



# The impact of COPD on health status: findings from the BOLD study

Christer Janson<sup>1</sup>, Guy Marks<sup>2</sup>, Sonia Buist<sup>3</sup>, Louisa Gnatiuc<sup>4</sup>, Thorarinn Gislason<sup>5</sup>, Mary Ann McBurnie<sup>6</sup>, Rune Nielsen<sup>7</sup>, Michael Studnicka<sup>8</sup>, Brett Toelle<sup>9</sup>, Bryndis Benediktstottir<sup>5</sup> and Peter Burney<sup>4</sup>

**Affiliations:** <sup>1</sup>Dept of Medical Sciences, Respiratory Medicine and Allergology, Uppsala University, Uppsala, Sweden. <sup>2</sup>Dept of Respiratory Medicine, Liverpool Hospital and Woolcock Institute of Medical Research, Sydney, and <sup>3</sup>Respiratory and Environmental Epidemiology Group, Woolcock Institute of Medical Research, Sydney, Australia. <sup>4</sup>Oregon Health and Science University, Portland, OR, and <sup>5</sup>Kaiser Permanente Center for Health Research, Portland, OR, USA. <sup>6</sup>Respiratory Epidemiology and Public Health, Imperial College London, London, UK. <sup>7</sup>Faculty of Medicine, University of Iceland and Respiratory Medicine and Sleep, Landspítali University Hospital, Reykjavik, Iceland. <sup>8</sup>Dept of Thoracic Medicine, Haukeland University Hospital, Bergen, Norway. <sup>9</sup>Dept of Respiratory Medicine, Paracelsus Medical University, Salzburg, Austria.

**Correspondence:** C. Janson, Dept of Medical Sciences, Uppsala University, Box 256, 75105 Uppsala, Sweden. E-mail: christer.janson@medsci.uu.se

**ABSTRACT** The aim of this study was to describe the impact of chronic obstructive pulmonary disease (COPD) on health status in the Burden of Obstructive Lung Disease (BOLD) populations.

We conducted a cross-sectional, general population-based survey in 11 985 subjects from 17 countries. We measured spirometric lung function and assessed health status using the Short Form 12 questionnaire. The physical and mental health component scores were calculated.

Subjects with COPD (post-bronchodilator forced expiratory volume in 1 s/forced vital capacity <0.70, n=2269) had lower physical component scores ( $44 \pm 10$  versus  $48 \pm 10$  units,  $p < 0.0001$ ) and mental health component scores ( $51 \pm 10$  versus  $52 \pm 10$  units,  $p = 0.005$ ) than subjects without COPD. The effect of reported heart disease, hypertension and diabetes on physical health component scores (-3 to -4 units) was considerably less than the effect of COPD Global Initiative for Chronic Obstructive Lung Disease grade 3 (-8 units) or 4 (-11 units). Dyspnoea was the most important determinant of a low physical and mental health component scores. In addition, lower forced expiratory volume in 1 s, chronic cough, chronic phlegm and the presence of comorbidities were all associated with a lower physical health component score.

COPD is associated with poorer health status but the effect is stronger on the physical than the mental aspects of health status. Severe COPD has a greater negative impact on health status than self-reported cardiovascular disease and diabetes.



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COPD is related to worse health status: impairment is greater than in self-reported cardiovascular diseases or diabetes <http://ow.ly/p1clx>

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## Introduction

Chronic obstructive pulmonary disease (COPD) is characterised by airflow limitation that is not fully reversible and accelerated decline of lung function. The disease is an important and growing cause of morbidity and mortality worldwide. COPD is expected to be the third leading cause of morbidity and the sixth leading cause of mortality in 2020 [1]. Patients with COPD experience respiratory symptoms and physical incapacity and often have several comorbid conditions. Consequently, they often have impaired health status or health-related quality of life, which in itself is an independent predictor of hospitalisations [2] and mortality [2, 3]. Low lung function [4], female sex [5], frequent exacerbations [4, 6], comorbidities [4] and a low level of physical activity [7] have been identified as factors that negatively influence health status in COPD, whereas physical exercise training [8, 9] and pharmacological interventions can have a positive effect on health status [10, 11]. However, the nature of the impact and the factors that influence health status are not well understood.

The major purpose of the Burden of Obstructive Lung Disease (BOLD) study is to estimate the social and economic burden of COPD around the world [12]. The study includes standardised measurement of spirometric lung function and a structured interview that incorporates the Short Form 12 (SF-12) questionnaire [13]. Previous BOLD analyses have concentrated on prevalence [12], risk factors [14] and economic aspects [15] of COPD. However, for the individual patient the major impact of the disease is manifest as deterioration in health status. The aims of the analyses in this paper are to describe the impact of COPD on health status in adults aged  $\geq 40$  years and to identify determinants of low health status in people with COPD.

