing by less than 5 % had to be produced to pass the criterion for repeatability. The highest FEV_1 and FVC value were used in the analyses.

The effect of age and height on FEV_1 was analysed in non-smokers without respiratory morbidity; and these analyses were done separately for each sample and each gender (11). Subsequently, individual predicted values of FEV_1 were calculated based on the derived equations, whereas FEV_1/FVC was reported as an absolute percentage (11). Furthermore, the obtained measurements of FEV_1 and FEV_1/FVC were also compared with European reference values (17).

Statistical methods

Data were analysed using the SPSS statistical programme version 12.0. Prevalence's were tested for differences between groups with a two sided X^2 test, and Yates` correction for continuity was applied for all 2 x 2 tables analysed. The Mantel-Haenszel X^2 test was used to examine for linear trends in the association between age groups and respiratory morbidity. The effect of asthma (yes or no), smoking (current smoker vs. non-smoker), and BMI (normal weight, over-weight, and obese) on FEV_1 and FEV_1/FVC was analysed by multiple linear regression separately for each of the three samples. Preliminary regression analyses of the data revealed no significant differences with regard to the effect of asthma, smoking, and BMI on FEV_1 and FEV_1/FVC between males and females, and the final model therefore comprises both males and females. Furthermore, interaction terms between asthma status and other independent variables, including BMI, were included in the regression model to test for differences in the influence of these variables on patients with and without asthma. In all analyses, p values of <0.05 were considered significant.

Results

Response rates

The overall response rates in the 20-35 year age-group at the three surveys included in the present analysis declined from 83.9 % at the 1976-78 survey to 55.1 % at the 2001-4 survey, similar to the overall response rate in the Copenhagen City Heart Study. Women responded more frequently than men at all surveys ($p < 0.008$), whereas there were no significant differences in response rates between age-stratified subgroups. The median age was 28, 31, and 28 years, respectively, at the three surveys.

Self-reported asthma, dyspnea, chronic mucus hypersecretion, and smoking

The prevalence of current smoking, chronic mucus hypersecretion, shortness of breath at exertion, and self-reported asthma by gender at the three surveys is shown in Table 1.

Asthma was reported with increasing frequency in both women (1.7 %, 4.8 %, and 7.7 %, respectively, $p < 0.001$) and men (1.2 %, 4.5 % and 5.9 %, respectively, $p < 0.001$) at the three surveys (Table 1). Although there was a trend towards a higher prevalence of asthma in females compared to males, this difference was only significant at the 2001-4 survey ($p < 0.041$). The prevalence of self-reported asthma did not differ within 5-year age-groups at any of the surveys.

Among the participants with self-reported asthma at the 1991-4 survey, 68.3 % reported asthma-symptoms triggered by allergen-exposure; and, furthermore, 49.0 % also reported symptoms of rhinitis in relation to allergen-exposure (Table 2). At the 2001-4 survey, more than 90 % of the participants with self-reported asthma, also reported wheeze in relation to known or unknown triggering factors; and, furthermore, 58.9 % of the asthmatics reported exercise-induced wheeze; further details are given in Table 2. The mean BMI was slightly higher among participants with self-reported asthma at all surveys, but this difference did not reach statistical significance, even though the prevalence of BMI > 25 was higher among asthmatics compared to non-asthmatics at the two most recent surveys (p=0.02 and p=0.03, respectively) (Table 2). Furthermore, the prevalence of obesity (BMI > 30) more than doubled over the study period, being 4.0 % and 10.3 % at the first and the last survey, respectively; again with the highest prevalence among subjects with self-reported asthma (14.9 % vs. 9.9 % at the last survey, p=0.03).

Overall, 4.0 % and 2.6 % of females and males, respectively, of the participants in the 1991-4 survey reported daily use of asthma medication, whereas use of asthma medication was reported by 6.9 % and 4.7 %, respectively, among females and males at the 2001-4 survey (p=0.02).

At the two most recent surveys 27.8 % and 24.3 %, respectively, of the participants reported shortness of breath at exertion. This symptom was reported almost twice as often by females compared to males (p= 0.002) (Table 1).

No significant change over time in prevalence of chronic mucus hypersecretion (CMH) was observed, but it was more prevalent among men than women at all surveys, although statistically significant only at the two most recent surveys ($p=0.007$ and $p=0.009$, respectively) (Table 1). The prevalence of CMH was approximately three times higher among current smokers compared to non-smokers at all surveys ($p<0.001$).

The prevalence of current smokers declined over time, being 61.2 %, 47.0 %, and 32.8 %, respectively, at the three surveys with no significant gender differences ($p< 0.001$) (Table 2).

