BMJ Open Respiratory Research

Influence of asthma and obesity on respiratory symptoms, work ability and lung function: findings from a cross-sectional Norwegian population study

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To cite: Klepaker G, Henneberger PK, Hertel JK, *et al*. Influence of asthma and obesity on respiratory symptoms, work ability and lung function: findings from a cross-sectional Norwegian population study. *BMJ Open Resp Res* 2021;**8**:e000932. doi:10.1136/bmjresp-2021-000932

► Additional supplemental material is published online only. To view, please visit the journal online (http://dx.doi.org/10.1136/bmjresp-2021-000932).

Received 23 March 2021
Accepted 21 July 2021

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ABSTRACT

Background Although asthma and obesity are each associated with adverse respiratory outcomes, a possible interaction between them is less studied. This study assessed the extent to which asthma and overweight/obese status were independently associated with respiratory symptoms, lung function, Work Ability Score (WAS) and sick leave; and whether there was an interaction between asthma and body mass index (BMI) ≥25 kg/m^2 regarding these outcomes.

Methods In a cross-sectional study, 626 participants with physician-diagnosed asthma and 691 without asthma were examined. All participants completed a questionnaire and performed spirometry. The association of outcome variables with asthma and BMI category were assessed using regression models adjusted for age, sex, smoking status and education.

Results Asthma was associated with reduced WAS (OR=1.9 (95% CI 1.4 to 2.5)), increased sick leave in the last 12 months (OR=1.4 (95% CI 1.1 to 1.8)) and increased symptom score (OR=7.3 (95% CI 5.5 to 9.7)). Obesity was associated with an increased symptom score (OR=1.7 (95% CI 1.2 to 2.4)). Asthma was associated with reduced prebronchodilator and postbronchodilator forced expiratory volume in 1 s (FEV_1) (β=−6.6 (95% CI −8.2 to −5.1) and −5.2 (95% CI −6.7 to −3.4), respectively) and prebronchodilator forced vital capacity (FVC) (β=−2.3 (95% CI −3.6 to −0.96)). Obesity was associated with reduced prebronchodilator and postbronchodilator FEV_1 (β=−2.9 (95% CI −5.1 to −0.7) and −2.8 (95% CI −4.9 to −0.7), respectively) and FVC (−5.2 (95% CI −7.0 to −3.4) and −4.2 (95% CI −6.1 to −2.3), respectively). The only significant interaction was between asthma and overweight status for prebronchodilator FVC (β=−3.6 (95% CI −6.6 to −0.6)).

Conclusions Asthma and obesity had independent associations with increased symptom scores, reduced prebronchodilator and postbronchodilator FEV_1 and reduced prebronchodilator FVC. Reduced WAS and higher odds of sick leave in the last 12 months were associated with asthma, but not with increased BMI. Besides a possible association with reduced FVC, we found no interactions between asthma and increased BMI.

Key messages

- Are asthma and increased body mass index (BMI) independently associated with respiratory health outcomes, and is there a possible interaction between asthma and BMI?
- Asthma and obesity were independently associated with an increased respiratory symptom score, reduced prebronchodilator and postbronchodilator forced expiratory volume in 1 s and reduced prebronchodilator forced vital capacity (FVC), and the only interaction was between asthma and overweight for prebronchodilator FVC.
- A better understanding of respiratory outcomes and interaction may aid clinical decision-making and inform more personalised treatments in patients with asthma and increased BMI.

INTRODUCTION

Asthma is characterised by variable respiratory symptoms, such as wheezing and dyspnoea during rest or exercise and variable airflow limitation. Studies have found more sick leave and disability among patients with asthma compared with healthy controls.[1 2] Similarly, obesity may also cause shortness of breath and wheezing both at rest and following activity.[3 4] The effect of obesity on lung function has been described in several review studies,[5–8] showing an association between obesity and reduced forced expiratory volume in 1 s (FEV_1) and forced vital capacity (FVC).[5] Obesity has also been associated with a higher frequency and longer duration of sick leave.[9 10] Work ability in subjects with obesity has been less studied, but an association between reduced work ability and higher body mass index (BMI) has been found in employed subjects.[11]

A recent review concluded that there is sufficient evidence for a causal relationship between BMI and asthma.[12] Obesity may increase the risk of de novo asthma, complicate asthma or worsen respiratory symptoms.[13] Studies indicate that asthma is a risk factor for obesity in children[14] and adults.[15] Low-grade

systemic inflammation and altered lung mechanics have been demonstrated in both asthma and obesity.[16] Obesity and asthma have several common comorbidities, such as obstructive sleep apnoea, gastro-oesophageal reflux and anxiety.[17] Previous studies of patients with both asthma and obesity have classified obese asthma as a distinct phenotype, characterised by late onset asthma, increased respiratory symptoms, reduced lung function and poorer response to treatment compared with patients with asthma without obesity.[13 18–20]

While asthma and obesity are each separately associated with adverse respiratory outcomes, a possible interaction between them is less studied. A better understanding of the combined effects of asthma and obesity may help inform new and more personalised treatment and follow-up for such patients. Nicolacakis *et al* assessed the interaction between asthma and obesity using different lung function tests.[21] This study found no synergistic interaction, but the study sample was small, and the analyses were not adjusted for smoking status. To the best of our knowledge, there are no other studies assessing the possible interaction between asthma and BMI and the effect on respiratory outcomes.

In the present study of asthma cases and controls without asthma, we studied the extent to which asthma and overweight/obese status were independently associated with respiratory symptoms, lung function, work ability and sick leave; and whether there is an interaction between asthma and BMI ≥25 kg/m^2 regarding these outcomes.

METHODS

Study population

The study population was a sample of 626 participants in the cross-sectional baseline survey of the Telemark study who answered affirmative to the question: 'Has a doctor/physician ever diagnosed you with asthma?'. A random sample of those who did not state that they had physician-diagnosed asthma (n=691) was included as controls (hereafter the term 'healthy controls' is used). The Telemark study is a population-based study that started in 2013 and is described in detail in a previous publication.[22] In brief, the Telemark study started with a random sample of 50 000 inhabitants living in Telemark county in Norway, aged 16–50 years, who received a postal questionnaire. Of these, 48 142 were eligible, and 16 099 responded (response rate: 33%).[23] The responders included 1857 (11.5%) who reported having physician-diagnosed asthma.

