

# Influence of Obesity on Work Ability, Respiratory Symptoms, and Lung Function in Adults with Asthma

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## Keywords

Asthma · Obesity · Lung function · Respiratory symptoms · Work ability

## Abstract

**Background:** Asthma is defined by variable respiratory symptoms and lung function, and may influence work ability. Similarly, obesity may contribute to respiratory symptoms, affect lung function, and reduce work ability. Thus, assessment of the influence of obesity on work ability, respiratory symptoms, and lung function in adults with asthma is needed. **Objectives:** We hypothesized that patients with obesity and asthma have more respiratory symptoms and reduced work ability and lung function compared with normal-weight patients with asthma. **Methods:** We examined 626 participants with physician-diagnosed asthma, aged 18–52 years, recruited from a cross-sectional general population study using a comprehensive questionnaire including

work ability score, the asthma control test (ACT), height and weight, and spirometry with reversibility testing. **Results:** Participants with a body mass index (BMI)  $\geq 30$  kg/m<sup>2</sup> (i.e., obese) had a higher symptom score (OR 1.78, 95% CI 1.14–2.80), current use of asthma medication (1.60, 1.05–2.46), and incidence of ACT scores  $\leq 19$  (poor asthma control) (1.81, 1.03–3.18) than participants with BMI  $\leq 24.9$  kg/m<sup>2</sup> (i.e., normal weight). Post-bronchodilator forced vital capacity (FVC) as a percentage of predicted ( $\beta$  coefficient –4.5) and pre-bronchodilator forced expiratory volume in 1 s as a percentage of predicted (FEV<sub>1</sub>) ( $\beta$  coefficient –4.6) were negatively associated with BMI  $\geq 30$  kg/m<sup>2</sup>. We found no statistically significant association of BMI  $> 30$  kg/m<sup>2</sup> (compared to BMI  $< 24.9$  kg/m<sup>2</sup>) with sick leave (1.21, 0.75–1.70) or reduced work ability (1.23, 0.74–2.04). **Conclusions:** There were indi-

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cations that patients with obesity had a higher symptom burden, poorer asthma control, higher consumption of asthma medication, and reduced lung function, in particular for FVC, compared with normal-weight patients.

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## Introduction

Both asthma and obesity are common globally, and the prevalence of both diseases, particularly obesity, is rising. It is estimated that 339 million people and 650 million adults have asthma and obesity, respectively [1, 2]. Previous studies have recognized the combination of asthma and obesity as a distinct phenotype [3–5]. Subjects with this phenotype are difficult to treat and are likely to be female, have asthma onset in midlife, report more respiratory symptoms, and have reduced lung function measured by spirometry [3, 4].

Obesity can affect lung function and cause respiratory symptoms through several mechanisms, one of which is increased intra-abdominal pressure [6]. Increased weight also represents an increased workload contributing to respiratory symptoms such as dyspnea on exertion [6]. The combination of obesity and asthma results in more respiratory symptoms and reduced lung function compared with either condition alone.

Several studies have reported an association between asthma severity and body mass index (BMI). One such study by Taylor et al. [7] found that, compared with normal-weight patients with asthma, patients with asthma and obesity were more likely to use asthma medication, to have more respiratory symptoms, and to have more severe asthma as measured by the Global Initiative for Asthma (GINA) severity score. Similar results were obtained by Bildstrup et al. [8], who found that asthma severity measured by GINA score increased significantly with higher BMI. However, the current recommendation for assessing asthma is to assess its control rather than its severity because this is regarded by many to be a better basis for treatment decisions [9–11]. Using the asthma control test (ACT), Schatz et al. [12] found that a higher BMI was an independent predictor of poor asthma control. However, there are few studies of asthma control assessed using ACT in patients with asthma and obesity, so additional studies are needed.

Sick leave and self-evaluated work ability can be used to describe the functional level of patients with asthma and obesity. For patients with asthma, this functional level may depend on asthma control and severity, but also

on the burden of symptoms and lung function. Subjects with obesity without any other diseases may also have reduced work ability and increased sick leave because of difficulties caused by their weight. A previous cross-sectional study in Denmark by Andersen et al. [13] demonstrated that a reduced work ability score (WAS), assessed by one of the questions in the work ability index (WAI), was associated with greater BMI regardless of the presence of asthma. In a Swedish longitudinal study (20-year follow-up), reported in 2017, asthma was shown to affect work ability [14]. To our knowledge, WAI assessed by WAS has not been studied in patients with asthma and obesity.