Asthmatic versus non-asthmatic participants

Over the study period, the crude difference in FEV_1 %predicted (FEV_1%pred) between asthmatic and non-asthmatic subjects gradually increased (Fig. 1). Subjects with self-reported asthma had, on average, poorer lung function than non-asthmatic participants (Table 2). After controlling for current smoking, the asthmatic subjects had, on average, a FEV_1 %pred which was 14.2 % lower than non-asthmatic participants ($p< 0.001$) at the 2001-4 survey. This difference was, therefore, much higher compared with the 1976-8 survey, when the difference in FEV_1%pred was 2.3% ($p=0.56$) (Table 3). Furthermore, at the 1976-8 survey BMI had no significant impact on the level of FEV_1 in participants with or without self-reported asthma. However, at the two most recent surveys, higher BMI was significantly associated with lower level of FEV_1 % predicted ($p=0.005$ and $p< 0.001$, respectively), not least for subjects with a BMI > 30, where the FEV_1 was reduced by 3.3 and 4.9 %pred, respectively, compared to normal-weight participants (Table 3). Furthermore, inclusion of a two-way interaction term between BMI (obese vs. non-obese) and asthma status was significant for participants with self-reported asthma ($p=0.043$), but not for non-asthmatic participants, suggesting that asthma and obesity have an additive effect on lung function level. The analyses, however, did reveal that obesity only partly explained the lung function deficit observed among participants with self-reported asthma.

Analysis of data for FEV_1/FVC % obtained at the three surveys revealed a similar trend, as the difference between the asthmatic and non-asthmatic participants increased from 1.9 at the 1976-8 survey to 8.2 % (absolute values) at the 2001-4 survey ($p< 0.001$).

Discussion

The present study shows a continuing increase in prevalence of asthma among young Danish adults over the time period 1976 to 2004. Furthermore, based on the spirometric data, the severity of asthma has also increased, which appears to be partly related to increasing BMI, especially obesity (BMI > 30). As the proportion of smokers declined from approximately 60 % to 30 % over the study period, it is unlikely that the increase in prevalence and severity of asthma is caused by an increase in smoking-related respiratory symptoms.

The observed changes in prevalence of CMH and dyspnoea at exertion throughout the study period were found to be non-significant, whereas the prevalence data for self-reported asthma and spirometric data revealed not only an increase in prevalence, but more interestingly also an increase in the impact of asthma on FEV_1. We therefore observed a surprising dissociation between, on one side, prevalence and severity of asthma and, on the other side, more non-specific respiratory symptoms. It has previously been shown that asthma symptoms are more prevalent among overweight subjects (19), and, furthermore, also that achieving good asthma control is, in spite of adequate treatment, less likely in overweight patients compared to normal weight patients (20). Our study revealed a change over time in the impact of BMI on level of lung function, and, furthermore, may suggest that there is an interaction between BMI and asthma status in subjects with self-reported asthma not found in subjects not reporting symptoms of asthma. Apart from sub-optimal asthma control due to compliance-related issues (21,22), it is, therefore, likely that the observed increase in severity of asthma, as judged by the level of FEV_1, may be due to an increasing trend towards being overweight and obese, not least among subjects with self-reported asthma. Our study, however, did not reveal major clues to the understanding of the mechanisms underlying the changes over time in prevalence of self-reported asthma.

Our study confirmed previous observations that chronic mucus hypersecretion (CMH) in young adults without symptoms suggesting a diagnosis of asthma is closely associated with smoking (23). The present study, however, also revealed a four times higher prevalence of CMH among asthmatics compared to non-asthmatics, which could not be ascribed to smoking. The presence of CMH in these young adults is therefore likely to reflect suboptimal asthma control, i.e. uncontrolled airway inflammation.

In spite of the availability of safe and effective therapy for asthma, a large proportion of asthmatics remain poorly controlled (1,22). One of the main reasons is poor compliance with controller medication, i.e. inhaled corticosteroids. In the present study, the proportion of subjects reporting daily use of asthma medication was substantially lower than the prevalence of self-reported asthma. It remains, therefore, a possibility that at least part of the lung function deficit observed among asthmatics is due to underuse of inhaled corticosteroids. However, the present study period represents a period where there has been a very steep increase in the prescription rate for inhaled corticosteroids in Denmark, not least among individuals <

40 years of age. Consequently, we had actually expected a normalisation of both FEV_1 and FEV_1/FVC among the asthmatics, rather than the surprising finding of an increasing lung function deficit in this group.