For the present study, all 1857 subjects with physician-diagnosed asthma and 1989 computer-randomised healthy subjects were invited to undergo further medical examinations in 2014 or 2015. Figure 1 shows a flowchart of the subjects in the present study and indicates the number of subjects excluded and reasons for exclusion.

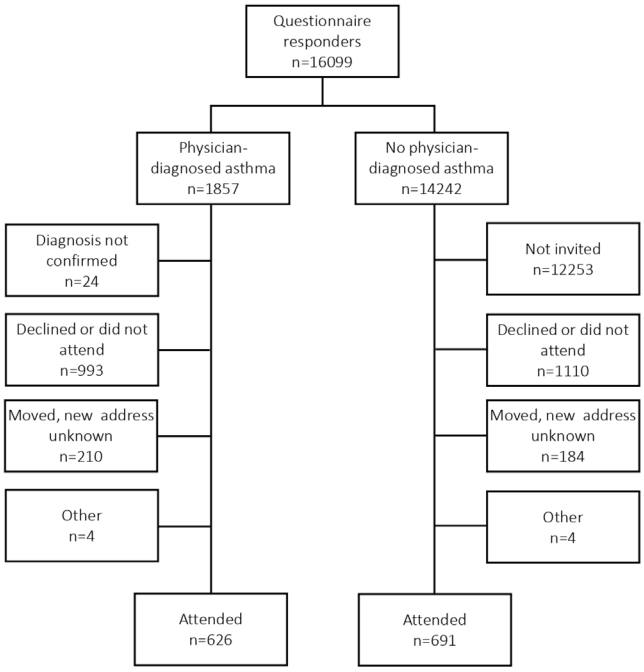

Figure 1 Flow chart of study subjects, including those excluded and the reasons for exclusion.

Questionnaire

All participants (n=1317) completed a questionnaire regarding respiratory symptoms, smoking status and other variables. The questionnaire was based on the European Community Respiratory Health Survey questionnaire as well as a questionnaire from a similar study conducted in Sweden.[24] Physician-diagnosed asthma was defined as an affirmative answer to the question: 'Has a doctor/physician ever diagnosed you with asthma?'. All missing data regarding symptoms and sick leave were recorded as not having that symptom or any sick leave. Age and sex were confirmed for accuracy using the Norwegian National Population Register. We calculated a score based on respiratory symptoms experienced within the last 12 months for each individual by adding all positive answers to questions Q1 to Q9 listed in online supplemental table 1, giving a maximum score of 9. The cut-off for dichotomising the symptom score was set at ≥3, which represented the upper tertile of the scores. Use of current asthma medication was defined as an affirmative answer to the question: 'Are you currently using any medications for asthma (spray, inhalation powder or tablets)?'. All subjects with physician-diagnosed asthma and respiratory symptoms during the past 12 months completed the Asthma Control Test (ACT) questionnaire, and a score was calculated.[25] In this questionnaire, answers are given a score of 1–5, where five is the best, and the maximum score is 25. A total score <19 indicates poorly controlled asthma.[25]

In the baseline study questionnaire the subjects were asked to state if they ever had sarcoidosis, other chronic lung diseases than asthma and Chronic obstructive pulmonary disease (COPD), sought help for mental

problems, physician-diagnosed COPD, and if they suffer from hay fever, pollen allergy or other allergic respiratory problems.

Anthropometric measures

All participants underwent a physical examination. Trained study personnel using the same instruments for all participants measured the subjects' height and weight. BMI was calculated as kg/m^2 and stratified into the following categories recommended by the WHO: normal weight (including underweight) <25.0 kg/m^2, overweight 25.0–29.9 kg/m^2 and obese ≥30 kg/m^2.[26]

Lung function tests

Spirometry was performed in accordance with the American Thoracic Society/European Respiratory Society guidelines[27] using Jaeger Master Screen Pulmonary Function Testing (Erich Jaeger GmbH & Co. KG, Würzburg, Germany). FVC, FEV_1 and FEV_1/FVC-ratio were recorded. Two trained physicians (GK and JK) manually validated all tests. If a participant had no valid curves, the results were not included. All reference values were calculated using Global Lung Function Initiative equations.[28]

Reversibility testing

All participants with at least one acceptable spirometry test (n=1258, 96%) were asked to inhale 0.4 mg salbutamol, and spirometry was repeated after 10–15 min.[29] All tests were manually validated, and tests without an acceptable curve were excluded. In total, 1091 (83%) participants had an acceptable test. Reasons for not performing the reversibility test included refusal by participants (n=91 (7%)), no valid curves (n=28 (2%)), contraindications (n=14 (1%)) or other reasons (n=15 (1%)).

Work ability

Work ability was defined via self-report using the first question of the Work Ability Index (WAI) questionnaire.[30] This question is referred to as the Work Ability Score (WAS).[30] The participants were asked to grade their current work ability on a scale from 0 ('I cannot work at all') to 10 ('my work ability is at its best right now'). WAS can be categorised into normal (score ≥8) and reduced (score <8) work ability.[31] Previous studies have demonstrated a strong association between WAS and the results of a complete WAI questionnaire.[31 32]

Sick leave

Sick leave was defined as an affirmative answer to the question, 'Have you been on sick leave over the course of the last 12 months?'. The subjects selected how many days they had been on sick leave from the following categories: 1–7 days, 8–14 days, 15 days–12 weeks and >12 weeks. A cut-off of 14 days was chosen to differentiate short-term from long-term sick leave. The cut-off and categorisation were chosen to reflect the official Norwegian sick leave system and important follow-up time points. Analyses of sick leave were restricted to subjects employed in paid work within the previous 12 months (n=1143).

Patient and public involvement

A representative from the Norwegian Asthma and Allergy Association (NAAA) was a member of the study steering committee and contributed to the development of questionnaires and examination methods. NAAA representatives have also been involved in study planning, design piloting and transfer of knowledge to the patient group.

Statistical analyses

The study participants were grouped into six categories according to their BMI and asthma status. To analyse differences between the groups, Pearson χ^2 and Fisher's exact tests were used for categorical data, and one-way analysis of variance (ANOVA) was applied to continuous data.