We hypothesized that patients with asthma and obesity have more respiratory symptoms and reduced work ability, asthma control, and lung function compared with normal-weight patients with asthma. Therefore, we aimed to assess the occurrence of self-reported respiratory symptoms, work ability, and lung function in patients with asthma stratified by BMI.

## Materials and Methods

### *Study Population*

The study population was a sample of 626 participants with physician-diagnosed asthma from the cross-sectional baseline of the Telemark study, a population-based study that started in 2013, which has been described in detail elsewhere [15]. In brief, the Telemark study commenced 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%) [16]. Among the 16,099 respondents, 1,857 (11.5%), reported having physician-diagnosed asthma. For the present study, all 1,857 subjects were invited to attend a medical examination in 2014–2015; 651 of these (response rate 35%) completed further medical examinations, of whom 24 (4%) were not confirmed to have physician-diagnosed asthma, and one of whom was excluded because of missing BMI data, leaving a total 626 patients. The subjects were first sent an open invitation by mail with contact information and invited to make an appointment for a medical examination. In total, 265 patients (42%) made an appointment and attended the examination. All those who did not make contact were given a specific time and date for the examination in a new letter resulting in 361 (58%) included participants. Among the 1,206 non-responders, 174 (14%) declined to attend, 210 (17%) had moved since address information was collected in 2013 and could not be reached, and 3 were excluded because of language problems. The remaining 819 (68%) simply did not attend their offered appointments.

### *Questionnaire*

Before the medical examination, all participants completed a questionnaire that inquired about their occupational history and exposures, respiratory symptoms, allergies, comorbidities, and

possible confounders. The questionnaire was based on the European Community Respiratory Health Survey questionnaire and a survey instrument from a similar study from western Sweden [17]. All missing data regarding symptoms were recoded as the absence of that symptom. Age and sex were checked for accuracy against the Norwegian inhabitant registry. All subjects who had asthma symptoms during the past 12 months completed the ACT questionnaire, and a score was calculated [18]. The ACT is a validated test for asthma control that consists of five questions [18]. All 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 [18].

A score based on respiratory symptoms in the last 12 months was calculated for each individual by adding all positive answers to the questions Q1–Q10 listed in Table 2; the maximum score was 10. The cutoff was set at  $\geq 6$ , which represented the upper tertile of the distribution of the symptom score.

### Health-Related Outcomes

#### Anthropometric Measures

Height and weight were measured by trained study personnel using the same instruments and tools for all participants. As defined by the World Health Organization (WHO), BMI was measured in kilograms per meter squared ( $\text{kg}/\text{m}^2$ ). In the analyses, BMI was stratified into the following categories recommended by the WHO: normal weight  $\leq 24.9 \text{ kg}/\text{m}^2$ , overweight  $25.0\text{--}29.9 \text{ kg}/\text{m}^2$ , and obese  $\geq 30 \text{ kg}/\text{m}^2$  [2]. Because some studies have used four BMI categories, also recommended by the WHO, we performed additional analyses stratified into the following categories: normal weight ( $\leq 24.9 \text{ kg}/\text{m}^2$ ), overweight ( $25.0\text{--}29.9 \text{ kg}/\text{m}^2$ ), obese ( $30.0\text{--}34.9 \text{ kg}/\text{m}^2$ ), and severely obese ( $\geq 35 \text{ kg}/\text{m}^2$ ).

#### Nitric Oxide in Exhaled Air

FeNO was measured according to the American Thoracic Society/European Respiratory Society (ATS/ERS) criteria [19] using the NIOX VERO (Aerocrine AB, Solna, Sweden). FeNO measurements were performed before the lung function testing. FeNO was obtained from 558 (89%) subjects who managed one acceptable test in three attempts.

#### Measurement of Total IgE

Blood samples were obtained and total IgE analyzed by chemiluminescent immunoassay (Immulate 2000 XPI; Siemens, Munich, Germany) in 621 (99%) subjects.