## Population and methods

The design and rationale for the BOLD Initiative and preliminary data on prevalence have been published elsewhere [13]. Sampling plans designed to randomly recruit a representative sample of the population were used for the recruitment of participants at all study sites. The present analysis included data from 18 sites in 17 countries for subjects in whom valid spirometry and health status data were obtained. The sites were: Adana (Turkey), Salzburg (Austria), Cape Town (South Africa), Reykjavik (Iceland), Hannover (Germany), Krakow (Poland), Bergen (Norway), Vancouver (Canada), Lexington (USA), Manila (Philippines), Sydney (Australia), London (United Kingdom), Uppsala (Sweden), Mumbai (India), Lisbon (Portugal), Maastricht (the Netherlands), Nampicuan/Talugtug (Philippines) and Tartu (Estonia).

Each participating site aimed to recruit a population-based sample of at least 600 adults (300 males and 300 females) who were not institutionalised, were aged  $\geq 40$  years, and were living in a well-defined administrative area in which the total population exceeded 150 000. Target recruitment numbers, as well as the sampling plans, were approved in advance by the Operations Center (Portland, OR, USA). Questionnaires were used to obtain information about respiratory symptoms, health status, comorbidities and risk factors for COPD. Pre- and post-bronchodilator spirometry testing was performed. Every site obtained approval from its local ethics committee and written informed consent from each participant.

The study population consisted of 14 450 subjects of whom 13 495 had recorded health status data and, of these, 11 985 subjects performed a technically satisfactory spirometry whereas 1510 did not have a technically satisfactory spirometry recording according to the pre-defined criteria of the BOLD protocol [13].

### *Spirometry and body mass index*

Lung function data were obtained at all BOLD sites using the ndd EasyOne Spirometer (ndd Medical Technologies, Andover, MA, USA). Lung function was measured before and 15 min after administration of 200  $\mu\text{g}$  of salbutamol. All spirograms were reviewed by the BOLD Pulmonary Function Reading Center and assigned a quality score based on acceptability and reproducibility criteria of the American Thoracic Society and European Respiratory Society guidelines [16]. Prediction equations derived from the third US National Health and Nutrition Examination Survey were used to compute predicted forced expiratory volume in 1 s (FEV<sub>1</sub>) [17]. Weight and height were measured at the clinic visit by trained technicians and body mass index (BMI) was calculated (weight (kg)/(length (m))<sup>2</sup>). The participants were categorised into four groups based on BMI: <20, 20–25, >25–30 and >30 kg·m<sup>-2</sup>.

### *Definition and classification of COPD*

COPD was defined according to the Global Initiative for Chronic Obstructive Lung Disease (GOLD) criteria as post-bronchodilator FEV<sub>1</sub>/forced vital capacity (FVC) <0.70 [18]. We also performed sensitivity analyses, defining COPD as post-bronchodilator FEV<sub>1</sub>/FVC predicted below the lower limit of normal (LLN) [17]. Subjects with COPD and FEV<sub>1</sub>  $\geq 80\%$  predicted were classified as GOLD grade 1; those with COPD and FEV<sub>1</sub> <80% but FEV<sub>1</sub>  $\geq 50\%$  predicted were classified as GOLD grade 2; those with COPD and

FEV<sub>1</sub> <50% but FEV<sub>1</sub> ≥30% predicted were classified as GOLD grade 3 and those with COPD and FEV<sub>1</sub> <30% predicted were classified as GOLD grade 4 [18].

#### **Questionnaire data**

Questionnaire data were obtained by face-to-face interviews administered by trained and certified staff in the participant's native language. Standard methods were used for forward and backward translation and reconciliation. All participants completed a core questionnaire, which was based on standardised instruments [13].

#### *Health status*

Health status was assessed by the SF-12 questionnaire (version 2), which is a generic instrument for assessing health status. The instrument was developed from the short form 36 (SF-36) questionnaire developed to catch the mental and physical score of the SF-36 using only 12 questions compared with the 36 questions in the SF-36 instrument. The physical (PCS) and mental health (MCS) component scores were calculated [19], with higher values indicating better health status.

#### *Educational level*

Educational level was calculated in years based on the question: "How many years of schooling have you completed?"

#### *Smoking history*

The participants were categorised as never-, ex- and current smokers. Smoking was defined as >20 packs of cigarettes in a lifetime or >1 cigarette each day for a year.

#### *Comorbidities*

Heart disease was defined as answering "yes" to the question: "Has a doctor or other healthcare provider ever told you that you had heart disease?". Hypertension, diabetes and stroke were defined in a similar manner.

Dyspnoea was graded using a modification of the Medical Research Council dyspnoea scale [20]. Stage 0 was defined as answering "no" to the question: "Are you troubled by shortness of breath when hurrying on the level or walking up a slight hill?" and stage IV as a positive answer to the question: "Are you too short of breath to leave the house or short of breath on dressing or undressing?"