The association of outcome variables with asthma and BMI was assessed using logistic and linear regression models adjusted for age, sex, smoking status and education. To assess interaction, a separate regression model was fit for each outcome and included covariates for asthma, BMI categories, asthma ×BMI interaction, age, sex, smoking and education. Additive interactions for dichotomous outcomes were assessed via the methods described by Andersson *et al* using the Synergy Index (SI), with a null value of 1.0 and a 95% CI.[33]

For responders and non-responders, we have self-reported data from the baseline survey on BMI, age, sex, education, smoking, sick leave and WAS. We used a conditional logistic regression model to test whether attendance at the medical examination was associated with these variables. In other analyses performed on the Telemark study population,[22] the inverse probability of participation weights was used to minimise selection bias from non-participation. Because this did not substantially change the exposure-outcome associations compared with the use of non-weighted variables in that study, weights were not used in the present study.

All analyses were performed using the statistical package SPSS V.25.0 (IBM SPSS). Statistical significance was defined as $p<0.05$, and $0.05 \leq p<0.10$ was considered borderline statistically significant.

RESULTS

Table 1 shows the characteristics for all subjects stratified by BMI-category and asthma status. Subjects with asthma and obesity had a higher age of onset of symptoms (mean 16.6 years of age), more frequently used asthma medication (65%) and had a poorer asthma control (43% with ACT score 5–19) than the subjects with normal weight and asthma. The subjects with asthma reported more

Table 1 Characteristics for subjects stratified by BMI-category and physician-diagnosed asthma

	No physician-diagnosed asthma			Physician-diagnosed asthma			P value
	Normal weight (BMI <25 kg/m^2)	Overweight (BMI 25–29.9 kg/m^2)	Obesity (BMI ≥30 kg/m^2)	Normal weight (BMI <25 kg/m^2)	Overweight (BMI 25–29.9 kg/m^2)	Obesity (BMI ≥30 kg/m^2)	(Comparing all strata)
	(n=309)	(n=255)	(n=127)	(n=228)	(n=230)	(n=168)	
Sex							**<0.001***
Women, N (%)	216 (70%)	132 (52%)	62 (49%)	157 (69%)	125 (54%)	110 (66%)	
Men N (%)	93 (30%)	123 (48%)	65 (51%)	71 (31%)	105 (46%)	58 (35%)	
Smoking status							0.16*
Never smoker N (%)	183 (59%)	140 (55%)	55 (43%)	134 (59%)	111 (48%)	83 (49%)	
Former smoker N (%)	68 (22%)	63 (25%)	39 (31%)	53 (23%)	65 (28%)	47 (28%)	
Occasional smoker N (%)	27 (9%)	25 (10%)	10 (8%)	17 (8%)	21 (9%)	13 (8%)	
Daily smoker N (%)	31 (10%)	27 (11%)	23 (18%)	24 (11%)	33 (14%)	25 (15%)	
Highest completed education							0.24*
Elementary N (%)	35 (11%)	30 (12%)	18 (14%)	37 (16%)	27 (12%)	24 (14%)	
Upper secondary N %)	98 (32%)	106 (42%)	52 (41%)	81 (36%)	87 (38%)	76 (45%)	
University N (%)	165 (53%)	111 (44%)	54 (43%)	102 (45%)	108 (47%)	65 (39%)	
Other/missing N (%)	11 (4%)	8 (3%)	3 (2%)	8 (4%)	8 (4%)	3 (2%)	
Age at examination, years, SEM categories, SD total	39.4 (0.55)	42.7 (0.48)	42.4 (0.74)	36.1 (0.68)	42.3 (0.63)	42.1 (0.59)	**<0.001****
Age of onset of asthma symptoms, years of age	NA	NA	NA	13.1 (0.75)	16.2 (0.88)	16.6 (0.89)	**0.005****
Current use of any asthma medication (spray, inhalation powder or tablets)							
► No	NA	NA	NA	109 (48%)	103 (45%)	59 (35%)	
► Yes	NA	NA	NA	119 (52%)	127 (55%)	109 (65%)	**0.036***
ACT score							
► Well controlled (20–25 points)	NA	NA	NA	109 (72%)	84 (65%)	63 (57%)	**0.034***
► Not controlled (5–19 points)	NA	NA	NA	45 (29%)	45 (35%)	48 (43%)	
Ever had sarcoidosis, yes N (%)	1	0	3	0	3	2	0.051*
Ever sought help for mental problems, yes N (%)	50 (19%)	44 (21%)	23 (18%)	56 (25%)	55 (24%)	46 (27%)	**0.014***

Continued

Table 1 Continued

	No physician-diagnosed asthma			Physician-diagnosed asthma			P value
	Normal weight (BMI <25 kg/m^2)	Overweight (BMI 25–29.9 kg/m^2)	Obesity (BMI ≥30 kg/m^2)	Normal weight (BMI <25 kg/m^2)	Overweight (BMI 25–29.9 kg/m^2)	Obesity (BMI ≥30 kg/m^2)	(Comparing all strata)
	(n=309)	(n=255)	(n=127)	(n=228)	(n=230)	(n=168)	
Ever had other chronic lung diseases than asthma and COPD, yes N (%)	1	4	3	12 (5%)	25 (11%)	12 (7%)	**<0.001***
Physician-diagnosed COPD, yes N (%)	1	1	0	7	6	6	**0.006***
Allergy with respiratory symptoms, yes N (%)	98 (32%)	76 (30%)	43 (34%)	138 (61%)	134 (58%)	112 (67%)	**<0.001***

P values are calculated using *χ^2 or ** One.way analysis of variance (ANOVA). NA=not applicable. Statistically significant findings, p<0.05, are bolded
ACT, Asthma Control Test; BMI, body mass index; COPD, Chronic obstructive pulmonary disease.

frequently other respiratory conditions such as respiratory allergy than the healthy controls.

In the logistic regression model to test whether attendance at the medical examination was associated with BMI, age, sex, education, smoking, sick leave and WAS, we observed positive associations with the age categories of 30–39 years (OR=2.2 (95% CI 1.8 to 2.7)) and 40–50 years (OR=3.8 (95% CI 3.2 to 4.6)) with 18–29 years as the reference. Negative associations were observed with male sex (OR=0.8 (95% CI 0.71 to 0.98)) and current smoking (OR=0.61 (95% CI 0.49 to 0.77)).

