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Body mass index as predictor for asthma: a cohort study of 118 723 men and women

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ABSTRACT

The objective of this study was to quantify the relationship between body mass index (BMI, kg/m^2) and asthma in middle-aged men and women and to evaluate change in BMI as a risk factor for asthma.

Asthma incidence was estimated from redeemed prescriptions of anti-asthmatic drugs from 2004 through 2007 retrieved from the nationwide Norwegian Prescription Database. BMI was measured during health surveys from 1994 to 1999 for more than 100 000 individuals born between 1952 and 1959. Change in BMI was based on self-report. Relative risks were estimated using Poisson regression.

The relative risk associated with 3 unit increase in BMI ranged from 1.14 (95% confidence interval: 1.10-1.18) for current smokers to 1.27 (1.22-1.32) for never-smokers after adjusting for confounders. The relative risk associated with 3 unit change in BMI was 1.21 (1.16-1.26) after adjusting for confounders, including gender, smoking, and BMI.

Asthma incidence as measured by anti-asthmatic drug use was positively related both to BMI and to change in BMI. For BMI the association was stronger for never-smokers than for ex-smokers and current smokers.

Key words: anti-asthmatic drugs, asthma, body mass index, body weight changes, smoking.

INTRODUCTION

Many studies have shown obesity to be a risk factor for asthma[1, 2], especially in women[3, 4]. The findings have been concordant in adolescents and adults[5]. One study also reported a positive relationship between hip/waist ratio and asthma incidence[6] and another found an inverse relationship between body height and asthma incidence[7]. Furthermore, one study found the body mass index (BMI)-asthma relationship only in non-atopic disease[6]. A recent meta-analysis of prospective studies concluded that asthma incidence increased by 50% in overweight/obese individuals[8]. This also concluded that there was a dose-response relationship, and that female gender does not disproportionately affect the obesity-asthma relationship[8].

Fewer studies have investigated the relationship between change in BMI and subsequent asthma, but in a prospective study of 85 911 female nurses, weight gain after the age of 18 years was strongly associated with an increased risk of adult onset asthma[9]. Romieu et al[10] found that both weight loss and weight gain was associated with an increased risk for asthma in a middle aged French female population. However, other studies suggest that weight loss seems to reduce the symptoms for individuals who do have asthma[11, 12].

Assessing the asthma prevalence in a population is challenging as no single instrument can be used to identify asthma with certainty. The use of self-reported asthma or asthma symptoms as a measure of asthma has been questioned by several studies[13, 14]. Using prescriptions of anti-asthmatic medications provides an alternative method [15]. A number of health care databases of prescriptions have shown the feasibility of using this kind of data to identify individuals with asthma[16-18]. A study from a prescribing database in general practice in the Netherlands found that a prescription of one or more anti-asthmatics identified 95% of adults with an asthma diagnosis[19]. In our study we have therefore estimated asthma

incidence on the basis of redeemed prescriptions of anti-asthmatic drugs retrieved from the nationwide Norwegian Prescription Database (NorPD) .

The objective of this study was to quantify the relationship between body mass index (BMI) and asthma in middle-aged men and women and to evaluate change in BMI as a risk factor for asthma.

MATERIALS AND METHODS

Study population

Data from health surveys conducted by the Norwegian government between 1994 and 1999 were linked to the information from NorPD which includes all drug prescriptions dispensed at pharmacies in Norway since 2004[20]. The health surveys were partly done by means of questionnaires (e.g. for smoking, exercise habits, level of education, and history of asthma, heart infarction, angina pectoris, stroke and diabetes), partly by physical measurements (e.g. height and weight). The questionnaires were filled in at home and delivered at the screening.

Altogether 107 001 men and 102 911 women born between 1952 and 1959 were invited to participate in the health surveys. A total of 159 331 attended (70% and 82% of the invited men and women, respectively), and 132 924 answered the question about asthma history ("do you have, or have you had, asthma" (yes/no)). The 8638 who answered "yes" were excluded, together with 4325 who were excluded for other reasons (see Figure 1), leaving 118 723 for analysis (55 940 men and 62 783 women). BMI (kg/m^2) was calculated as weight (kg) divided by height (m) squared.