#### *Symptoms*

The following symptoms were included in the analyses: wheeze: "wheezing or whistling in the chest at any time in the last 12 months"; chronic cough: "cough on most days for as much 3 months each year"; and chronic phlegm: "bringing up phlegm from the chest, having phlegm in the chest that is difficult to bring up on most days for as much as 3 months each year".

#### *Medication*

The level of medication for breathing problems was categorised into four groups based on the participants answer to the questions. "In the past 12 months, have you taken any medications for your breathing?" If the participants answered yes, the name and formulation of the medication was asked for. In the present analyses, medication level 0 was no bronchodilators or inhaled corticosteroids (ICSs); level 1 was short-acting  $\beta_2$ -agonists or ipratropium but no long-acting  $\beta_2$ -agonists (LABAs), tiotropium, theophylline or ICSs; level 2 was LABAs, tiotropium or theophylline but no ICSs; and level 3 was ICSs with or without bronchodilators.

#### *COPD exacerbation*

COPD exacerbation was defined as a reported medical visit for an episode of breathing problems that interfered with usual daily activities in a subject with COPD.

#### **Statistical analysis**

All analyses were performed in STATA software, version intercooled STATA 11 (Stata Corporation, College Station, TX, USA). Differences between subjects with and without COPD were tested by the t-test and Chi-squared test. The association between FEV<sub>1</sub> and health status in subjects with COPD was evaluated by linear regression. Multiple linear regression was used in the multiple variable analyses with PCS and MCS, respectively, as dependent variables in the whole population and in the subpopulation with COPD. In these analyses, adjustments were made for age, sex, BMI, smoking history and educational level. Regression models were fitted separately for each site and results for the association between health status and COPD were pooled across sites using random effects meta-analysis in order to detect heterogeneity between the

centres [21]. Heterogeneity was quantified using the  $I^2$  statistic [22]. A p-value of  $<0.05$  was considered statistically significant.

## Results

The characteristics of the 11 985 subjects who had both health status data and a technically satisfactory spirometry, grouped by COPD status, are presented in table 1. Participants with COPD ( $n=2269$ ) were significantly older, more often male, had a lower BMI, lower educational level and had a higher prevalence of heart disease, hypertension and stroke than those without COPD (table 1).

### Sample population

Participants with COPD had lower PCS ( $44 \pm 10$  versus  $48 \pm 10$  units,  $p<0.0001$ ) and MCS ( $51 \pm 10$  versus  $52 \pm 10$  units,  $p=0.005$ ) than participants without COPD. The severity of COPD was inversely correlated with both these scales (figure 1).

In the multivariate analyses, both PCS and MCS were inversely related to COPD severity (table 2). The strength of the relationship between health status and COPD, as well as other diseases, is presented in figure 2 and table 2. The presence of heart disease, hypertension and diabetes was associated with lower PCS and MCS. Stroke was only significantly related to lower PCS. The effect of these non-COPD diseases on PCS was of approximately the same magnitude as the effect of having COPD GOLD grade 2, but considerably less than the effect of GOLD grade 3 and 4 (fig. 2). The estimated effect of having COPD of any severity was of the same level of magnitude as having self-reported heart disease and diabetes.

The combined effect of COPD severity level and the presence of comorbidities on PCS are presented in figure 3. Having COPD GOLD grade 1 was only associated with lower PCS if the subject also had heart disease, hypertension, diabetes or stroke. Subjects with COPD grade 3 and 4 and any of these comorbidities had the lowest PCS.

Female sex, current smoking and having a BMI  $<20$  kg·m<sup>-2</sup> were also associated with lower PCS and MCS (table 2). Ex-smoking status, a lower educational level and having a BMI  $>30$  kg·m<sup>-2</sup> were all associated with a lower PCS. Finally, older age was associated with a lower PCS but a higher MCS.

The random effects meta-analysis estimate of the effect of having COPD grade 2 and higher was a PCS that was mean (95% confidence interval) 4.3 (3.6–4.9) units lower (fig. 4). There was no significant between-centre heterogeneity in the association between PCS and GOLD grade 2+ (fig. 4). Having COPD was associated with a 1.8 (0.8–2.8) units lower MCS (fig. 5). There was significant and large between-centre heterogeneity in the association between MCS and GOLD grade 2+ (fig. 5). This heterogeneity was largely explained by a stronger association between COPD grade 2+ and MCS in Mumbai, India. With Mumbai

TABLE 1 Characteristics of the participants according to severity of airflow limitation grouped by Global Initiative for Chronic Obstructive Lung Disease grade

