Added value of co-morbidity in predicting health-related quality of life in COPD patients

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The extent to which a chronic obstructive pulmonary disease (COPD) patient is impaired in health-related quality of life (HRQoL) is only to a small extent reflected in clinical and demographical measures. As the influence of co- morbidity on HRQoL is less clear, we investigated the added value of 23 common diseases in predicting HRQoL in COPD patients with mild to severe airways obstruction.

COPD patients from general practice who appeared to have an forced expiratory volume in 1 sec/inspiratory vital capacity (FEV1/IVC)< predicted -1·64 SD, FEV1 <80% predicted, FEV1 reversibility <12% and a smoking history, were included (n=163). HRQoL was assessed with the short-form-36 (SF-36) and the presence of co- morbidity was determined by a questionnaire, which asked for 23 common diseases.

All domains of the SF-36 were best predicted by the presence of three or more co-morbid diseases. FEV1 % predicted, dyspnoea and the presence of one or two diseases were second-best predictors. Co-morbidity explained an additional part of the variance in HRQoL, particularly for emotional functioning (R^2=0·11). When individual diseases were investigated, only insomnia appeared to be related to HRQoL.

As HRQoL is still only partly explained, co-morbidity and other patient characteristics do not clearly distinguish between COPD patients with severe impairments in HRQoL and COPD patients with minor or no impairments in HRQoL. Therefore, it remains important to ask for problems in daily functioning and well-being, rather than to rely on patient characteristics alone.

INTRODUCTION

Previous studies have shown that health-related quality of life (HRQoL) of COPD patients may be seriously impaired (1-10). These impairments in HRQoL not only affect physical functioning, but also emotional and social functioning. Determinants of HRQoL are, however, less understood. Lung function parameters, which objectively indicate the stage of the disease and which are good predictors of prognosis and survival, are only weakly related to HRQoL (1,2,4,8-20). Dyspnoea, a more subjective measure of severity of COPD, has been found to correlate better with HRQoL than pulmonary function tests (9-13,19,21). Nevertheless, HRQoL remains largely unexplained by these determinants. Furthermore, demo-graphical characteristics such as age, gender and socio- economic status are weakly or not related to

HRQoL (1,2,8,13,14,17-20,22,23). Therefore, the extent to which a COPD patient is impaired in daily life and functioning is only to a small extent reflected in parameters which are commonly measured in clinical practice.

In previous studies on HRQoL in COPD patients, the predictive value of co-morbidity on HRQoL has not been investigated (1-23). Nevertheless, co-morbidity may fre- quently occur in COPD patients and it may be assumed that co-morbidity has a substantial impact on HRQoL. To investigate whether COPD patients with an impaired HRQoL can be identified by the presence of co-morbidity, we studied the added value of co-morbidity in predicting HRQoL in COPD patients. We analysed the influence of 23 co-morbid diseases, together with several other clinical and demographical parameters, on HRQoL in a population of COPD patients with mild to severe airways obstruction.

MATERIALS AND METHODS

SELECTION OF COPD PATIENTS

Twenty-eight general practices from urban and suburban regions in the western part of The Netherlands participated in the study. These practices covered almost 55 000 patients at the time of study. Selection of patients was carried out in four steps: (a) all patients who were registered with a diagnosis of asthma or COPD in their general practice and who were 40 years or older were selected; (b) the general practitioners were then asked to exclude patients who met the following criteria: poor cognitive functioning (n=47), a poor mastering of the Dutch language (n=46) and presence of an end-stage disease (n=33); (c) 1106 patients were eligible, of whom 659 were willing to participate (60% response); (d) to include patients with COPD only, patients with an forced expiratory volume in 1 sec/inspiratory vital capacity (FEV1/IVC) ratio before and after inhalation of 400 mg salbutamol below the reference ratio 71?646SD [according to the calculation of the lower 5th percentile of reference values, recommended by the European Respira- tory Society (24)], FEV1580% predicted, FEV1 reversi- bility 512% of predicted and a history of smoking were included (n=163). The study was approved by the Medical Ethics Committee of the Academic Medical Center, University of Amsterdam.