#### Lung Function Tests

Spirometry was performed in accordance with the ATS/ERS guidelines [20] using a Jaeger Master Screen PFT (Erich Jaeger GmbH and Co. KG, Würzburg, Germany). All tests were performed under the guidance of one of three trained physicians. Forced vital capacity (FVC) as percent of predicted, forced expiratory volume in 1 s ( $\text{FEV}_1$ ) as percent of predicted, and the  $\text{FEV}_1/\text{FVC}$  ratio were recorded. All tests were manually validated by two trained physicians (G.K. and J.K.) using flow-volume and time-volume curves according to ATS/ERS guidelines [20]. If a participant had no valid curves, their results were not included. All reference values were calculated using the equations from the Global Lung Function Initiative guidelines [21].

**Reversibility Testing.** All participants with at least one acceptable spirometry test ( $n = 597$ , 95% of 626) were asked to inhale 0.4

mg salbutamol, and spirometry was repeated after 10–15 min. An improvement in  $\text{FEV}_1$  of  $\geq 12\%$  and  $>200 \text{ mL}$  was defined as a positive result [22]. All tests were manually validated according to ATS/ERS guidelines, and tests without an acceptable curve were discarded. In total, 534 (85%) of the participants had an acceptable test. Reasons for not performing reversibility testing were refusal by the participant ( $n = 34$ , 5%), not having at least one acceptable spirometry curve ( $n = 13$ , 2%), contraindications (e.g., severe cardiovascular disease or pregnancy;  $n = 7$ , 1%), and other reasons ( $n = 10$ , 1%).

#### Work Ability

Work ability was defined by the self-reported first question of the WAI questionnaire. This question is referred to as the WAS [23]. Briefly, the participants are asked to grade their work ability on a scale from 0 (I cannot work at all) to 10 (my employability is at its best right now). The WAS can be categorized into normal (score  $\geq 8$ ) and reduced (score  $< 8$ ) work ability [24]. Previous studies have demonstrated a strong association between WAS and the results of the complete WAI questionnaire [24, 25].

#### Sick Leave

Sick leave was defined as an affirmative answer to the question: “Have you been on sick leave over the course of the past 12 months?” Analyses of sick leave were restricted to participants engaged in paid work within the previous 12 months.

#### Statistical Analyses

To analyze BMI results, we used Pearson’s  $\chi^2$  test for categorical data and one-way analysis of variance (ANOVA) for continuous data, except for total IgE and FeNO where the Kruskal-Wallis test was used because of non-normal data distribution.

All dichotomous outcomes were analyzed and adjusted for age, sex, smoking, and education using multiple logistic regression. Continuous outcomes were analyzed by linear regression and adjusted for the same confounders as the categorical outcomes. The symptom score was analyzed by ANOVA and the dichotomized symptom score by logistic regression adjusted for age, sex, smoking, and education.

All analyses were performed using the statistical package SPSS version 23.0 (IBM SPSS Inc., Armonk, NY, USA).

## Results

The characteristics of the 626 participants with asthma stratified by BMI category are shown in Table 1. The majority of the participants were women ( $n = 392$ , 63%). Smoking status and level of education were similar across the categories. About half (52%) of all subjects had never smoked, and 44% had completed a university education. Participants in the two highest BMI categories were older at examination and had a later onset of asthma symptoms than those in the lowest BMI category (Table 1). Values of FVC and  $\text{FEV}_1$  before and after reversibility testing were both significantly lower among the participants in

**Table 1.** Characteristics of subjects with asthma from a general population: all subjects and stratified by BMI category