	No COPD	Grade 1	Grade 2	Grade 3	Grade 4	p-value <sup>#</sup>
<b>Subjects n</b>	9716	1027	945	257	40	
<b>Females</b>	54.0	41.0	44.2	42.4	47.5	$<0.0001$
<b>Age years</b>	$55.2 \pm 10.8$	$64.9 \pm 12.2$	$64.0 \pm 11.2$	$63.4 \pm 11.7$	$60.1 \pm 9.9$	$<0.0001$
<b>Years of education</b>	$11 \pm 5$	$11 \pm 4$	$10 \pm 4$	$9 \pm 4$	$8 \pm 4$	$<0.0001$
<b>Smoking history</b>						$<0.0001$
Never-smoker	49.3	33.8	27.7	19.5	22.5	
Ex-smoker	29.5	39.8	37.4	42.4	50.0	
Current smoker	21.2	26.4	34.9	38.1	27.5	
<b>Body mass index kg·m<sup>-2</sup></b>						$<0.0001$
$<20$	5.9	4.8	14.2	28.0	47.5	
20–25	31.8	35.3	29.6	27.6	37.5	
$>25$ –30	38.0	42.3	32.9	25.2	12.5	
$>30$	24.4	17.6	23.3	19.3	2.5	
<b>Comorbidities</b>						
Heart disease	12.6	19.6	22.9	18.3	5.0	$<0.0001$
Hypertension	30.2	36.4	39.4	31.9	24.4	$<0.0001$
Diabetes	7.4	7.2	9.0	11.7	7.5	0.09
Stroke	2.6	3.6	5.7	3.9	5.0	$<0.0001$

Data are presented as % or mean  $\pm$  sd, unless otherwise stated. COPD: chronic obstructive pulmonary disease. <sup>#</sup>: no COPD versus COPD.

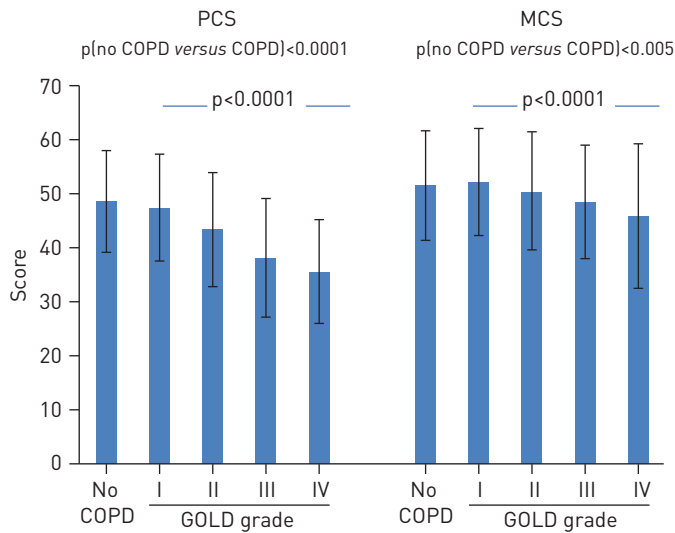


FIGURE 1 Physical component score (PCS) and mental health component score (MCS) in the participants that chronic obstructive pulmonary disease (COPD). Participants with COPD are divided by COPD Global Initiative for Chronic Obstructive Lung Disease (GOLD) grades. Data are presented as mean  $\pm$  SD.

removed from the meta-analysis, the between centre heterogeneity was no longer statistically significant ( $I^2=18.2$ ,  $p_{\text{heterogeneity}}=0.24$ ).

Redefining COPD using FEV<sub>1</sub>/FVC ratio  $<LLN$  rather than the FEV<sub>1</sub>/FVC ratio  $<0.70$  as the criterion for airflow limitation reduced the number of subjects with COPD from 2269 (18.9%) to 1520 (12.7%), but had no effect on the association between COPD grades and health status (table 3).

Participants who did not perform a technically satisfactory spirometry had lower PCS ( $45 \pm 11$  versus  $48 \pm 10$  units,  $p < 0.0001$ ) than those that performed a satisfactory spirometry, while there was no difference in MCS (51 units in both groups).

#### COPD population

Among subjects with COPD grade 1 or higher, lower FEV<sub>1</sub> was independently related to lower PCS but not significantly associated with MCS, after adjusting for the other covariates (table 4). Dyspnoea was the most important determinant of a low PCS and MCS ( $p_{\text{trend}} < 0.0001$ ). PCS and MCS were also negatively related to female sex and wheeze. Higher age was associated with lower PCS and higher MCS. In addition a low PCS was related to chronic cough, chronic phlegm, heart disease, diabetes and stroke and a BMI  $>30 \text{ kg}\cdot\text{m}^{-2}$ , while a low MCS was related to a BMI  $<20 \text{ kg}\cdot\text{m}^{-2}$  and current smoking (adjusted effect estimate (95% CI)  $-1.49$  ( $-2.71$ – $-0.28$ )).