DATA COLLECTION PROCEDURES

In this study, the term HRQoL refers to physical, social and emotional aspects of life that may be impaired due to disease. These aspects include functional status and general health perceptions according to the model of HRQoL of Wilson and Cleary (25). Generic HRQoL was measured instead of disease-specific HRQoL, because disease-specific instruments, in contrast to generic instruments, are designed to detect aspects of one particular disease and might therefore not able to detect aspects of co-morbid diseases.

HRQoL was determined by the short-form- 36 (SF-36), a generic measure which is broadly used and validated (26).

The questionnaire is composed of 36 questions, organized into eight multi-item domains: physical functioning, role limitations due to physical health problems, social functioning, mental health, role limitations due to emotional problems, vitality, bodily pain and general health. All raw domain scores are linearly converted to a 0-100 scale, with higher scores indicating a better HRQoL.

To determine the presence of diseases, patients were asked to complete a questionnaire on 23 diseases. This questionnaire is developed by the Statistics Netherlands (a government institution which conducts yearly surveys to collect information on the Dutch society on various topics among which indicators of health) and is broadly used in demographical studies in The Netherlands (27). Diseases included in the questionnaire had a prevalence of more than 2% in the general population and were long-lasting by nature. In the questionnaire, patients were asked whether they were suffering from each of the 23 diseases at that moment. Diseases were described so as to be under- standable for patients. For example, the term `high blood pressure' was used instead of `hypertension'. The following diseases were asked for: locomotive diseases (rheumatoid arthritis, arthrosis, slipped disc, disorder of the back for43 months), hypertension, insomnia, serious heart diseases or myocardial infarction, sinusitis, migraine, depression, dizziness with falling, ulcer of the stomach/duodenum, cancer, atherosclerosis, thyroid diseases, diabetes, serious intestinal diseases for43 months, serious skin diseases, gall bladder diseases, stroke, chronic cystitis, kidney stones, thrombosis, epilepsy, liver diseases and renal diseases.

In addition, questions were asked on gender, age, highest form of education received, coughing (usually at day/night or daily at least 3 months a year), phlegm (usually at day/ night or daily at least 3 months a year),

dyspnoea (when walking at normal pace on flat ground or when going upstairs), and smoking (smoking status, number of years smoked, number of cigarettes smoked per day). Lung function impairment was assessed by spirometry before and after inhalation of 400 mg salbutamol using a pneumotach (MasterScope, Jaeger, Germany) according to the Eur- opean Respiratory Society guidelines for measurement (24), and carried out by trained personnel.

ANALYSIS

In the questionnaire all participants were asked about the highest form of education they received (seven levels). The percentage of patients with a high and a low education was calculated. We defined a lower level of education as: primary school, lower vocational training, school for lower general secondary education (4 years education). The high educational level was defined as: high general secondary education (5 or 6 years education), high vocational training or university. The number of pack-years was calculated with the following formula: (number of cigarettes smoked per day6number of years smoked)/20. Fourteen persons did not answer all 23 questions on chronic diseases.

Therefore, the presence of one or more chronic diseases (co-morbidity) was calculated only for those persons who called in all questions on the existence of chronic diseases.

t-tests were carried out to test whether patients with and without co-morbidity differed on each domain of the SF-36.

A linear regression analysis was carried out for each domain to determine the predictive value of co-morbidity together with other clinical and demographic parameters on HRQoL. In the linear regression models the SF-36 domain was the dependent variable. These analyses were carried out in two steps. First, the independent variables introduced were age, gender, education, number of pack-years, cough, phlegm, dyspnoea and FEV1 % predicted. Second, co- morbid diseases were added as independent variables to the model to study the added value of co-morbidity in predicting HRQoL. Co-morbid diseases were added in two different ways. First, the number of co-morbid diseases was added and second, the eight most common individual diseases were added step-wise forward. To check whether necessary assumptions in multiple regression were not violated, normal plots of the residuals of the regression models were produced. All analyses were carried out using SPSS 8-0-2 for Windows.

RESULTS

INCLUSION

Of the 1106 eligible patients with a known diagnosis of asthma or COPD, 659 were willing to participate (60%).