A total of 114 577 subjects also reported their minimum and maximum weight during the five years before screening. Women were asked not to report weight during pregnancy. Change in BMI was calculated from the measured height and the reported minimum weight

(w_{min}) and maximum weight (w_{max}) as $\Delta_{BMI} = (w_{max}-w_{min})/height^2$. Relative change in BMI was calculated as Δ_{BMI} / BMI * 100%, where BMI is the measured BMI.

In addition the following variables were included from the health surveys: Smoking (never, ex, current), physical activity (low, medium, high), education (5 levels), year of birth, urban/rural residence, and receipt of disability pension (yes/no).

Physical activity was addressed by asking for time spent on light (no sweating or heavy breathing) or hard activity. The alternatives in both categories were 0 hours, <1 hour, 1-2 hours and 3+ hours per week, averaged over the year. We joined the two questions in a new variable with three levels: 1) <1 hour with light activity and 0 hours with hard activity, and 2) less than three hours with hard activity, and 3) three or more hours with hard activity.

Educational level was given as one of 5 categories: 1) elementary school (to age 16), 2) technical college or similar (1-2 years), 3) further education/high school or similar (3 years), 4) university/college < 4 years, and 5) university/college 4+ years.

Subjects living in municipalities with more than 50 000 inhabitants were classified as urban, others as rural. However the two largest cities in Norway were not screened during 1994-99.

Measuring asthma incidence

Asthma incidence (new cases of asthma between screening and 2007) was estimated from redeemed prescriptions of inhaled anti-asthmatic drugs from 2004 through 2007 retrieved from NorPD. From 1 January 2004, all pharmacies in Norway have been obliged by law to send electronic data on all prescriptions to the Norwegian Institute of Public Health[20]. NorPD contains information on all individuals who have received prescription drugs dispensed at pharmacies. All prescriptions, whether reimbursed or not, are stored in the

database. The drugs are classified according to the Anatomical Therapeutic Chemical Classification System (ATC)[21]. Among the data collected are the patient's unique identification number (encrypted), gender and age, the date of dispensing, detailed information on the drug (brand name, package size, number of packages, ATC code, defined daily dose, price), and code of reimbursement if relevant.

As endpoint we used at least two prescriptions, with the last one being dispensed at least 6 months after the first one, of reimbursed inhaled anti-asthmatic drugs, i.e. drugs with ATC code R03AC (selective β_2-agonists), R03BA (glucocorticoids), and/or R03AK (long-acting β_2-agonists/glucocorticoids combined in one inhaler). The system for general reimbursement in Norway is basically a "positive list" system, based on a list of diseases or conditions for which pharmaceutical treatment can be reimbursed. Reimbursement is granted only under the condition that the patient has a chronic disease (e.g. asthma) for which "long-term" medication (more than 3 months) is necessary[22].

Use of glucocorticoids indicates a more persistent asthma than use of β_2-agonists only. We also did an analysis where the endpoint was defined as at least two prescriptions, with the last one being dispensed at least 6 months after the first one, of reimbursed glucocorticoids (ATC code R03BA or R03AK).

The drug prescription data were linked to the health survey data using the unique personal identification number assigned to every Norwegian citizen at birth or immigration (encrypted). Permission for the linkage was given by the Norwegian Data Inspectorate and the Regional Committees for Medical Research Ethics.

Statistical methods

We used log-Poisson regression to estimate associations (expressed as relative risks (RR)) between effect variables (BMI and change in BMI) and the outcome variable (incident asthma) for never-smokers, ex-smokers, and current smokers separately[23]. The estimate was carried out using the glm function in the statistical package R[24]. The effect variables were entered as categorical as well as continuous. We present RR-estimates adjusted for age (year of birth; continuous variable), gender, physical activity, education, urban/rural residence, and disability pension (categorical variables). In the analyses with BMI change as effect variable, BMI (continuous variable) was adjusted for as well.

We tested for interactions between gender and the effect variables (BMI and BMI change), and between smoking and the effect variables, by including the relevant interaction terms in the model in addition to gender, smoking category and the potential confounders listed above. The effect variables were entered as continuous.

We tested for trends in the potential confounders as a function of BMI at baseline using linear regression for continuous variables and logistic regression for yes/no variables, with BMI entered as a continuous variable. Individuals with BMI < 20 were not included in the trend tests.