Among subjects with COPD, 18.2% were using bronchodilators or ICSs. Adjusting for level of medication use did not change the previously reported associations. Having had at least one exacerbation of COPD within the last 12 months, which was reported by 7.3% of subjects with COPD, was associated with lower PCS (adjusted estimate (95% CI)  $-2.58$  ( $-4.53$ – $-0.63$ )), whereas no significant association was found between MCS and exacerbations. Including exacerbations in the model did not change the associations reported above.

Among subjects with COPD, the relationship between each of these risk factors and health status was not modified by sex.

#### Discussion

The main finding in this article is that COPD is an important determinant of health status, but that the effect is stronger on the physical than the mental aspects of health status. COPD severity and current smoking were both independently related to poorer health status. Among people with COPD, physical health status was independently related to lower lung function, the level of dyspnoea and cardiovascular comorbidities, while mental health status was mainly related to the level of dyspnoea.

In our analyses, only subjects with COPD GOLD grade 2 and higher had worse health status than those without COPD. Health status did not differ between subjects with COPD grade 1 and subjects without COPD. As in several other studies, the impact of COPD was larger on the physical than the mental aspects of health status [5, 23, 25]. In accordance with previous studies the negative impact on health status increased with increasing COPD severity [25–27]. The actual SF-12 scores in BOLD participants were similar to those from other population-based studies [5], but the scores were considerably higher, indicating better health status, than in a large European study of patients in primary healthcare setting [26].

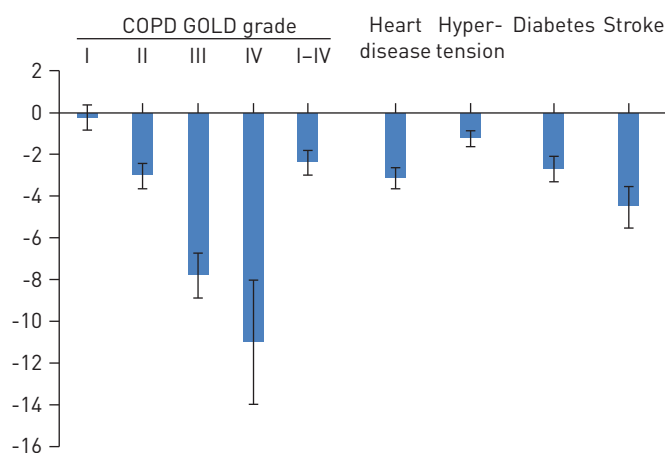
**TABLE 2** Associations between Short Form (SF)-12 physical component score (PCS) and mental health component score (MCS) with chronic obstructive pulmonary disease (COPD) defined as having a post-bronchodilator forced expiratory volume in 1s (FEV<sub>1</sub>)/forced vital capacity (FVC) <0.70

	PCS SF-12	MCS SF-12
<b>No COPD</b>	Reference	Reference
<b>COPD (FEV<sub>1</sub>/FVC &lt;0.70)</b>		
Grade 1	-0.19 [-0.78-0.39]	0.07 [-0.55-0.69]
Grade 2	-3.0 [-3.6- -2.4]	-1.4 [-2.1- -0.77]
Grade 3	-7.8 [-8.9- -6.7]	-3.1 [-4.3- -2.0]
Grade 4	-11 [-14- -8.9]	-5.2 [-8.1- -2.3]
<b>Age per 10 years</b>	-1.2 [-1.6- -0.8]	0.84 [0.67-1.0]
<b>Females compared with males</b>	-2.0 [-2.3- -1.6]	-2.2 [-2.5- -1.8]
<b>Years of education per year</b>	0.23 [0.19-0.28]	0.05 [0.00-0.10]
<b>Smoking history</b>		
Never	Reference	Reference
Ex	-0.39 [-0.77- -0.01]	-0.38 [-0.79-0.03]
Current	-1.8 [-2.2- -1.3]	-1.8 [-2.3- -1.3]
<b>Body mass index kg·m<sup>-2</sup></b>		
<20	-1.0 [-1.7- -0.37]	-1.0 [-1.8- -0.32]
20-25	Reference	Reference
>25-30	-0.54 [-0.92- -0.15]	0.05 [-0.36-0.46]
>30	-2.9 [-3.3- -2.4]	0.05 [-0.43-0.54]
<b>Comorbidities</b>		
Heart disease	-3.1 [-3.6- -2.6]	-0.78 [-1.3- -0.26]
Hypertension	-1.2 [-1.6- -0.85]	-0.80 [-1.2- -0.41]
Diabetes	-2.7 [-3.3- -2.1]	-0.76 [-1.4- -0.10]
Stroke	-4.5 [-5.4- -3.5]	-0.23 [-1.2-0.77]

Data are adjusted for the variables in the table and centre are presented as adjusted estimates [95% confidence interval].