Characteristics	All subjects ( <i>n</i> = 626)	Body mass index categories			<i>p</i> value
		normal weight ≤24.9 kg/m <sup>2</sup> ( <i>n</i> = 228)	overweight 25–29.9 kg/m <sup>2</sup> ( <i>n</i> = 230)	obese ≥30 kg/m <sup>2</sup> ( <i>n</i> = 168)	
Categorical variables, <i>n</i> (%)					
Women	392 (63)	157 (69)	125 (54)	110 (65)	0.004 <sup>a</sup>
Men	234 (37)	71 (31)	105 (46)	58 (35)	
Smoking status					0.380 <sup>a</sup>
Never smoker	328 (52)	134 (59)	111 (48)	83 (49)	0.334 <sup>a</sup>
Former smoker	165 (26)	53 (23)	65 (28)	47 (28)	
Occasional smoker	51 (8)	17 (8)	21 (9)	13 (8)	
Daily smoker	82 (13)	24 (11)	33 (14)	25 (15)	
Highest level of education completed					
Elementary	88 (14)	37 (16)	27 (12)	24 (14)	0.334 <sup>a</sup>
Upper secondary	244 (39)	81 (36)	87 (38)	76 (45)	
University	275 (44)	102 (45)	108 (47)	65 (39)	
Other/missing	19 (3)	8 (4)	8 (4)	3 (2)	
Continuous variables, mean (SD for total cases, SEM for BMI categories)					
Age at examination, years	40.0 (9.32)	36.1 (0.68)	42.3 (0.53)	42.1 (0.59)	<0.001 <sup>b</sup>
Age at onset of asthma symptoms, years	15.1 (11.95)	13.0 (0.75)	16.2 (0.88)	16.6 (0.89)	0.005 <sup>b</sup>
Before bronchodilation					
FVC% predicted	97.8 (12.85)	100.4 (0.82)	98.1 (0.82)	93.6 (1.10)	<0.001 <sup>b</sup>
FEV <sub>1</sub> % predicted	91.7 (15.07)	92.9 (0.93)	93.1 (1.01)	87.8 (1.30)	0.001 <sup>b</sup>
FEV <sub>1</sub> /FVC ratio, %	76.2 (7.80)	76.3 (0.54)	76.4 (0.50)	75.6 (0.65)	0.706 <sup>b</sup>
After bronchodilation					
FVC% predicted	98.6 (12.31)	100.4 (0.86)	98.7 (0.82)	95.9 (1.14)	0.004 <sup>b</sup>
FEV <sub>1</sub> % predicted	95.5 (13.88)	96.6 (0.93)	96.0 (0.96)	93.2 (1.30)	0.066 <sup>b</sup>
FEV <sub>1</sub> /FVC ratio, %	78.6 (8.12)	78.9 (0.67)	78.5 (0.49)	78.5 (0.66)	0.839 <sup>b</sup>
Symptom score (0–10)	3.85 (3.14)	3.68 (0.20)	3.60 (0.21)	4.45 (0.25)	0.015 <sup>b</sup>
Continuous variables, median (interquartile range)					
FeNO, ppb	13 (12)	13 (12)	13 (11)	12 (13)	0.729 <sup>c</sup>
Total IgE, kU/L	48.5 (114)	50 (117)	52 (117)	43 (103)	0.683 <sup>c</sup>

<sup>a</sup>  $\chi^2$  test, comparing the three BMI categories, <sup>b</sup> One-way ANOVA, comparing the three BMI categories, <sup>c</sup> Kruskal-Wallis, comparing the three BMI categories.

the highest BMI category than those in the lowest BMI category. However, there were no significant differences in the FEV<sub>1</sub>/FVC ratio. The mean symptom score was 3.85 (SD 3.14) for all subjects and was significantly higher (4.45, SEM 0.25) among obese participants (*p* = 0.004). Median values of FeNO and total IgE were similar across the BMI categories.

Odds ratios (ORs) for the association of respiratory symptoms, control of asthma, and work ability with BMI categories are presented in Table 2. After adjustment for age, sex, education, and smoking, no specific respiratory symptom was associated with increased BMI. However, the risk of a symptom score ≥6 was significantly higher in the highest BMI category compared with the lowest (OR

1.78, 95% CI 1.14–2.80). The highest BMI group also had an increased OR for current use of asthma medication (OR 1.60, 95% CI 1.05–2.46) and a reduced ACT score (OR 1.81, 95% CI 1.03–3.18).

The outcome variables of symptom score, FEV<sub>1</sub>% predicted, FVC% predicted, and the FEV<sub>1</sub>/FVC ratio were analyzed as continuous variables and adjusted for age, education, smoking status, and sex, as shown in Table 3. The symptom score was significantly higher for participants with a BMI ≥30 kg/m<sup>2</sup> ( $\beta$  coefficient = 0.68, 95% CI 0.048–1.31). Both pre- and post-bronchodilator FVC were significantly negatively associated with BMI ≥30 kg/m<sup>2</sup>, with  $\beta$  coefficients of –6.5 and –4.5%, respectively. The comparable decrements for FEV<sub>1</sub> were not as large,