The percentage of men was not significantly different between non-participants (43%) and participants (49%), but there was a significant difference in age between non- partcipants (66 years, SD=15) and participants (62 years, SD=13). Of the participants, 163 (25%) were found to have a persistent airway obstruction, a reversibility in FEV^1 % predicted less than 12% and a history of smoking. They fulfilled our criteria for COPD and were included in the analyses. Patients who were excluded on the basis of these criteria and who were thus not considered COPD patients, were less often men (41 vs. 72% men) and were younger [61 (SD=12) vs. 67 (SD=10)] than those who were included.

GENERAL CHARACTERISTICS

In Table 1, the general characteristics of COPD patients in this study are presented. As can be seen, the mean age was 67 years, 72% of the patients were male, the majority had a low education (86%) and the mean number of pack-years was 36. Most patients had a moderate (FEV^1 50-70% predicted) (40%) or severe ($FEV^1$550% predicted) (37%) airways obstruction and the mean per cent reversibility of FEV^1 was 5?1. The majority of patients reported symptoms of airway disease. Dyspnoea was the most frequently mentioned symptom (78%).

Seventy-two per cent of the patients had one or more of 23 co-morbid diseases. Most patients were suffering from one (31%) or two (22%) diseases, while 20% suffered from three or more diseases. The ten most frequently mentioned diseases were: locomotive diseases (38%), hypertension (20%), heart diseases (16%), insomnia (12%), ulcer of the stomach/duodenum (10%), sinusitis (9%), cancer (9%), dizziness with falling (7%), migraine (6%) and stroke (6%).

CO-MORBIDITY AND HEALTH-RELATED QUALITY OF LIFE, UNIVARIATE ANALYSIS

Table 2 shows the mean scores on the eight domains of the SF-36 for patients with different types of co-morbidity.

Each group of COPD patients with co-morbidity was compared with COPD patients without. Patients with one or more co-morbid diseases had significantly lower scores on physical functioning (50 vs. 59), role functioning due to physical problems (48 vs. 69), social functioning (71 vs. 83), mental health (71 vs. 80) and role functioning due to emotional problems (68 vs. 87). Patients with one or two other diseases were not significantly more impaired on all domains, while patients with three or more diseases were significantly more impaired on all domains.

Furthermore, when compared to patients without co- morbidity, scores on physical functioning were especially low in patients with dizziness and stroke, while scores on role functioning due to physical problems, social function- ing, mental health, role functioning due to emotional problems, vitality and general health were low in patients with insomnia. Scores on role functioning due to physical or emotional problems, vitality, bodily pain and general health were also low in patients with sinusitis. Scores on role functioning due to emotional problems and bodily pain finally appeared to be low in patients with migraine.

[TABLE 1]

[TABLE 2]

CO-MORBIDITY AND HEALTH-RELATED QUALITY OF LIFE, MULTIVARIATE ANALYSIS

The multivariate analyses were carried out to study which diseases were associated with HRQoL independently of each other and independently of demographical and clinical characteristics of COPD patients. In Table 3, the results for the influence of the number of co-morbid diseases on HRQoL, are presented. The linear regression analyses with each domain as dependent variable were carried out in two steps. First, only demographical and clinical characteristics were related to the domains. Second, the number of co- morbid diseases was added to this model. As the b of the first and the second model did not differ greatly, only the b of the second model are presented.

Table 3 shows that gender was associated with physical functioning, social functioning, and role functioning due to emotional problems, indicating that men were less impaired than women. Age, education and pack-years were not related to any domain. With respect to the clinical characteristics, FEV^1 was related to physical functioning, social functioning, vitality and general health. Dyspnoea was related to physical functioning, role functioning due to physical problems, mental health and vitality. Chronic cough and chronic phlegm were not significantly related to any domain. The presence of one or two diseases was associated with worse scores on role functioning due to physical problems, mental health, and role functioning due to emotional problems. The presence of three or more diseases was significantly related to all domains.

It appeared that all domains were best predicted by the presence of three or more co-morbid diseases. Physical functioning, social functioning and general health were second best predicted by FEV^1 % predicted. Role functioning due to physical problems and vitality on the other hand was second-best predicted by dyspnoea. Mental health and role functioning due to emotional problems finally were second-best predicted by the presence of one or two diseases.