This investigation is unique in the sense that it includes many countries and cultures. Despite this, we found no evidence of geographical differences in the strength of association between physical health status and COPD. As an example, the association between PCS and having COPD stage II or higher was of equal magnitude in high income countries, such as Norway and Canada, to India. The weak association between mental health status and COPD was also geographically consistent with the exception of a very strong negative association between COPD grade 2 and higher and MCS in India.

In the present study we used the SF-12 questionnaire. A large number of instruments have been used when assessing health status or health-related quality of life in COPD. These include both disease-specific instruments, such as St George’s Respiratory Questionnaire [28], and generic instruments, such as SF-36 [29]. Recently, shorter questionnaires have been used in order to facilitate measurement of health status in



**FIGURE 2** Adjusted estimates (95% confidence interval) of associations of chronic obstructive pulmonary disease (COPD) and comorbidities with the Short Form (SF)-12 physical component score. GOLD: Global Initiative for Chronic Obstructive Lung Disease.

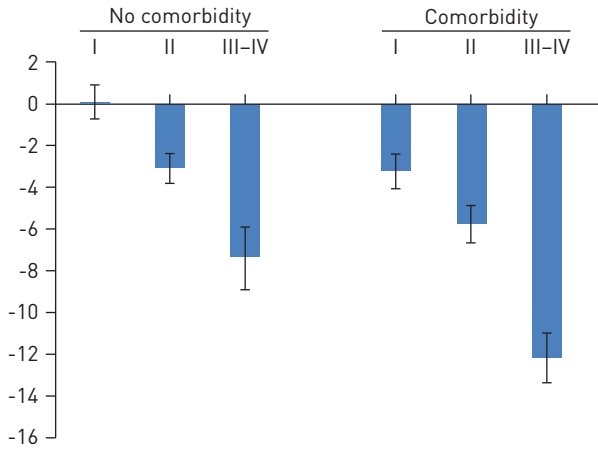


FIGURE 3 Adjusted estimates (95% confidence interval) of associations of chronic obstructive pulmonary disease Global Initiative for Chronic Obstructive Lung Disease grades in subjects without and with comorbidities (heart disease, hypertension, diabetes and stroke) with the Short Form-12 physical component score.

clinical or epidemiological settings. Examples of shorter health status questionnaires are disease-specific instruments, such as Clinical COPD Questionnaire [30, 31] and the COPD Assessment Test (CAT) [4], and generic instruments, such as EuroQol 5 dimension and SF-12 [32].

The advantage of a generic questionnaire is that it enabled us to compare the effect of different diseases on health status. In this study, the negative influence of self-reported heart disease, diabetes and stroke was of similar magnitude to the effect of COPD grade 2, but considerably less than the effect of COPD grades 3 and 4. It is well known that many patients with COPD have extrapulmonary comorbidities that generate significant healthcare costs [33, 34], have a negative effect on rehabilitation outcome [35] and increase the risk of hospitalisations and mortality in COPD patients [36]. Comorbidity may also influence health status in COPD [24]. In the present study, self-reported heart disease had a negative influence on PCS but not MCS. This finding is in accordance with other studies [26, 37]. We also found that diabetes was independently related to lower health status in our participants with COPD. This has been observed in some