The prevalence of outcomes by possible confounders is presented in table 2 and shows an association of most outcomes with sex and smoking status. Additionally, most lung function variables were associated with age and education.

Table 3 shows the WAS, sick leave in the last 12 months, symptom score and mean % of predicted prebronchodilator and postbronchodilator spirometry for the six groups defined by asthma and BMI status. Overweight subjects with asthma had significantly reduced WAS and were more frequently on sick leave compared with overweight subjects without asthma. There was no significant difference in sick leave >14 days within the two groups. Comparing obese subjects with and without asthma to their normal weight counterparts, we found a significantly increased symptom score (p=0.02 and p=0.01, respectively). Lung function prebronchodilator and postbronchodilator was significantly lower in the groups with asthma than in those without, with the exception of pre-FVC and post-FVC for normal weight and obese subjects. The results also demonstrated that, regardless of asthma status, subjects with obesity had reduced FEV_1 and FVC both prebronchodilator and postbronchodilator compared with normal weight subjects. However, the FEV_1/FVC-ratio was similar. The frequencies of each respiratory symptom by asthma and BMI categories are presented in online supplemental table 1.

Table 4 shows adjusted coefficients, interaction terms and SIs from the regression models. The adjusted ORs for the categorical outcomes show that asthma is significantly associated with a reduced WAS (OR=1.9 (95% CI 1.4 to 2.5)), an increased likelihood of sick leave in the last 12 months (1.4 (95% CI 1.1 to 1.8)) and an increased symptom score (7.3 (95% CI 5.5 to 9.7)). Obesity was associated with an increased symptom score (1.7 (95% CI 1.2 to 2.4)) but not WAS or sick leave, and overweight was associated with none of these three outcomes. The models for each respiratory symptom showed that obesity was associated with several symptoms (online supplemental table 2). The SI was used to evaluate additive interactions. An elevated SI was found for the combination of overweight and asthma with WAS and the two sick leave outcomes, but none of these index values were statistically significant (table 4). Multiplicative interactions for the dichotomous outcomes were not significant, although asthma and overweight had a borderline statistically significant interaction (p=0.095) for reduced WAS.

Table 2 Work Ability Score, sick leave, respiratory symptom score and % of predicted FEV_1, FVC and FEV_1/FVC-ratio prebronchodilator and postbronchodilator by possible confounders: sex, smoking status, highest completed education and age category

Outcome, summary statistics	Number	Sex			Smoking status				Highest completed education				Age category			
		Male	Female	P value	Never smoker	Former smoker	Daily smoker	P value	Elementary	Upper secondary	University	P value	18–30	31–40	41–52	P value
Work Ability Score <8, n/n total in group (%)	261/1295 (20%)	85/508 (17%)	176/787 (22%)	**0.016**	112/697 (16%)	78/328 (24%)	71/270 (27%)	**<0.001**	52/168 (31%)	130/525 (25%)	79/602 (13%)	**<0.001**	26/212 (12%)	66/310 (21%)	169/773 (22%)	0.007
Sick-leave in the last 12 months, n/n total in group (%)	413/1143 (36%)	113/453 (25%)	300/690 (43%)	**<0.001**	182/610 (30%)	125/297 (42%)	106/236 (45%)	**<0.001**	44/116 (38%)	180/464 (39%)	189/563 (34%)	0.203	47/156 (30%)	108/237 (46%)	258/714 (36%)	0.148
Sick leave >14 days, n/n total in group (%)	199/1143 (17%)	43/453 (9%)	156/690 (23%)	**<0.001**	78/610 (13%)	63/297 (21%)	58/236 (25%)	**<0.001**	20/116 (17%)	88/464 (19%)	91/563 (16%)	0.428	15/156 (10%)	57/237 (24%)	127/714 (18%)	0.060
Symptom score ≥3, n/n total in group (%)	403/1317 (31%)	120/515 (23%)	283/802 (35%)	**<0.001**	194/706 (27%)	107/335 (32%)	102/276 (37%)	**0.012**	50/171 (29%)	177/541 (33%)	176/605 (29%)	0.379	63/216 (29%)	96/314 (31%)	244/787 (31%)	0.874
Symptom score, n, mean (SEM)	1317	515 1.87 (0.11)	802 2.58 (0.10)	**<0.001**	706 2.10 (0.10)	335 2.37 (0.15)	276 2.72 (0.18)	**0.004**	171 2.26 (0.21)	541 2.49 (0.12)	605 2.14 (0.11)	0.095	216 2.26 (0.18)	314 2.26 (0.15)	787 2.33 (0.10)	0.911
Pre-FEV_1 % of predicted value, n, mean (SEM)	1257	489 94.26 (0.67)	768 96.00 (0.49)	**0.033**	671 95.44 (0.52)	322 96.57 (0.77)	264 93.50 (0.99)	**0.031**	158 93.12 (1.08)	515 94.06 (0.63)	584 97.02 (0.58)	**<0.001**	199 94.45 (0.83)	296 96.11 (0.81)	762 95.25 (0.54)	0.428
Pre-FVC % of predicted value n, mean (SEM)	1257	489 98.25 (0.44)	768 98.25 (0.56)	**0.028**	671 98.86 (0.46)	322 100.14 (0.68)	264 98.93 (0.82)	0.284	158 97.37 (0.99)	515 98.34 (0.54)	584 100.46 (0.50)	**0.002**	199 99.25 (0.81)	296 99.91 (0.66)	762 98.92 (0.47)	0.498
Pre-FEV_1/ FVC-ratio in %, n, mean (SEM)	1257	489 0.79 (0.002)	768 0.77 (0.003)	**<0.001**	671 0.79 (0.002)	322 0.77 (0.003)	264 0.76 (0.005)	**<0.001**	158 0.79 (0.006)	515 0.77 (0.003)	584 0.78 (0.003)	0.093	199 0.81 (0.005)	296 0.79 (0.004)	762 0.77 (0.002)	**<0.001**
Post-FEV_1 % of predicted value, n, mean (SEM)	1091	425 96.79 (0.67)	666 99.16 (0.50)	0.004	588 98.22 (0.53)	279 99.88 (0.76)	224 96.25 (1.00)	**0.009**	131 95.97 (1.16)	442 97.10 (0.64)	518 99.78 (0.57)	**<0.001**	177 97.99 (0.84)	264 99.10 (0.78)	650 97.95 (0.55)	0.478
Post-FVC % of predicted value, n, mean (SEM)	1091	425 98.57 (0.58)	666 99.88 (0.46)	0.077	588 98.78 (0.49)	279 100.67 (0.70)	224 99.28 (0.80)	0.093	131 97.21 (1.12)	442 98.85 (0.56)	518 100.36 (0.51)	**0.012**	177 98.92 (0.85)	264 100.03 (0.69)	650 99.23 (0.48)	0.559