RESULTS

The average BMI at baseline was higher in men (26.2 kg/m^2) than in women (24.7 kg/m^2), but severe obesity (BMI $\geq$ 35 kg/m^2) was more common in women than in men (Table 1). Women also reported a larger BMI change than men, both in absolute and relative terms. Smoking habits and education were comparable for men and women, but more men were physically active, and more women received disability pension (Table 1). Overweight at baseline was associated with low education, low physical activity, rural residence, high

prevalence of disability pension, low prevalence of smoking, later year of birth, and large change in BMI (Table 1). Incident asthma was typically associated with the same baseline characteristics as was overweight, except that smoking and high physical activity (for men) was more common at screening among the incident asthma cases than among the others (Table 1). The incident asthma cases were also born and screened slightly earlier than the others.

BMI and asthma incidence

In total, the asthma incidence was 3.4%. The incidence was highest in current smokers and lowest in never-smokers, higher in women than in men (Table 2, Figure 2), and positively related to BMI (Table 2, Figure 2). There was no statistically significant interaction between BMI and gender ($p = 0.25$), but the BMI-asthma relationship was significantly weaker in current smokers than in never-smokers (p interaction < 0.001). As measured by the risk difference the three smoking groups were more similar (Figure 2; parallel curves would indicate equal risk difference). The prescription rate was more than 3 times higher for very obese ($BMI \geq 35$) never-smokers than for normal-weight ($20 \leq BMI < 25$) never-smokers. Treating BMI as a continuous variable, the RR associated with an increase of 3 kg/m^2 in BMI ranged from 1.14 for current smokers to 1.27 for never-smokers when adjusting for confounders. The RRs obtained by adjusting for gender and age only were very similar to those shown in Table 2.

The overall incidence of persistent asthma, as defined by use of corticoids, was 2.7%, and the association with BMI was typically marginally stronger for incident persistent asthma than for incident asthma (see Section S1 in the supplementary material).

Change in BMI and asthma incidence

We don't know the direction of the BMI change, but assuming a weight gain in subjects whose measured weight at screening was closer to the reported maximum than to the reported minimum, and a weight loss in the others, the direction of the change had a minor impact (Table S2.1). Thus it seems reasonable to use absolute (direction free) BMI change as effect variable. There was no statistically significant interaction between self-reported change in BMI during the last 5 years before screening and gender ($p = 0.97$) or smoking ($p > 0.47$). Change in BMI was positively associated with incident asthma. A 3 kg/m^2 increase in the change in BMI during the 5 years before screening, was associated with a 35% increase in the risk for asthma incidence (Table 3) after adjusting for gender, age, and smoking category. After adjustment for all confounders, including BMI, the RR was still as high as 1.21 (1.16-1.26).

Within each category of BMI, in the range $20 \leq BMI < 35$, the relative risk for being prescribed anti-asthmatic drugs was higher for individuals who reported a relative change in BMI $\geq 10\%$ of their screened BMI, as compared to those with a smaller change (Table S2.2 in the supplementary material). That was true for all smoking categories.

DISCUSSION

The risk of developing asthma in middle-age as estimated by use of reimbursed inhaled anti-asthmatic drugs increased with increasing BMI. The relationship was strongest in never-smokers and weakest in current smokers as measured by the relative risk. The risk for incident asthma in very obese ($BMI \geq 35$) never-smokers was 3.5 times higher than for normal-weight ($20 \leq BMI < 25$) never-smokers, after adjusting for confounders. The risk for incident asthma in individuals with a self reported BMI change of 10 kg/m^2 or more during the last five years

before screening was twice as high as in those with a change of 2.5 kg/m^2 or less, after adjusting for BMI and other confounders.

Strengths and limitations

The main strength of this study is that it was based on information on measured BMI and several important confounders for more than 100 000 healthy individuals in a narrow age-range, as well as on all dispensed prescriptions of inhaled anti-asthmatic drugs between 1/1 2004 and 1/1 2008 for the same individuals. This approach eliminates the problem of recall bias as regards incident asthma, and attenuates any effect of the seasonal variation in asthma, which may affect prevalence estimates based on cross-sectional surveys with self-reported asthma symptoms and/or doctor-diagnosed asthma.