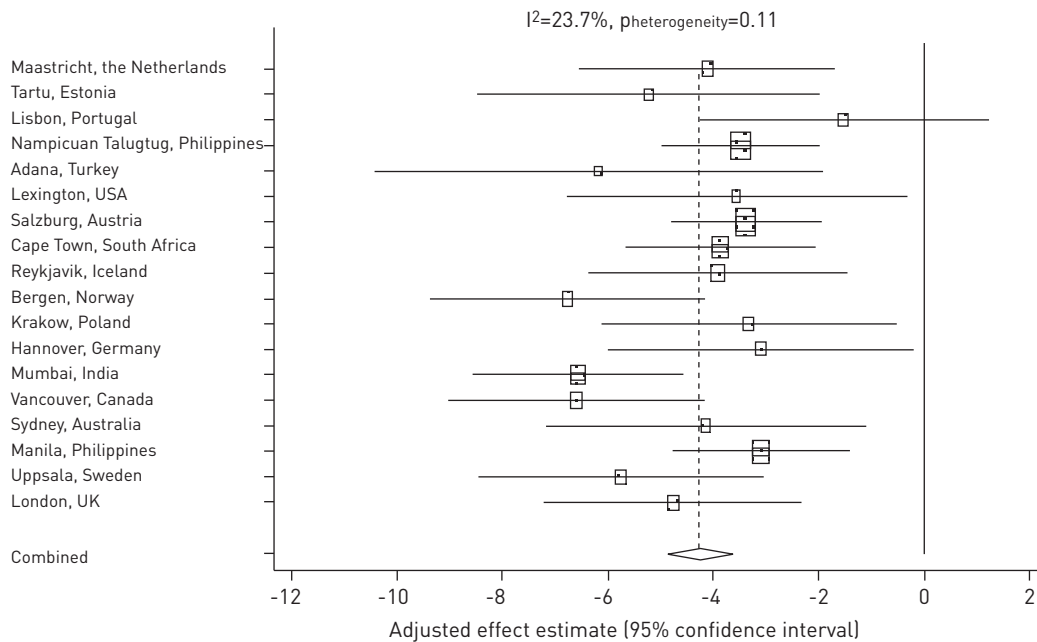


FIGURE 4 Effect estimates and 95% confidence intervals for the association between the Short Form-12 physical component score and chronic obstructive pulmonary disease (COPD) Global Initiative for Chronic Obstructive Lung Disease grade 2 and higher compared with participants without COPD (adjusted within centre for age, sex, educational level, smoking history, comorbidities and body mass index) with a combined effect estimate (diamond indicates 95% confidence interval) from the model with centre as the random effect. The size of each square is proportional to the sample size.



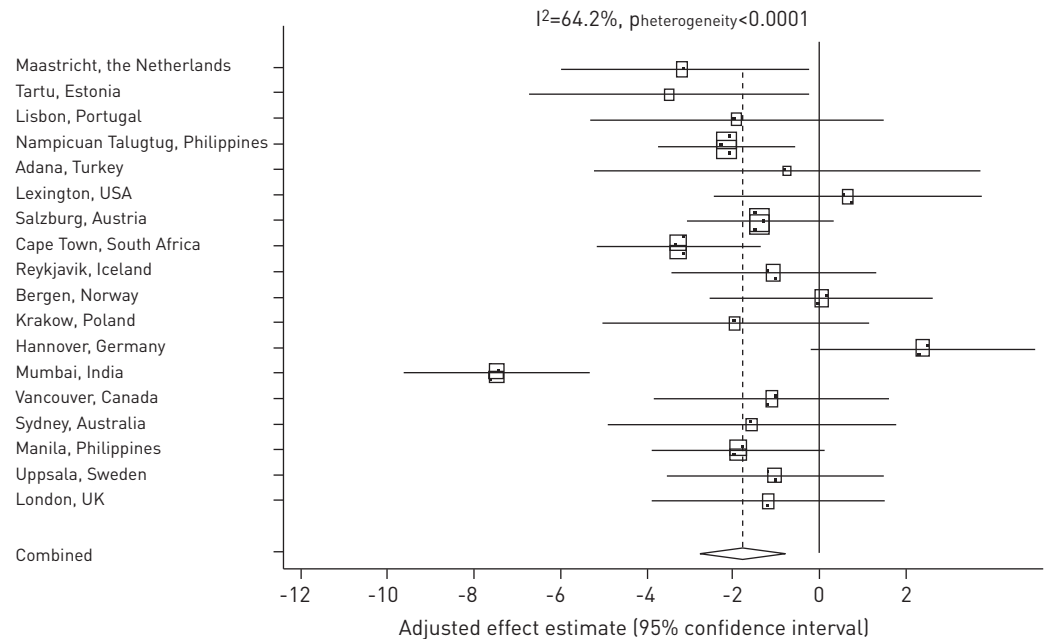


FIGURE 5 Effect estimates and 95% confidence intervals for the association between the SF-12 mental component score and chronic obstructive pulmonary disease (COPD) Global Initiative for Chronic Obstructive Lung Disease grade 2 and higher compared with participants without COPD (adjusted within centre for age, sex, educational level, smoking history, comorbidities and body mass index) with a combined effect estimate (diamond indicates 95% confidence interval) from the model with centre as the random effect. The size of each square is proportional to the sample size.

[38], but not all, previous studies [39]. There was an additive effect of COPD severity and comorbidities on impairment of health status in subjects with COPD.

Dyspnoea was independently negatively related to both PCS and MCS in both the present study and in a previous study [40]. Apart from dyspnoea and FEV<sub>1</sub>, PCS was also related to chronic cough, chronic phlegm and wheeze. In recent years, increased attention has been paid to symptoms associated with COPD. This might be due to the fact that dyspnoea and other respiratory symptoms indicate a worse prognosis in COPD, independent of the level of airflow limitation [41, 42]. Another reason might be that in subjects with COPD, improvement in symptoms may be easier to achieve than improvement in lung function.

In the present study, females with COPD had lower health status than males with COPD. This is a replication of findings from several other studies [5, 40, 43]. A low BMI was related to lower MCS and a higher BMI to lower PCS in our investigation. Several other studies have found that both being underweight and being obese are related to decreased health status [39, 44, 45]. In accordance with other studies, higher educational level was associated with better health status [46, 47].