**Table 2.** Adjusted multiple logistic regression analyses of the association (OR<sup>a</sup> and 95% CI of respiratory symptoms, control of asthma, and work ability with BMI level)

Dependent variable	Normal weight ≤24.9 kg/m <sup>2</sup>	Overweight 25–29.9 kg/m <sup>2</sup>	Obese ≥30 kg/m <sup>2</sup>
Q1: Have you had wheezing or whistling in the chest at some point over the course of the last 12 months?	1	0.83 (0.56–1.22)	1.34 (0.87–2.05)
Q2: Have you ever felt breathless due to wheezing or whistling in your chest?	1	0.94 (0.64–1.39)	1.43 (0.94–2.17)
Q3: Have you had whistling or wheezing in your chest without having a cold?	1	0.72 (0.49–1.07)	1.39 (0.91–2.11)
Q4: Have you experienced shortness of breath when at rest at any time in the last 12 months?	1	1.23 (0.78–1.93)	1.34 (0.84–2.15)
Q5: Have you experienced shortness of breath after being exposed to cold at any time in the last 12 months?	1	1.01 (0.67–1.52)	1.52 (0.99–2.33)
Q6: Have you experienced shortness of breath after exerting yourself at any time in the last 12 months?	1	0.94 (0.63–1.40)	1.54 (0.99–2.38)
Q7: Have you woken up due to coughing attacks during the last 12 months?	1	1.37 (0.90–2.10)	1.46 (0.93–2.28)
Q8: Have you woken up with a feeling of tightness in your chest at any time in the last 12 months?	1	1.06 (0.70–1.59)	1.16 (0.75–1.79)
Q9: Have you been woken up by shortness of breath at any time in the last 12 months?	1	0.92 (0.55–1.52)	0.96 (0.56–1.63)
Q10: Have you experienced an asthma attack in the last 12 months?	1	1.14 (0.71–1.82)	1.49 (0.92–2.41)
Q11: Do you currently use any medication (spray, inhalation powder, or tablets) for asthma?	1	1.16 (0.79–1.72)	<b>1.60 (1.05–2.46)</b>
Symptom score ≥6	1	1.22 (0.79–1.88)	<b>1.78 (1.14–2.80)</b>
Reduced asthma control test score ≤19	1	1.38 (0.79–2.40)	<b>1.81 (1.03–3.18)</b>
Have you been on sick leave over the course of the last 12 months?	1	1.08 (0.69–1.69)	1.21 (0.75–1.70)
Work ability score ≤8	1	1.57 (0.97–2.55)	1.23 (0.74–2.04)

Normal weight is the reference category.

<sup>a</sup> Each line represents a separate model adjusted for age, sex, education, and smoking. Statistically significant findings are in bold.

and only the pre-bronchodilator value differed significantly between groups. The  $\beta$  coefficients for the FEV<sub>1</sub>/FVC ratios were positive for both the middle and highest BMI categories in both the pre- and post-bronchodilator tests, consistent with the observation that the decrements were greater for FVC than for FEV<sub>1</sub>.

Similar results were obtained when we stratified BMI into four categories (data not shown).

## Discussion/Conclusion

The results of this study showed that participants with BMI ≥30 kg/m<sup>2</sup> had a significantly increased risk of a symptom score ≥6 compared with those with BMI ≤24.9 kg/m<sup>2</sup> (OR 1.78, 95% CI 1.14–2.80). The average symptom

score was also significantly higher for participants in the highest BMI category ( $p = 0.015$ ). When symptom scores were analyzed using a linear regression model, we found similar results. To our knowledge, no previous studies have used a similar symptom score in subjects with asthma and obesity. The participants with BMI ≥30 kg/m<sup>2</sup> also had higher ORs for current use of asthma medication (OR 1.60, 95% CI 1.05–2.46) and reduced asthma control (OR 1.81, 95% CI 1.03–3.18) compared with subjects with BMI ≤24.9 kg/m<sup>2</sup>.