The main limitations of the study are (cf. the discussion below) the possibility of false negatives (undetected cases of mild asthma) and false positives (asthma medication may have been prescribed for COPD - especially in smokers - or for other diseases), and the use of self-reported data to calculate change in BMI. Also, about 25% of those who were invited to the health surveys did not attend. If the association between BMI and asthma was different in the non-attenders and the attenders, our effect estimates would be biased, but we believe that the participation rate is more likely to influence prevalence estimates than effect estimates. Further, we excluded individuals with a self-reported asthma history, which might have been hampered by recall bias, but again, our effect estimates are only biased to the extent that the association between asthma and BMI differed between those who recalled their asthma history correctly and those who did not.

The use of drug prescriptions as a proxy for asthma

False positives: In Norway, anti-asthmatic drugs are prescribed by doctors after they have recognized the patient's symptoms as asthma-like. We believe that using a minimum of two such prescriptions separated by an interval of at least 6 months as a proxy for having asthma should minimize the number of false positives. A formal validation of our approach has not been performed, but a study from the Netherlands found that in the age group 18-49 years asthma patients could be identified reliably from a prescribing database in general practice (a positive predictive value of 0.79 when using ≥ 2 anti-asthmatic medications in 12 months as definition criterion)[19]. Our study population was older (48-56 years in 2007), and may include non-asthma patients treated with anti-asthmatics. The most relevant example is patients with Chronic Obstructive Pulmonary Disease (COPD), which is strongly related to smoking. A study of an adult Norwegian study population found adjusted odds ratios for current smokers and ex-smokers of 9.6 (95%CI 3.6–25.2) and 5.0 (95%CI 1.8–13.8), respectively, compared to never-smokers[25]. We therefore believe that the number of COPD patients was small in our group of never-smokers (48-56 years old in 2007), but in the groups of ex-smokers and current smokers it was probably higher. However, in a study of 485 men aged 40-75 years without COPD at baseline, 13.1% of those with BMI ≤ 24.3 kg/m2 (tertile 1) developed COPD in a 10 year period, compared to only 4.6% of those with BMI > 26.6 kg/m2 (tertile 3)[26, 27]. This suggests that the proportion of COPD patients was probably lower among the obese than among the normal weighted in our study population as well, and that the relationship between asthma and BMI would have been stronger than the actually observed relationship if we were able to eliminate the COPD-patients.

False negatives: The definition criterion of two prescriptions with a six month interval may have led to a loss of some cases of mild asthma. Some of these were probably undiagnosed and were not prescribed any anti-asthmatic drugs during 2004-2007. The chance of a mild asthma case being diagnosed would increase if a person visited a doctor for any

reason, and the general medication prevalence increased with BMI. The percentage of men who received at least one prescription for any drug during 2004-2007 was 86% in the normal-weight group and 96% in the 35+ kg/m^2 group. For women the corresponding numbers were 94% and 98%. Only 12% of the men and 5% of the women did not receive any prescription during 2004-2007, and a relatively high percentage of these would need to have undetected asthma to influence the results of this study in a significant way.

Some individuals probably got an asthma diagnosis before 2004 without being in need of anti-asthmatic drugs during 2004-2007. Among those who reported an asthma history in the health survey, and were excluded from this study, only 44% would have been defined as asthma patients by our criterion. For those who were more than 20 years old at the first asthma incidence (self-reported age), the percentage was 52, and relatively independent of BMI at screening. This indicates that not all of the subjects who developed asthma before screening were in need of anti-asthmatic drugs during 2004-2007. Thus, it is also possible that some subjects may have developed asthma after the screening without needing anti-asthmatic drugs during 2004-2007. Among the subjects without an asthma history at screening who redeemed anti-asthmatic drugs and got the first prescription in 2004, 12% did not receive any prescription during 2006 and 2007, the fraction being approximately the same in the various BMI groups. In conclusion, there might have been some cases of incident asthma that were not identified in this study, but as the probability of not being identified seems to be relatively independent of BMI, the observed relationship between BMI and adult onset asthma should still be valid.