Continued

Table 2 Continued

Outcome, summary statistics	Number	Sex			Smoking status				Highest completed education				Age category			
		Male	Female	P value	Never smoker	Former smoker	Daily smoker	P value	Elementary	Upper secondary	University	P value	18–30	31–40	41–52	P value
Post-FEV_1/FVC ratio in %, n, mean (SEM)	1091	425 0.78 (0.004)	666 0.81 (0.002)	**<0.001**	588 0.81 (0.003)	279 0.80 (0.003)	224 0.78 (0.005)	**<0.001**	131 0.81 (0.006)	442 0.80 (0.003)	518 0.81 (0.003)	**0.029**	177 0.85 (0.005)	264 0.81 (0.004)	650 0.79 (0.003)	**<0.001**

P values were calculated using Fisher's exact, Pearson χ^2 or one-way ANOVA.Statistically significant findings, p<0.05, are bolded
ANOVA, Analysis of variance; FEV, forced expiratory volume; FEV_1, forced expiratory volume after 1 s; FVC, forced vital capacity.

We found no statistically significant multiplicative or additive interactions between asthma status and elevated BMI category with any specific respiratory symptom (online supplemental table 2).

Adjusted linear regression models showed that asthma was significantly associated with a higher symptom score (2.4 points (95% CI 2.2 to 2.7)), reduced prebronchodilator and postbronchodilator FEV_1 %-predicted (β=−6.6 (95% CI −8.2 to −5.1) and −5.2 (95% CI −6.7 to −3.4)), prebronchodilator FVC %-predicted (β=−2.3 (95% CI −3.6 to −0.96)) and prebronchodilator and postbronchodilator FEV_1/FVC-ratio (−0.04 (95% CI −0.05 to −0.03) and −0.03 (95% CI −0.04 to −0.03)) (table 4). Overweight status was associated only with an increased prebronchodilator FEV_1/FVC-ratio (β=0.01 (95% CI 0.003 to 0.020)). Obesity was associated with a higher symptom score (0.6 points (95% CI 0.3 to 0.97)) and reduced FEV_1 and FVC % of predicted prebronchodilator and postbronchodilator (FEV_1 β=−2.9 (95% CI −5.1 to −0.7) and −2.8 (95% CI −4.9 to −0.7), FVC β=−5.2 (95% CI −7.0 to −3.4) and −4.2 (95% CI −6.1 to −2.3), respectively). The interaction between asthma and overweight status was statistically significant for prebronchodilator FVC (β=−3.6 (95% CI −6.6 to −0.6)), but not for postbronchodilator FVC (β=−3.1 (95% CI −6.3 to 0.05)). We found no other interactions between asthma and overweight or obesity status when analysing lung function and the other continuous variables.

DISCUSSION

In the present study, we found that asthma and increased BMI were independently associated with an increased respiratory symptom score and reduced lung function. Asthma, but not increased BMI, was associated with reduced self-reported work ability and more frequent sick leave in the last 12 months. The only statistically significant interaction we found was between asthma and overweight for prebronchodilator FVC %.

All groups with asthma, regardless of BMI category, reported a higher symptom score compared with the group with no asthma in the same BMI category. As expected, in the adjusted model, we found an elevated OR for increased symptom scores in subjects with asthma. Obese subjects with and without asthma reported a significantly higher symptom score compared with the normal-weight group. In the adjusted model, obesity was associated with an increased symptom score with an OR of 1.7 (95% CI 1.2 to 2.4), which was substantially lower than that for asthma (7.3 (95% CI 5.5 to 9.7)). The same contrast was evident when modelling symptom score as a continuous variable, with effect estimates greater for asthma (2.4 (95% CI 2.2 to 2.7)) than obesity (0.6 (95% CI 0.3 to 0.97)) and for individual symptoms as dichotomous outcomes (online supplemental table 2). The stronger association of symptoms with asthma was expected because asthma is a respiratory disease, while obesity is not.

Table 3 Work Ability Score, sick leave, respiratory symptom score and % of predicted FEV_1, FVC and FEV_1/FVC-ratio prebronchodilator and postbronchodilator, stratified by physician-diagnosed asthma and BMI category†‡

	BMI category			P values for elevated vs normal weight within asthma strata	
Outcome, summary statistics	**Normal weight (BMI <25 kg/m²)**	**Overweight (BMI 25–29.9 kg/m²)**	**Obesity (BMI ≥30 kg/m²)**	**Overweight vs normal**	**Obesity vs normal**
Work ability score <8, n/n total in group (%)					
No asthma	46/308 (15%)	36/250 (14%)	23/125 (18%)	0.86	0.37
Asthma	45/223 (20%)	65/223 (29%)	46/166 (27%)	**0.03**	0.08
P values for asthma vs no asthma within BMI categories	0.11	**>0.001**	0.07		
Sick leave in the last 12 months, n/n total in group (%)					
No asthma	87/269 (32%)	69/230 (30%)	41/111 (37%)	0.57	0.39
Asthma	74/193 (38%)	80/202 (40%)	62/138 (45%)	0.80	0.23
P values for asthma vs no asthma within BMI categories	0.18	**0.04**	0.20		
Sick leave >14 days, n/n total in group (%) *					
No asthma	37/85 (43%)	29/69 (42%)	18/41 (44%)	0.85	0.97
Asthma	39/74 (53%)	42/80 (53%)	34/62 (55%)	0.98	0.80
P values for asthma vs no asthma within BMI categories	0.25	0.20	0.28		
Symptom score ≥3, n/n total in group (%)					
No asthma	35/309 (11%)	25/255 (10%)	26/127 (21%)	0.60	**0.01**
Asthma	109/228 (48%)	107/230 (47%)	101/168 (60%)	0.78	**0.02**
P values for asthma vs no asthma within BMI categories	**>0.001**	**>0.001**	**>0.001**		
Symptom score, mean (SEM)					
No asthma	1.04 (0.10)	0.98 (0.11)	1.57 (0.19)	0.70	**0.01**
Asthma	3.46 (0.18)	3.37 (0.19)	4.15 (0.23)	0.75	**0.02**
P values for asthma vs no asthma within BMI categories	**>0.001**	**>0.001**	**>0.001**		
Pre-FEV_1 % of predicted value, mean (SEM)					
No asthma	98.6 (0.68)	100.2 (0.77)	95.4 (1.27)	0.13	**0.01**
Asthma	92.9 (0.93)	93.1 (1.01)	87.8 (1.30)	0.97	**>0.001**
P values for asthma vs no asthma within BMI categories	**>0.001**	**>0.001**	**>0.001**		
Pre-FVC % of predicted value, mean (SEM)					
No	100.9 (0.62)	102.0 (0.76)	96.5 (1.17)	0.37	**>0.001**
Yes	100.4 (0.82)	98.1 (0.82)	93.6 (1.10)	**0.04**	**>0.001**
P values for asthma vs no asthma within BMI categories	0.59	**0.001**	0.08		
Pre-FEV_1/FVC-ratio in %, mean (SEM)					
No asthma	79.7 (0.39)	79.3 (0.35)	79.8 (0.47)	0.54	0.82
Asthma	76.3 (0.54)	76.4 (0.50)	75.7 (0.65)	0.94	0.56