In the regression models adjusted for covariates, no specific respiratory symptom had a significant association with increased BMI, although several did have ORs that were of borderline significance ( $0.05 < p < 0.10$ ): Q2 ( $p = 0.10$ ), Q5 ( $p = 0.06$ ), Q6 ( $p = 0.05$ ), and Q7 ( $p = 0.10$ ). Other studies have shown that some respiratory symp-

**Table 3.** Results of adjusted multiple linear regression analyses of the association ( $\beta$  coefficient and 95% CI) of lung function and symptom score with BMI level<sup>a</sup>

Outcome variable	Normal weight $\leq 24.9 \text{ kg/m}^2$	Overweight $25\text{--}29.9 \text{ kg/m}^2$	Obese $\geq 30 \text{ kg/m}^2$
Symptom score	0	–0.006 (–0.60 to 0.59)	<b>0.68 (0.048 to 1.31)</b>
Before bronchodilation			
FEV <sub>1</sub> % predicted	0	0.95 (–1.95 to 3.85)	<b>–4.57 (–7.71 to –1.42)</b>
FVC % predicted	0	<b>–1.90 (–4.36 to –0.56)</b>	<b>–6.47 (–9.14 to –3.80)</b>
FEV <sub>1</sub> /FVC, %	0	<b>2.1 (0.6 to 3.5)</b>	1.0 (–0.6 to 3.5)
After bronchodilation			
FEV <sub>1</sub> % predicted	0	0.55 (–2.26 to 3.35)	–2.77 (–5.81 to 0.27)
FVC% predicted	0	–1.58 (–4.10 to 0.93)	<b>–4.54 (–7.27 to –1.81)</b>
FEV <sub>1</sub> /FVC, %	0	<b>2.08 (0.52 to 3.65)</b>	<b>1.71 (0.12 to 3.40)</b>

Normal weight is the reference category.

<sup>a</sup> Each line represents a separate model adjusted for age, sex, education, and smoking. Statistically significant  $\beta$  coefficients are in bold.

toms are more prevalent among patients with asthma and obesity, but the literature is contradictory. Kwon et al. [26] examined 852 patients with asthma and found that wheezing within the previous 3 months had an OR of 3.2 ( $p = 0.002$ ) in overweight subjects compared with normal-weight subjects, but that the incidence of cough and dyspnea in the previous 3 months was not related to BMI. Other studies have also found an association between obese asthma and wheezing [27, 28]. Bildstrup et al. [8] demonstrated more 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. A possible interpretation of our results is that patients with asthma and obesity report the same respiratory symptoms as normal-weight asthma patients. A possible explanation for the conflicting results is a lack of statistical power and the small number of participants with sufficiently high BMI in our study because the effects may be related to extreme obesity. However, when we stratified BMI into four categories, we found comparable results, although the small number of subjects in the upper two categories (i.e., obese and severely obese) resulted in low statistical power (data not shown).

Control of asthma can be assessed by different questionnaires. One of the most frequently used is the ACT, but several similar tests are available. An advantage of the ACT is that it can be completed by patients and does not require any spirometry results or other medical tests. In the present study, participants with BMI  $\geq 30 \text{ kg/m}^2$  had a lower ACT score (OR 1.81, 95% CI 1.03–3.18), indicating that they had poorer asthma control than subjects

with BMI  $\leq 24.9 \text{ kg/m}^2$ . Although Schatz et al. [12] reported that a higher BMI was an independent predictor of poor asthma control, the proportion of individuals in their study with an ACT score  $< 20$  was higher than that in our study. A possible explanation may be that Schatz et al. [12] included subjects  $> 65$  years of age, all of whom currently used asthma medication and had at least one asthma-related medical encounter within the previous 2 years. Pisi et al. [29] studied a tertiary-care asthma outpatient population and reported an OR 1.6 (95% CI 1.04–2.55) for reduced ACT score among overweight patients ( $25 < \text{BMI} \leq 30 \text{ kg/m}^2$ ) compared with normal-weight patients ( $18.5 \leq \text{BMI} \leq 25 \text{ kg/m}^2$ ). They did not analyze patients with higher BMIs. Because our study was population based, we expected our estimates to be lower than for a selective patient study, but the trend to reduced asthma control with increasing BMI seems to be consistent.