The use of self-reported max/min weight as basis for change in BMI

Change in BMI was calculated from self-reported minimum and maximum weight during the last five years before screening, and was thus less accurate than the measurements of BMI per

se. It is known that self-reported weights and heights tend to be too low and too high, respectively, and the corresponding BMI too low[28, 29]. Whether there was a systematic under- or over-reporting of change in BMI with increasing BMI we do not know, but the fact that the relative change in BMI increased with increasing BMI may indicate an over-reporting of BMI change with increasing BMI. However, the association between change in BMI and asthma was still statistically significant after adjusting for BMI.

We don't know the direction of the BMI change, but assuming a weight gain in subjects whose measured weight at screening was closer to the reported maximum than to the reported minimum, and a weight loss in the others, the direction of the change had a minor impact (see table S2.2 in the supplementary material). Thus, although our way of defining weight loss and weight gain were imprecise, they were both associated with increased asthma incidence, which agrees with the results in Romieu et al[10]. On the other hand, weight loss studies on the basis of behavioural change and bariatric studies have shown substantial improvements in the clinical status of many obese patients with asthma who lost weight[11, 12].

BMI versus waist-to-hip ratio and waist circumference

Waist circumference and waist-to-hip ratio have been suggested as better screening tools than BMI for cardiovascular risk factors[30]. In a subsample of 71 424 subjects, for which we had measurements of waist and hip, the waist-to-hip ratio and the waist circumference were associated with asthma in roughly the same way as BMI. They were both significantly associated with incident asthma, also after adjusting for BMI (see section S3 in the supplementary material).

Obesity and asthma: possible mechanisms

Many authors have found an association between obesity and asthma incidence, but it is not clear whether the association is causal or whether the two conditions share the same environmental, behavioural or genetic influences. Although the exact mechanisms responsible for the relationship between obesity and asthma incidence remain unknown, some possible explanations have been put forward[31]. These include the effect of obesity on lung mechanics, systemic inflammation and co-morbidities[32]. The co-morbidities include dyslipidemia, type 2 diabetes, gastro-oesophageal reflux disease (GORD), and hypertension. Excluding the 23 141 individuals who, during 2004-2007, were dispensed antihypertensives (ATC group C02), lipid modifying agents (C10), drugs for GORD (A02B), or drugs used in diabetes (A10), the RR associated with 3 kg/m^2 increase in BMI in Table 2 changed by less than 0.02 in all smoking categories. This shows that these co-morbidities do not explain the association between BMI and asthma found in our study.

Enhancement of proinflammatory cytokines and the effect of oestrogens has also been mentioned[33]. However, the literature is ambiguous. Barr et al found that postmenopausal hormone use was associated with an increased rate of newly diagnosed asthma[34]. On the other hand, Carlson et al found that postmenopausal women who used HRT had higher levels of FEV_1, which again is expected to give lower risk of asthma[35]. In a mouse asthma model Matsubara et al characterised how oestrogens can suppress airway hyperresponsiveness[36]. In our population the proportion that used oestrogens decreased with increasing BMI, but excluding the 7000 women who were dispensed oestrogens (ATC group G03C) during 2004-2007, did not change the BMI-asthma association in Table 2. However we cannot exclude the possibility that some women used oestrogens during the interval from screening to the start of NorPD. Both the timing and duration of use, as well as the dose seems to be very important

when assessing the potential effects of hormones. This was clearly demonstrated in the Women Health Initiative study regarding the effect on coronary heart disease[37].

Table 1. Baseline characteristics at screening in different BMI groups and in those who were and were not incident asthma cases.

	Men							
	BMI (kg/m^2)						Incident asthma*	
	< 20	20-24.9	25-29.9	30-34.9	≥ 35	P trend†	no	yes
N	700	20382	28241	5722	895		54493	1447
Change in BMI	1.2	1.6	2.3	3.5	5.2	<0.001	2.2	2.6
Rel. ch. in BMI (pct)	6.3	6.8	8.4	11.1	13.8	<0.001	8.1	9.6
Year of birth	1955.5	1955.5	1955.6	1955.8	1955.9	<0.001	1955.6	1955.4
Never-smokers (%)	28.3	39.1	40.2	38.3	39.2	0.463	39.7	30.0
Ex-smokers (%)	9.7	19.7	26.4	29.7	29.1	<0.001	24.1	24.0
Current smokers (%)	62.0	41.2	33.4	32.0	31.7	<0.001	36.2	46.0
High education‡ (%)	28.5	36.1	32.7	26.6	20.2	<0.001	33.2	28.8
Physically active§ (%)	14.0	19.3	17.0	13.3	11.0	<0.001	17.3	20.0
Disability pension (%)	7.5	2.5	2.2	3.5	7.0	<0.001	2.5	5.0
Urban recidence (%)	18.3	18.2	16.8	14.9	15.0	<0.001	17.2	15.0

Table 1 cont.