The use of self-reported asthma, as opposed to a diagnosis supported by objective measurements, may lead to inclusion of subjects with non-asthmatic respiratory symptoms, including symptoms due to smoking (24). However, by only including adults under the age of 35 years in our analyses makes it unlikely that a substantial number of patients with COPD have been misclassified as asthmatics; and, furthermore, such potential misclassification is unlikely to have changed substantially over time as the analyses did not reveal a time trend in respiratory symptoms and smoking habits. This is further supported by the observation of a high prevalence of asthma-related features, incl. rhinitis and wheeze triggered by allergen-exposure, among participants classified as having asthma. However, we cannot exclude the possibility that asthma-like symptoms due to, e.g. poor physical fitness or obesity, in a smaller number of cases may have been reported as asthma.

The prevalence of self-reported asthma, which in a substantial proportion of cases most likely reflects doctor-diagnosed asthma, may change over a 30-year period solely due to changes in public and/or clinical understanding of asthma (4, 25). Interpretation of our observations with regard to asthma prevalence should therefore take into account that it seems unlikely that there has been no change whatsoever over the study period in the general understanding of asthma. However, the validity of the present observations is strongly supported by the fact that the difference in level of lung function was largest in the most recent survey, as this indicates that our findings is not due to a greater awareness of asthma or tendency to diagnose milder cases of asthma.

Our study has a number of limitations. Firstly the declining response rate; although it most likely represents current trends in willingness to participate in epidemiological studies (26). Register based follow-up of the non-responders in the Copenhagen City Heart Study shows a higher age adjusted mortality and morbidity than in responders. A visit was planned to a sample of the non-responders at the end of the 1976-8 survey, but only 30 % of this sample was successfully contacted. However, these subjects had a slightly higher prevalence of asthma and CMH than in responders. The true prevalence of asthma might therefore be higher than we have observed in our study. In addition, we have no indications that the proportion of subjects with asthma among non-responders have changed over time. Secondly, the questionnaire differed between the surveys, as they were balanced between current – new – knowledge, the wish to obtain valuable information, and acceptability for the participants. Furthermore, the participant's responses to identical questions may also change over time due to current beliefs etc. In the present study, this seems likely to explain the observed changes in prevalence of exercise-induced shortness of breath and exercise-induced wheeze (Table 2).

In conclusion, our study has revealed a continuing increase in prevalence and severity of asthma among young Danish adults over the last three decades, where the latter appeared to be related to, but not fully explained by, changes in BMI.

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Table 1

Prevalence (%) of current smoking, chronic mucus hypersecretion (CMH), exercise-Induced shortness of breath (SOB-E), and asthma at 3 surveys, 1976 and 2004, among 20-35 year old Danes.

	Females	Males
Current smokers		
1976-8	60.4 (403)	62.1 (391)*
1991-4	46.8 (310)	47.2 (290)*
2001-4	32.8 (127)	32.9 (107)*
CMH		
1976-8	7.1 (47)	9.2 (58)*
1991-4	7.5 (50)	10.8 (66)**
2001-4	8.0 (31)	10.9 (35)**
SOB-E		
1976-8	#	#
1991-4	34.2 (227)	20.9 (128)***
2001-4	29.7 (115)	18.0 (59)***
Asthma		
1976-8	1.7 (11)	1.2 (8)*
1991-4	4.8 (33)	4.5 (28)*
2001-4	7.7 (30)	5.9 (19)**

Data not available; actual numbers in brackets. For comparison between males and females: * NS, ** $p < 0.05$, and *** $p < 0.002$.

Table 2
Characteristics of participants with and without self-reported asthma, respectively, at three surveys, 1976 to 2004, among 20-35 year old Danes.

	1976-78 Survey		1991-94 Survey		2001-4 Survey	
Asthma	+Asthma	-Asthma	+Asthma	-	+Asthma	-Asthma
Age (yrs)	26.8 (4)	28.3 (4)	29.7 (4)	29.8 (4)	28.3 (5)	27.6 (4)
Current smokers (%)	53.3 [10]	61.0 [779]	45.0 [28]	53.8 [654]	22.6 [11]	29.2 [194]
CMH (%)	26.7 [5]	7.4 [95]	23.1 [14]	7.6 [92]	15.1 [7]	4.3 [29]
SOB (%)			9.6 [6]	1.3 [16]	7.7 [4]	0.5 [23]
SOB-E (%)			57.7 [35]	20.0 [243]	32.1 [16]	13.1 [87]
SOB at night (%)			46.2 [28]	2.5 [3]	23.1 [11]	2.2 [15]
EI-cough (%)			57.7 [35]	12.7 [154]	58.5 [29]	13.0 [86]
Cough at night (%)			53.8 [33]	12.9 [157]		
Wheeze (%)			88.5 [54]	21.3 [259]	67.9 [33]	18.6 [123]
EI-wheeze (%)			31.0 [19]	4.2 [51]	69.2 [34]	20.3 [135]
Asthma medication (%)			55.8 [34]	0.4 [5]	58.5 [29]	0.5 [33]
Allergic rhinitis (%)			49.0 [30]	17.6 [214]		
BMI (kg/height^2)	23.1 [4.3]	22.4 [3.4]	23.6 [3.2]	22.6 [3.5]	24.1 [3.9]	23.1 [3.2]
BMI > 25 (%)	13.3 [3]	21.0 [268]	41.3 [25]	31.0 [377]	43.9 [22]	37.7 [250]
FEV_1 %pred	95.2 (15)	96.5 (14)	86.2 (15)	97.1 (13)	83.1 (13)	97.0 (10)
FEV1/FVC %	81.2 (11)	83.6 (9)	78.2 (10)	86.9 (7)	75.9 (10)	84.1 (7)