We wanted to use sick leave and self-evaluated work ability as a way to describe the functional level of patients with asthma and obesity. The reasons for a high frequency of sick leave and low work ability because of illness are complex and dependent on many different factors. For asthma, work ability may depend on asthma control and severity, but also on the burden of symptoms and lung function. After adjustment for age, sex, education, and smoking, we found no increased sick leave or reduced WAS among subjects with asthma and overweight or obesity. When the analyses were performed using four BMI groups, we found an OR of 2.0 (95% CI 0.99–4.0) for reduced WAS and of 1.2 (95% CI 0.56–2.54) for sick leave when BMI was  $\geq 35 \text{ kg/m}^2$ . However, when we used four

BMI categories, the small number of subjects in the top two strata resulted in low statistical power.

Previous studies have shown an effect of BMI on sick leave regardless of concurrent asthma. In a review by Neovius et al. [30], obesity was associated with a higher frequency and longer duration of sick leave. The associations with overweight were less clear. Another review that included only longitudinal studies came to similar conclusions [31]. Similarly, several studies have reported more sick leave among patients with asthma, regardless of their weight, than healthy controls [32, 33]. To our knowledge, only one study has reported a higher level of sick leave among patients with asthma and obesity [34]. This Swedish study found that obesity was more common in subjects who were on sick leave because of respiratory problems than in the general population. However, the study included only a relatively small sample ( $n = 237$ ) of patients on sick leave for  $>2$  weeks who were recruited from a compulsory insurance registry.

To our knowledge, the work ability measured as WAS in patients with asthma and obesity has not been studied previously. Work ability among subjects with increased BMI was assessed in a previous cross-sectional study by Andersen et al. [13], which demonstrated a reduced work ability with increasing BMI, with an OR of 1.69 (95% CI 1.10–2.62) for lower work ability among working subjects with grade III obesity ( $\text{BMI} \geq 40 \text{ kg/m}^2$ ). In a longitudinal study (20-year follow-up) that did not consider obesity, asthma was shown to affect the WAI of participants, and the effect was increased by the severity of asthma [14]. These studies indicate separate effects of asthma and obesity on work ability and sick leave. In many of the previous studies of work ability in subjects with obesity, the average BMI of participants has been considerably higher than the highest category in our study. Moreover, our study was a general population-based study of relatively young subjects, which may have affected our results. If these effects of obesity occur at higher BMI than that of most of our subjects, we lacked the statistical power to replicate such results.

We found a significant negative effect of BMI on FVC and  $\text{FEV}_1$ . After reversibility testing with 0.4 mg salbutamol, the effect of obesity on  $\text{FEV}_1$  in participants with asthma was no longer significant, and the  $\text{FEV}_1/\text{FVC}$  ratio in the obese participants improved ( $\beta = 1.7$ , 95% CI 0.12–3.4), because the increase in  $\text{FEV}_1$  exceeded the increase in FVC, consistent with the observation that the decrement in  $\text{FEV}_1$  was less than the decrement in FVC. Studies of lung function in patients with asthma have shown that they have reduced  $\text{FEV}_1$  and  $\text{FEV}_1/\text{FVC}$  ratio,

indicating airway obstruction [35]. The effect of obesity on lung function is also well documented [36–39]. Both  $\text{FEV}_1$  and FVC can be affected [36], but because the  $\text{FEV}_1/\text{FVC}$  ratio is often preserved, spirometry demonstrates a restrictive pattern in obese patients [38]. Several studies have shown an effect on spirometry in patients with asthma and overweight/obesity [29, 40, 41], but there are also studies that show no such effect [8]. In another study, obese adults without asthma had a lower  $\text{FEV}_1$ , residual volume, and total lung capacity than normal-weight subjects with asthma, suggesting that obesity may have stronger effects on  $\text{FEV}_1$  and FVC in subjects without asthma than in those with asthma. Consistent with this, individuals with obesity have been reported to have lower  $\text{FEV}_1$  and FVC than overweight individuals [39].