	Women							
	BMI (kg/m^2)						Incident asthma*	
	< 20	20-24.9	25-29.9	30-34.9	≥ 35	P trend†	no	yes
N	3493	34688	18559	4688	1355		60181	2602
Change in BMI	1.5	2.1	3.2	4.7	6.5	<0.001	2.6	3.3
Rel. ch. in BMI (pct)	8.0	9.2	11.9	14.8	16.9	<0.001	10.4	12.5
Year of birth	1955.5	1955.6	1955.6	1955.8	1955.9	<0.001	1955.6	1955.5
Never-smokers (%)	35.9	36.9	38.1	40.1	43.6	<0.001	38.0	27.4
Ex-smokers (%)	13.8	24.1	26.3	26.0	26.7	<0.001	24.5	20.4
Current smokers (%)	50.3	39.0	35.6	33.9	29.7	<0.001	37.5	52.2
High education‡ (%)	33.3	33.6	27.7	22.1	19.6	<0.001	30.9	24.8
Physically active§ (%)	9.0	10.7	9.3	7.6	4.7	<0.001	9.8	9.7
Disability pension (%)	5.4	3.5	4.9	7.1	11.4	<0.001	4.2	9.3
Urban recidence (%)	19.9	18.2	15.7	14.2	12.3	<0.001	17.2	15.1

Means are given for continuous variables and percentages for dichotomous variables (indicated by %).

Definition of abbreviations: BMI = body mass index; rel. ch. = relative change, pct = percentage.

* Received at least two prescriptions of reimbursed inhaled anti-asthmatic drugs between 2004 and 2007, with the last one being dispensed at least 6 months after the first one.

† P-value for trend is calculated for subjects with BMI ≥ 20.

‡ University/college or higher (level 4 or 5).

Q§ Three or more hours/week with hard activity (level 3).

Table 2. Adjusted relative risks for incident asthma by body mass index, stratified by smoking. 5491 individuals were excluded because of missing data for one or more of the variables adjusted for.

	RR (95% CI) by category of BMI (kg/m^2)					RR (95% CI) for 3 units increase
	< 20	20-24.9	25-29.9	30-34.9	≥ 35	in BMI
Never-smokers						
RR*	0.9 (0.6-1.4)	Ref	1.5 (1.3-1.7)	2.2 (1.8-2.7)	3.5 (2.6-4.5)	1.27 (1.22-1.32)
N†	28 (2.0)	390 (1.9)	456 (2.6)	153 (4.0)	61 (7.0)	1088 (2.5)
Ex-smokers						
RR*	0.7 (0.4-1.3)	Ref	1.2 (1.0-1.4)	1.9 (1.6-2.4)	2.6 (1.9-3.7)	1.22 (1.16-1.28)
N†	11 (2.1)	313 (2.6)	346 (2.9)	127 (4.6)	39 (6.7)	836 (3.0)
Current smokers						
RR*	1.1 (0.9-1.3)	Ref	1.3 (1.2-1.4)	1.6 (1.4-1.9)	1.7 (1.3-2.3)	1.14 (1.10-1.18)
N†	102 (5.0)	840 (4.0)	710 (4.7)	196 (6.1)	47 (7.5)	1895 (4.5)
All						
RR‡	1.0 (0.9-1.2)	Ref	1.3 (1.2-1.4)	1.8 (1.6-2.0)	2.4 (2.0-2.9)	1.19 (1.17-1.22)
N†	141 (3.6)	1543 (2.9)	1512 (3.4)	476 (4.9)	147 (7.1)	3819 (3.4)

Definition of abbreviations: BMI = body mass index; CI = confidence interval; RR = relative risk; ref = reference group.