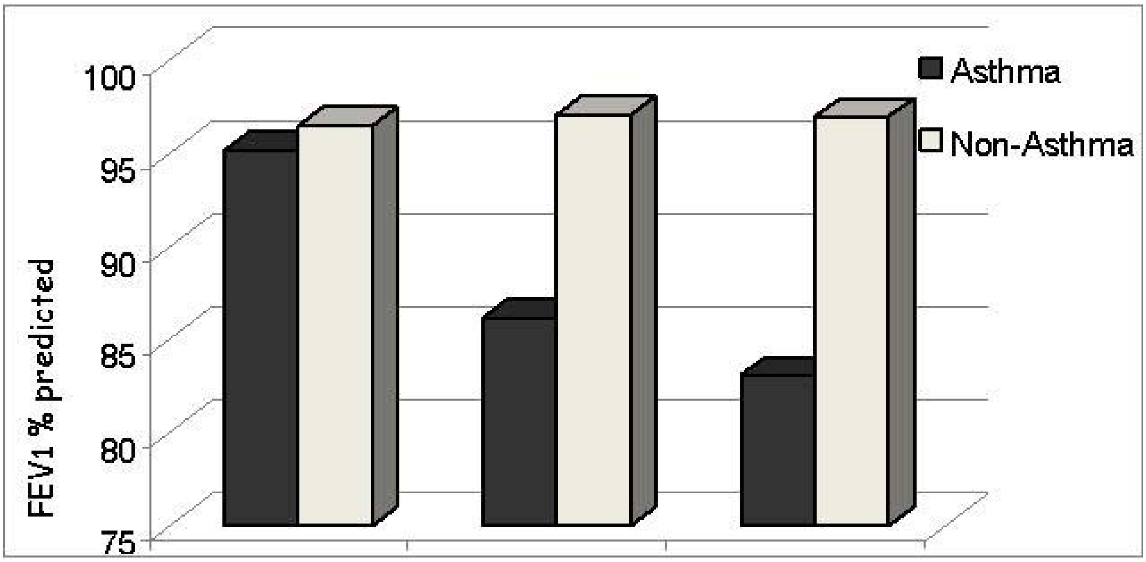
CMH: Chronic mucus hypersecretion, SOB: shortness of breath, SOB-E: exercise-induced shortness of breath, EI-wheeze: exercise-induced wheeze.
Actual numbers in [brackets], and standard deviations in (parentheses).

Table 3

Multiple linear regression analyses of data obtained at 3 surveys (1976 to 2004) of random samples of 20-35 year old Danes with FEV_1 %predicted as the dependent variable.

	FEV_1 (% predicted)
1976-78 Survey	Smoking -2.0 (-3.1 to -0.3) BMI 25-30 -0.3 (-1.0 to 0.8) 30+ -0.9 (-2.1 to 1.1) Asthma -2.3 (-9.4 to 4.6)
1991-94 Survey	Smoking -2.9 (-5.9 to -0.3) BMI 25-30 -1.4 (-2.2 to -0.6) 30+ -3.3 (-5.2 to -1.6) Asthma -10.7 (-13.4 to -7.9)
2001-4 Survey	Smoking -4.6 (-5.8 to -3.4) BMI 25-30 -1.5 (-2.9 to -0.3) 30+ -4.9 (-6.1 to -3.8) Asthma -14.2 (-16.5 to -12.1)

Figures in the table are regression coefficients, and 95% confidence intervals in brackets, in units of the dependent variable (FEV_1 %predicted).
Smoking and asthma status were included in the model as dichotomous variables (with non-smoker and no asthma as reference), whereas BMI was included in the model in three categories, i.e. BMI > 25, BMI 25-30, and BMI > 30 (with BMI < 25 as the reference).


FEV1 % predicted
100
95
90
85
80
75
Asthma
Non-Asthma