Continued

Table 3 Continued

Outcome, summary statistics	BMI category			P values for elevated vs normal weight within asthma strata	
	Normal weight (BMI <25 kg/m^2)	Overweight (BMI 25–29.9 kg/m^2)	Obesity (BMI ≥30 kg/m^2)	Overweight vs normal	Obesity vs normal
P values for asthma vs no asthma within BMI categories	**>0.001**	**>0.001**	**>0.001**		
Post-FEV$_1$ % of Post-FEV$_1$ % of predicted value, mean (SEM)predicted value, mean (SEM)					
No asthma	101.0 (0.70)	102.3 (0.82)	97.4 (1.43)	0.31	**0.003**
Asthma	96.6 (0.93)	96.0 (0.97)	93.2 (1.30)	0.81	**0.02**
P values for asthma vs no asthma within BMI categories	**>0.001**	**>0.001**	**0.03**		
Post-FVC % of predicted value, mean (SEM)					
No asthma	100.4 (0.66)	101.5 (0.82)	95.9 (1.25)	0.38	**>0.001**
Asthma	100.4 (0.86)	98.7 (0.82)	95.9 (1.14)	0.20	**0.001**
P values for asthma vs no asthma within BMI categories	0.99	**0.02**	0.99		
Post-FEV$_1$/FVC ratio in %, mean (SEM)					
No asthma	82.1 (0.42)	81.2 (0.36)	82.0 (0.51)	0.12	0.59
Asthma	79.4 (0.55)	78.5 (0.49)	78.5 (0.66)	0.26	0.31
P values for asthma vs no asthma within BMI categories	**>0.001**	**>0.001**	**>0.001**		

Prebronchodilator spirometry: 661 acceptable tests among controls, 596 acceptable tests among cases.
Postbronchodilator spirometry: 559 acceptable tests among controls, 532 acceptable tests among cases.
Statistically significant findings are given in bold.
*The participants with reported sick leave >14 days were limited to those who reported taking sick leave in the last 12 months.
†P values were based on χ^2 test for categorical variables and one-way ANOVA for continuous variables.
‡The distribution by BMI category for all 691 participants without asthma was 269 normal weight, 230 overweight and 111 obese; for all 626 participants with asthma, 193 had normal weight, 202 had overweight and 138 had obese. The actual numbers varied by outcome variable, depending on the number of missing values.
ANOVA, Analysis of variance; BMI, body mass index; FEV, forced expiratory volume; FEV$_1$, forced expiratory volume after 1 s; FVC, forced vital capacity.

Reduced WAS and sick leave in the last 12 months were both associated with asthma but not with overweight or obesity status. When assessing lung function, both asthma and obesity were associated with reduced spirometry. This was not the case for postbronchodilator FVC % of predicted for asthma and prebronchodilator and postbronchodilator FEV$_1$/FVC ratio for obesity. The results are consistent with greater effect estimates for FEV$_1$ than FVC for asthma and the reverse for obesity (table 4).

Jarvis *et al* employed some of the same questions as in the present study and assessed the associations between increased BMI and respiratory symptoms.[4] In line with our findings, these authors reported more wheezing in the absence of cold and shortness of breath following strenuous activity; significantly more wheezing with shortness of breath and waking with shortness of breath was also reported (online supplemental table 2). Other studies have reported an increase in self-reported dyspnoea and wheezing at rest and exertion in obese subjects compared with normal-weight subjects,[3] but to our knowledge, no other studies used a respiratory symptom score. As expected, all groups with physician-diagnosed asthma reported a higher symptom score compared with subjects without asthma in the same BMI category (table 3). Our previous study of the same population of physician-diagnosed subjects showed no statistically significant difference between obese and normal weight asthma cases for any specific respiratory symptom, but the group with obesity did have a higher symptom score.[34] Other studies have shown that some respiratory symptoms are more prevalent among patients with asthma and obesity, but the literature is conflicting.[35–37] Bildstrup *et al* demonstrated an increased incidence of severe cough and tightness in the chest with increased BMI in patients with asthma, whereas wheezing and shortness of breath were not related to BMI.[38] The findings in previous studies were observed mainly for the BMI category ≥35 kg/m^2 or for groups with an average

Table 4 Association of work ability, sick leave, respiratory symptom score and spirometry with asthma and BMI categories and tests of interaction**