* Adjusted for gender, age (year of birth), education, physical activity, disability pension, and rural/urban status.

† Number (percentage) of incident asthma cases.

‡ Adjusted for gender, age (year of birth), education, physical activity, disability pension, rural/urban status, and smoking category.

Table 3. Adjusted relative risks for incident asthma by self-reported change in body mass index (direction of change is ignored). 8861 individuals were excluded because of missing data for change in BMI or for one or more of the variables adjusted for.

	RR (95% CI) by category of change in BMI (kg/m^2)					RR (95% CI) for 3 units increased
	< 2.5	2.5-5	5.1-7.5	7.5-9.9	≥ 10	change in BMI
RR*	ref	1.5 (1.4-1.6)	1.9 (1.7-2.1)	2.5 (2.1-3.0)	3.3 (2.6-4.1)	1.35 (1.31-1.39)
RR†	ref	1.4 (1.3-1.6)	1.8 (1.6-2.0)	2.3 (1.9-2.7)	2.9 (2.2-3.6)	1.31 (1.27-1.35)
RR‡	ref	1.3 (1.2-1.4)	1.5 (1.3-1.7)	1.7 (1.4-2.1)	2.0 (1.5-2.5)	1.21 (1.16-1.26)
N§	1903 (2.7)	1235 (4.1)	377 (5.6)	119 (7.5)	72 (9.8)	3706 (3.4)

Definition of abbreviations: BMI = body mass index; CI = confidence interval; RR = relative risk; ref = reference group.

* Adjusted for gender, age (year of birth) and smoking category.

† In addition adjusted for education, physical activity, disability pension, and rural/urban status.

‡ In addition adjusted for BMI.

§ Number (percentage) of incident asthma cases.

Figure captions

Figure 1. Flow chart of the study population. Norwegian health surveys 1994-1999 linked to the nationwide Norwegian Prescription Database 2004-2007.