TABLE 3 Associations between Short Form (SF)-12 physical component score (PCS) and mental health component score (MCS) with chronic obstructive pulmonary disease (COPD) defined as having a post-bronchodilator forced expiratory volume in 1 s (FEV<sub>1</sub>)/forced vital capacity (FVC) predicted below the lower limit of normal (LLN)

	PCS SF-12	MCS SF-12
<b>No COPD</b>	Reference	Reference
<b>COPD (FEV<sub>1</sub>/FVC &lt;LLN)</b>		
Grade 1	-0.26 (-1.05–0.53)	-0.28 (-1.13–0.56)
Grade 2	-3.2 (-3.9– -2.5)	-1.2 (-1.9– -0.44)
Grade 3	-7.9 (-9.0– -6.8)	-2.9 (-4.1– -1.7)
Grade 4	-12 (-14– -8.8)	-5.1 (-8.0– -2.2)

Data are presented as adjusted estimates (95% confidence interval). Estimates are adjusted for age, sex, educational level, smoking history, body mass index, cardiovascular diseases, diabetes and centre.



**TABLE 4** Associations between Short Form (SF)-12 physical component score (PCS) and mental health component score (MCS) in subjects with chronic obstructive pulmonary disease (COPD)

	PCS SF-12	MCS SF-12
<b>FEV<sub>1</sub> per 10% predicted</b>	0.89 [0.68–1.1]	-0.07 [-0.29–0.16]
<b>Dyspnoea</b>		
Grade 0	Reference	Reference
Grade 1	-1.9 [-3.0–-0.79]	-0.59 [-1.8–0.64]
Grade 2	-4.1 [-5.4–-2.8]	-1.3 [-2.8–0.15]
Grade 3	-5.5 [-7.2–-3.9]	-3.2 [-5.1–-1.4]
Grade 4	-8.6 [-11–-6.6]	-6.2 [-8.4–-4.0]
<b>Age per 10 years</b>	-1.3 [-1.7–-0.96]	0.75 [0.34–1.2]
<b>Females compared with males</b>	-1.4 [-2.2–-0.57]	-2.2 [-3.1–-1.3]
<b>Symptoms</b>		
Chronic cough	-1.4 [-2.8–-0.07]	-0.48 [-2.0–1.0]
Chronic phlegm	-1.9 [-3.3–-0.53]	-1.4 [-3.0–0.17]
Wheeze	-1.1 [-2.0–-0.25]	-1.5 [-2.5–-0.46]
<b>Body mass index kg·m<sup>-2</sup></b>		
<20	0.09 [-1.3–1.5]	-2.5 [-4.1–-1.0]
20–25	Reference	Reference
>25–30	0.06 [-1.0–0.88]	0.78 [-0.43–1.6]
>30	-1.4 [-2.5–-0.19]	0.64 [-0.68–2.0]
<b>Comorbidities</b>		
Heart disease	-1.5 [-2.6–-0.46]	-0.12 [-1.3–1.1]
Hypertension	-0.23 [-1.1–0.46]	-0.51 [-1.5–0.46]
Diabetes	-2.0 [-3.6–-0.53]	-0.69 [-2.4–1.0]
Stroke	-3.0 [-5.1–-1.0]	0.82 [-1.4–3.1]

Data are presented as adjusted estimates (95% confidence interval). Estimates are adjusted for the variables in the table, smoking history, educational level and centre. FEV<sub>1</sub>: forced expiratory volume in 1 s.

The BOLD study is one of several large epidemiological studies that have examined health status in people with COPD. The Epidemiologic Study of COPD in Spain (EPI-SCAN) has highlighted the importance of impaired health status in people with undiagnosed COPD [48]. The Latin American Project for the Investigation of Obstructive Lung Disease (PLATINO) has focused on sex differences and has shown that health status was lower in females than males [5]. The Canadian Obstructive Lung Disease prevalence study has been used to validate the CAT. Components of CAT can be of value for identifying subjects with previously undiagnosed COPD [49].

Strengths of this study include the large sample size and the use of a standardised method of data collection, together with a high level of quality control that increases the internal validity of the analyses [12, 13]. Also, BOLD includes subjects from a large number of countries, which increases the external validity of our findings. The use of questionnaires in different languages may introduce problems. However, in BOLD, the translations of the original questionnaires have been validated. Another possible limitation is that we did not collect data on depression, which has been shown to be related to health status in patients with COPD [50]. As the protocol did not include the CAT, we were not able to classify the subjects according to the newly developed GOLD groups A–D [18]. Finally, lack of a disease-specific health status questionnaire and the fact that the information on comorbidities was self-reported should be taken into account when interpreting our findings.

We confirm that COPD is related to worse health status and that the effect on the physical aspects of health status is stronger than the effect on the mental aspects. In severe COPD, the degree of impairment in health status is greater than the effect seen in people with self-reported cardiovascular diseases and diabetes. In subjects with COPD, health status is related to low lung function, dyspnoea, symptoms and comorbidities.

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