Health-related outcome, effect estimate or units	Coefficients from regression models (95% CI)*			Coefficients for interaction terms in regression models† for all outcomes and Synergy Index for dichotomous outcomes			
		Elevated BMI vs normal weight		Interaction terms in regression models (95% CI)†		Synergy Index (95% CI)‡	
	Asthma, yes vs no	Overweight	Obesity	Asthma×overweight	Asthma×obesity	Asthma×overweight	Asthma×obesity
Dichotomous outcomes							
Work Ability Score ≤8, OR	**1.9 (1.4 to 2.5)**	1.2 (0.8 to 1.6)	1.2 (0.8 to 1.7)	1.76 (0.90 to 3.41) §	1.08 (0.51 to 2.28)	3.3 (0.35 to 32)	1.26 (0.35–4.5)
Sick leave in the last 12 months, OR¶	**1.4 (1.1 to 1.8)**	1.05 (0.8 to 1.4)	1.3 (0.9 to 1.8)	1.28 (0.71 to 2.30)	1.01 (0.51 to 2.00)	2.75 (0.06 to 112)	1.17 (0.21 to 6.45)
Sick leave >14 days, OR¶	1.5 (0.99 to 2.2)	0.9 (0.6 to 1.5)	0.9 (0.6 to 1.6)	1.35 (0.64 to 2.86)	1.05 (0.45 to 2.47)	2.50 (0.05 to 129)	1.22 (0.13 to 11.4)
Symptom score ≥3, OR	**7.3 (5.5 to 9.7)**	0.9 (0.7 to 1.3)	**1.7 (1.2 to 2.4)**	1.05 (0.54 to 2.04)	0.71 (0.35 to 1.44)	0.94 (0.61 to 1.47)	1.37 (0.87 to 2.17)
Continuous outcomes							
Symptom score (0–9), score	**2.4 (2.2 to 2.7)**	−0.03 (−0.3 to 0.3)	**0.6 (0.3 to 0.97)**	−0.1 (−0.7 to 0.5)	0.01 (−0.7 to 0.7)		
Pre-FEV_1 % of predicted	**−6.6 (−8.2 to −5.1)**	1.7 (−0.2 to 3.5)	**−2.9 (−5.1 to −0.7)**	−1.7 (−5.1 to 1.7)	−2.2 (−6.2 to 1.8)		
Pre-FVC, % of predicted	**−2.3 (−3.6 to −0.96)**	−0.08 (−1.6 to 1.5)	**−5.2 (−7.0 to −3.4)**	**−3.6 (−6.6 to −0.6)**	−2.4 (−6.0 to 1.2)		
Pre-FEV_1/FVC-ratio, %	**−0.04 (−0.05 to − 0.03)**	**0.01 (0.003 to 0.020)**	0.009 (−0.001 to 0.019)	1.3 (−0.4 to 2.9)	−0.3 (−2.2 to 1.7)		
Post-FEV_1, % of predicted	**−5.2 (−6.7 to −3.4)**	1.1 (−0.7 to 2.8)	**−2.8 (−4.9 to −0.7)**	−2.0 (−5.4 to 1.5)	0.1 (−4.0 to 4.2)		
Post-FVC, % of predicted	−1.0 (−2.5 to 0.4)	−0.05 (−1.7 to 1.6)	**−4.2 (−6.1 to −2.3)**	−3.1 (−6.3 to 0.05) §	0.03 (−3.7 to 3.8)		
Post-FEV_1/FVC ratio, n %	**−0.03 (−0.04 to − 0.03)**	0.008 (−0.001 to 0.02)	0.009 (−0.001 to 0.02)	0.9 (−0.8 to 2.5)	−0.1 (−2.0 to 1.9)		

Predilator spirometry: 661 acceptable tests among controls, 596 acceptable tests among cases.
Postdilator spirometry: 559 acceptable tests among controls, 532 acceptable tests among cases.
*A separate regression model was fit for each outcome and included covariates for asthma, BMI categories, age, sex, smoking and education.
†A separate regression model was fit for each outcome and included covariates for asthma, BMI categories, asthma ×BMI interaction, age, sex, smoking and education. The coefficients for the interaction terms test for interaction on the multiplicative scale for dichotomous outcomes and on the additive scale for continuous outcomes.
‡Synergy Index is an indicator of an additive interaction for dichotomous outcomes and has a null value of 1.0.
§Results are borderline statistically significant, 0.05<p<0.10.
¶Results for sick leave are limited to the 1143 participants employed in the last 12 months.
**Statistically significant findings are given in bold. The operational definitions of asthma and BMI categories are described in the Methods section.
BMI, body mass index; FEV_1, forced expiratory volume after 1 s; FEV, forced expiratory volume; FVC, forced vital capacity.

BMI in the top BMI group that was higher than in our study.

When using WAS to assess self-reported work ability, we found a reduced WAS associated with asthma but not increased BMI. A Danish cross-sectional study by Andersen *et al* demonstrated reduced work ability with increasing BMI in working subjects.[11] They found an OR of 1.69 (95% CI 1.10 to 2.62) for lower work ability among working subjects with BMI ≥40 kg/m^2. For BMI of 30 to <35 kg/m^2, the OR was 1.11 (95% CI 1.01 to 1.22); however, the researchers used a different instrument to evaluate work ability that focused on physical demands. This may explain the different results compared with our study, as WAS is a measure of total work ability. In a review by Neovius *et al*, obesity was associated with higher frequency and longer duration of sick leave.[9] A Dutch review, using only longitudinal studies, had similar conclusions.[10] Two other studies have found more frequent sick leave among patients with asthma regardless of weight compared with healthy controls.[1 2] Hansen *et al* showed that patients with asthma receive more welfare, sick leave and disability compared with subjects without asthma.[1] In the present study, we found more frequent sick leave within the past 12 months among subjects with asthma, but there was no indication of increased duration of sick leave longer than 14 days. This finding may suggest that subjects with asthma are more frequently on sick leave, but that the sick leave periods are relatively short. A limitation of this study is that we do not have data on the cause for the sick leave.

Increased BMI alone was not associated with more sick leave in our study. There are several possible explanations for these conflicting results on self-reported work ability and sick leaves for the current study vs other studies.[9 10] First, we had few subjects with BMI >40 kg/m^2 (n=22); thus, we lacked the statistical power to show an effect. Neovius *et al* reported an OR of 1.3–2.1 for frequency of sick leave in studies comparing subjects with obesity to those with normal weight and found that subjects with obesity had about ten additional days of sick leave per person year compared with those with normal weight.[9] In the present study, the subjects were relatively young (the oldest was 52 years old) and all subjects were working, which possibly introduced a healthy worker effect bias. Moreover, in Norway, there is a high awareness of reducing sick leave and employers will make great efforts to adjust work tasks and provide alternative jobs so that the workers can stay at work.