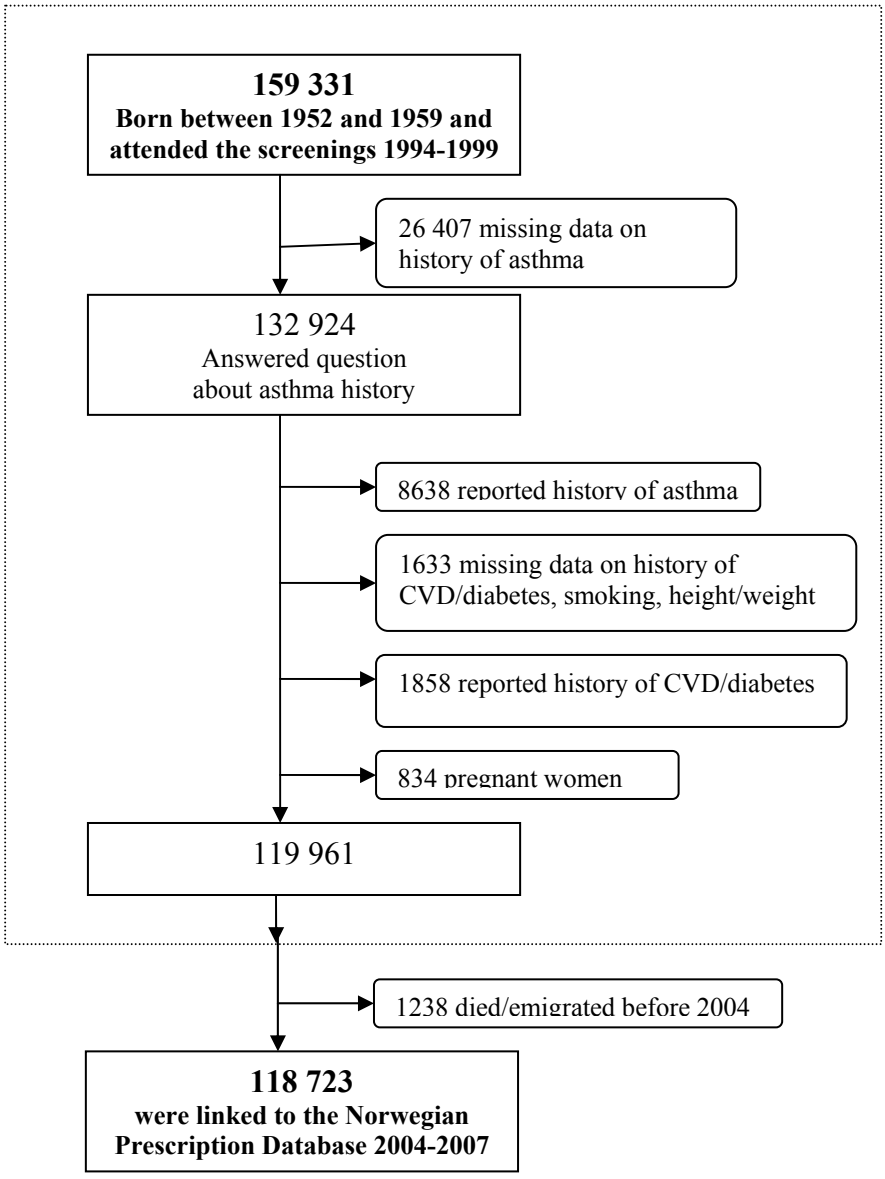

Figure 1.

Figure 2. Asthma incidence as a function of BMI. Points: Asthma incidence (number of new asthma cases divided by number of subjects at risk) within each BMI (<20, 20-24.9, 25-29.9, 30-34.9, ≥35) and smoking category. The x-coordinates correspond to the average BMI in each category. Curves: fitted Poisson regression curves from univariate models. Histograms: distribution of BMI. The scale of the histograms is the same for each of the six combinations of gender and smoking category.

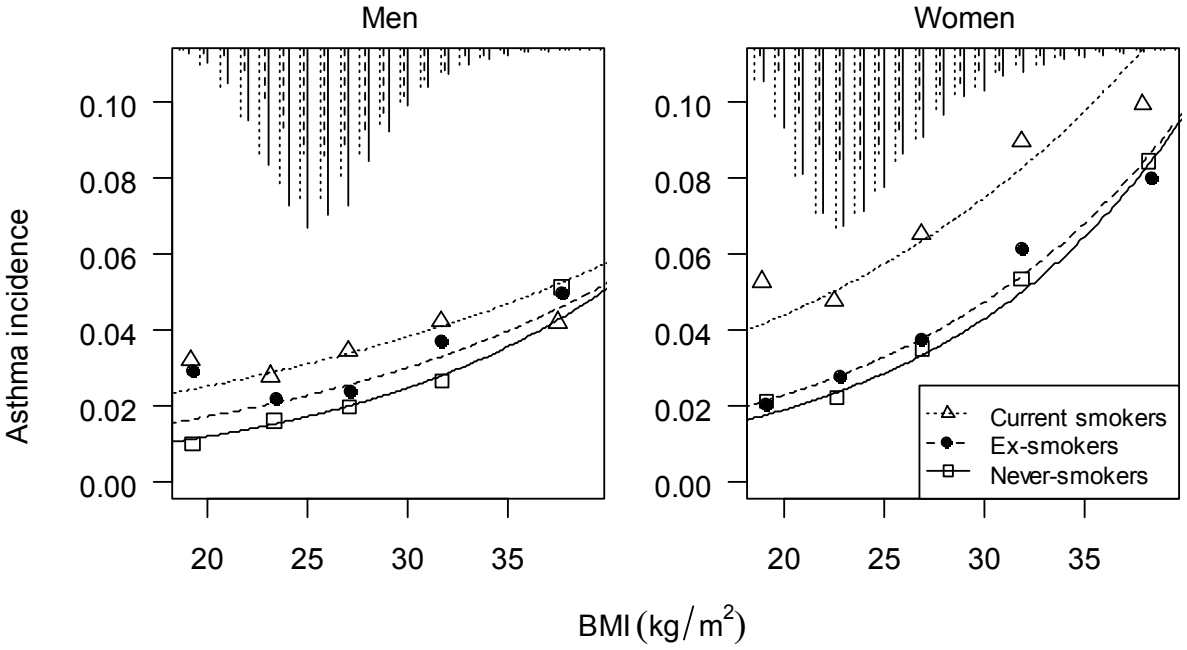

Figure 2.

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