### *Strengths and Limitations*

An important limitation of our study is that most outcomes were self-reported. However, we have used validated questionnaires that have also been used in other large epidemiological studies of respiratory health [17]. Although validated questionnaires can reduce information bias, such bias may still be important and reduce or inflate the associations of symptoms with exposure. Although most epidemiological studies are susceptible to bias because of selection and non-response, analyses of non-responders in our baseline study indicated that the frequencies of respiratory symptoms were similar in participants and non-participants [16]. To reduce selection bias, all eligible participants were invited for further medical examinations. We had a relatively low response rate among those invited, which may introduce selection bias and could be considered as a limitation of the present study. We have self-reported data from the cross-sectional baseline survey on BMI, sex, education, smoking habits, sick leave, and WAS in both responders and non-responders. A forward conditional logistic regression to test whether attendance to the medical examination was associated with BMI, sex, education, smoking habits, sick leave, and WAS revealed statistically significant results only for somewhat older age (30–39 years: OR 2.2 (1.6–3.1); 40–50 years: OR (3.5 [2.7–4.7])), and current smoking (OR 0.67 [0.50–0.89]). While more robust participation by somewhat older individuals and reduced participation by current smokers may alter prevalence estimates, it is unlikely to bias the associations examined in this study. Such bias cannot, however, be ruled out entirely. To further decrease the likelihood of biased results, all analyses in this paper are adjusted for age, smoking, sex, and education.

Approximately 30% of the participants had a BMI  $\geq 30$  kg/m<sup>2</sup>, a seemingly high proportion that may be an overestimation relative to the source population. In a survey conducted by the Norwegian National Statistics Agency in 2015, the proportion of obese inhabitants in the south eastern region of Norway (which includes Telemark county) in the age groups 25–44 and 45–64 years was 15 and 18%, respectively [42]. Those data were self-reported, while ours were objectively measured. For all 16,099 participants in the baseline study, 15% reported obesity, while 20% reported obesity among the subjects with asthma. Furthermore, 21% of the individuals with asthma who attended the medical examination reported obesity in the baseline survey while 27% were measured to be obese when attending the medical examination, suggesting an underestimation of obesity in the self-reported data, a pattern that has also been observed by other investigators [43]. Based on these findings, we therefore assume that this proportion of obesity is in accordance with the prevalence of obesity in south eastern Norway.

In our analyses, participants were defined by self-report of physician-diagnosed asthma. With our study design, we were not able to verify the diagnosis of asthma. However, a review by Tor  n et al. [44] demonstrated that self-reported physician-diagnosed asthma has high specificity and gives a valid estimate. Using this approach also allows the inclusion of participants who have had childhood asthma without recent symptoms, which may lower the frequency of positive responses among the participants. To assess this, we performed an additional analysis restricted to participants with active asthma, defined as having any respiratory symptoms during the previous 12 months. The analysis produced results comparable to those of the full analysis.

Another limitation of the study is using only BMI as a measure of obesity. Although BMI is widely used, it may not necessarily be the best measure of obesity. According to the WHO, BMI can be classified into six categories [45]. Even though our study cohort was of reasonable size ( $n = 626$ ), the groups, particularly those in the extreme categories, became too small when we used these six categories as defined by the WHO. Larger studies or study designs other than population-based studies may be needed to assess the effect of obesity classes II (35–39.9 kg/m<sup>2</sup>) and III ( $>40$  kg/m<sup>2</sup>).

Because both asthma and obesity can individually contribute to respiratory symptoms and effects, we cannot determine the degree to which the associations we found were related to obesity and asthma. To our knowledge, few studies of the interaction of asthma and obesity have been conducted.

In conclusion, we found no clear evidence that any specific respiratory symptom was related to obesity in asthma. However, we did find indications of a higher symptom burden, reduced asthma control, and higher consumption of asthma medication in participants with asthma and obesity than in patients with asthma and normal weight. Obesity was found to be associated with reduced spirometry results, in particular for FVC. Although subjects with asthma and obesity had a higher respiratory symptom burden, poorer asthma control, and reduced lung function compared with subjects with asthma and normal weight, the work ability and sick leave seemed to be similar for both groups. Because of the small number of participants in our study with BMI  $\geq 35$  kg/m<sup>2</sup>, we recommend further studies on this subpopulation.

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### Statement of Ethics

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

### Disclosure Statement

The authors have no conflicts of interest to declare.

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### Author Contributions

G.K. drafted the paper and was involved in study design, data collection, data analyses, and data interpretation. M.V.S. was involved in study design, data collection, data management, data analyses, and critical revision of the manuscript. J.K.H. and   .L.H. were involved in data interpretation and critical revision of the manuscript. P.K.H., J.K., and A.K.M.F. were involved in study design, data analyses, data interpretation, and critical revision of the manuscript. All authors approved the final manuscript.



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