Among subjects without asthma, we found a significant negative effect on FVC both prebronchodilator and postbronchodilator among subjects with BMI ≥30 kg/m^2 compared with those with normal weight. In a review by Dixon and Peters, the authors concluded that FVC and FEV_1 were slightly reduced in the presence of obesity and that the FEV_1/FVC ratio was often unaffected unless BMI was over 60 kg/m^2. They also found that body fat distribution was more strongly associated with lung function than BMI and weight.[39] The effect of obesity on lung function has also been described in other review studies,[5–8] showing an effect on both FEV_1 and FVC.[5] Several studies have shown an effect of overweight/obesity status on spirometry among patients with asthma,[40–42] but there are also studies that do not find an effect.[38] In meta-analyses, the effect on FVC and FEV_1 among subjects with asthma and obesity was confirmed.[8] Thus, our results seem to be in line with those of previous studies indicating an independent effect of both obesity and asthma on lung function.

To our knowledge, few studies have assessed the possible interactions between asthma and obesity. Nicolacakis *et al* found no synergistic interaction between asthma and obesity and concluded that the effects on lung function were a result of the combined effects.[21] However, this was a small study (n=210 divided into four groups), and the results were not adjusted for smoking status. The researchers attributed the lack of interaction to the existence of different pathways: obesity reduces lung volumes and influences the thoracic wall movement, while asthma affects the smooth muscle tone, leading to airway obstruction. However, we found only a possible interaction of asthma and overweight with FVC, and no interaction with the other assessed outcomes.

Strengths and limitations

An important limitation of our study was that the outcomes, apart from lung function, were self-reported. However, we used validated questions from questionnaires used in other large epidemiological studies on respiratory health. Validated questionnaires may improve the accuracy of the responses; however, they may still introduce recall bias and random errors that could distort estimates of associations.

Epidemiological studies are susceptible to bias due to selection and non-response. The controls were randomly selected from the Telemark study baseline cohort for medical examination, and all asthma cases were invited to reduce selection bias. Another important limitation is the relatively low response rate among the invited participants, which may have introduced selection bias. Nevertheless, non-response analyses of our baseline study indicated that the frequency of respiratory symptoms was similar between participants and non-participants.[23] Analyses of the baseline population showed that non-response was associated with younger age, living in rural areas, male sex and past smoking status, and responders more frequently used asthma medications and had more chronic cough.[23] While more robust participation by somewhat older individuals and women and reduced participation by current smokers may have altered prevalence estimates, they were unlikely to have biased the estimates of associations examined in this study. However, such a bias cannot be ruled out entirely. To decrease the likelihood of confounding factors, all analyses were adjusted for age, smoking status, sex and educational level.

In the present study, asthma was defined by a self-reported physician-diagnosis of asthma. Using our current study design, we could not verify the diagnosis of asthma. However, validation studies of self-reported physician-diagnosed asthma have found good sensitivity (68%) and high specificity (94%).[43] Our study design included cases of childhood asthma, without any recent symptoms. This may lower the frequency of positive responses among the cases. To assess this possibility, we performed a sensitivity analysis restricted to participants with active asthma, defined as having any respiratory symptoms in the last 12 months. The analysis showed comparable results, with somewhat higher estimates for all three BMI groups with asthma (data not shown).

BMI is widely used but may not necessarily be the best measure of obesity and its effects.[39] According to WHO, BMI can be classified into six categories.[44] Even though our study was of reasonable size (N=1317), the use of categories defined by the WHO led to small sample sizes in the extreme BMI categories. This resulted in uncertainty in the analyses owing to statistical power issues. Larger studies or study designs other than population-based studies may be needed to better assess the effect of asthma with obesity grade II (35–39.9 kg/m^2) and III (>40 kg/m^2). Some effects of obesity may occur at higher BMI than most of our cases; thus, we may lack the statistical power to replicate the results reported by some other studies.

As this was a cross-sectional study, we could not assess causality. The participants may have had a debut of asthma in childhood with normal weight but were now obese and still had asthma. However, as we have shown, it is possible to examine the interaction between obesity and asthma. As recommended by Knol and VanderWeele, we assessed interaction on additive and multiplicative scales for dichotomous outcomes.[45] There are several measures of interaction on an additive scale, for example, relative excess risk due to interaction (RERI), attributable proportion due to interaction (AP) and the SI. In the present study, SI was used because it is regarded to be more stable across strata of potential confounders than RERI and AP.[46]

A strength of this study is that it is based on a relatively large sample from the general population aged between 16 and 52 years and residing in Telemark county. We also included a control group from the same population, reducing the possibility of systematic differences. A few well-trained healthcare workers performed all medical examinations.

In conclusion, asthma and obesity were independently associated with an increased respiratory symptom score, reduced prebronchodilator and postbronchodilator FEV_1 and reduced prebronchodilator FVC. The association between symptom score and asthma was considerably stronger than that with obesity. Reduced WAS and higher odds of sick leave in the last 12 months were associated with asthma but not increased BMI in the adjusted models. Other than the additive interaction of asthma and overweight status on prebronchodilator FVC, we found no other significant additive or multiplicative interactions between asthma and BMI. Due to the small number of participants with BMI ≥35 kg/m^2 in our study, we recommend further studies on this subpopulation.

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Acknowledgements We wish to thank Gølin Finckenhagen Gundersen, Martin Veel Svendsen and Regine Abrahamsen for participating in data collection and preparation.

Contributors GK drafted the paper and was involved in the study design, data collection, data management, data analyses and data interpretation. JKH and ØLH were involved in data interpretation and critical revision of the manuscript. PKH, JK and AKMF were involved in the study design, data analyses, data interpretation and critical revision of the manuscript. All authors approved the final manuscript.

Funding This work was supported by funding from the Telemark Hospital, Norway.

Disclaimer The findings and conclusions in this paper are those of the authors and do not necessarily represent the views of the National Institute for Occupational Safety and Health of the USA.

Competing interests None declared.

Patient consent for publication Not required.

Ethics approval This study was approved by the Regional Committee for Medical and Health Research Ethics in Norway (REC 2012/1665). All study participants provided written informed consent.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available upon reasonable request. The datasets generated and/or analysed during the current study are not publicly available because of privacy policy regulations, but they are available from the corresponding author upon reasonable request.

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