The demographical and clinical characteristics together explained 30% of the variance of physical functioning, 16% of the variance of role functioning due to physical problems and 14% of the variance of vitality. The proportion of the variance explained was less for the other domains (R^2= 0·10). When co-morbidity was added to the model, all R^2 increased. The largest increase was noted for mental health (DR^2=0·11) and role functioning due to emotional problems (DR^2=0 ·11).

Instead of the number of co-morbid diseases, we also added the eight most common individual diseases step-wise forward to the model with only demographic and clinical variables (Table 4). In Table 3 all domains were best predicted by three or more co-morbid diseases. When the eight most common individual diseases were analysed, it appeared that only mental health, bodily pain and general health were best predicted by a co-morbid disease, namely insomnia. Physical functioning, role functioning due to physical

problems and vitality were on the other hand best predicted by dyspnoea. Social functioning was best predicted by gender.
For the models in Table 4, the variance was less explained for all domains than for the models in Table 3, except for physical functioning. Nevertheless, the R^2 was higher for all domains than the model with only demo- graphic and clinical characteristics. The largest increases were noted for mental health (DR^2=0·11) as a result of insomnia. Insomnia was related to all domains except role functioning due to physical problems, and was most strongly related to mental health. Locomotive diseases, hypertension, stomach or duodenal ulcers and sinusitis were not significantly related to any domain.

DISCUSSION

In this study, the relationship between several co-morbid diseases, together with demographical and clinical char- acteristics and HRQoL in patients with mild to severe COPD was investigated. The results of this study indicate that the presence of three or more co-morbid diseases in COPD patients was more predictive of HRQoL than any demographic variable or clinical variable, such as FEV^1 or airway symptoms. FEV^1, dyspnoea and the presence of one or two diseases were second-best predictors of HRQoL.
When the relationships between individual diseases and HRQoL were investigated, only insomnia appeared to be significantly related to HRQoL. Co-morbid diseases were of added value in predicting HRQoL, particularly with respect to emotional status (mental health and role functioning due to emotional problems).
Although there was some drop-out in this study, the COPD patients included in our study had a wide range of ages and airway obstruction. Furthermore, males and females, patients with a high and a low education, and patients with and without respiratory symptoms or co- morbidity were all represented. The patients in our study thus represented COPD patients with all relevant char- acteristics to study the independent influence of these characteristics on HRQoL.

[TABLE 3]

[TABLE 4]

In previous studies, dyspnoea appeared to be one of the best predictors of generic and disease-specific HRQoL.
Pulmonary function tests, particularly FEV^1, were associated with generic and disease-specific HRQoL, but the relationships were weak. Our study confirmed these findings, although the influence of dyspnoea in our study was less marked when all co-morbid diseases were included in the multivariate models. Some co-morbid diseases, such as heart diseases, may also be associated with dyspnoea. As a result, co-morbidity may have partly removed the effect of dyspnoea on HRQoL.
As the associations of co-morbidity, dyspnoea and FEV^1 with HRQoL were independent of each other, these factors all provided complementary information about HRQoL of COPD patients. Co-morbidity, as the best predictor of HRQoL, provided most information. In one study the effects of FEV^1 and co-morbidity were investigated (9). This study showed that the influence of co-morbidity on HRQoL was particularly seen in patients with relative mild airways obstruction ($FEV^1$450% predicted) and that the influence of airways obstruction (FEV^1) was particularly seen in patients without co-morbidity. However, the relative con- tribution of these factors to HRQoL was not presented and data on the separate domains of HRQoL were not given.
Except for insomnia, we could not identify individual diseases which were significantly related to HRQoL. As the In previous studies, dyspnoea appeared to be one of the best predictors of generic and disease-specific HRQoL.
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Except for insomnia, we could not identify individual diseases which were significantly related to HRQoL. As the ing). Although co-morbidity added 5-11% to the explained variance, the largest part of the variance in HRQoL is thus still unexplained. In previous studies the proportion of the variance in HRQoL explained ranged from 8% to 71% (1,2,4,8,10,13,16,17,20,22,23). However, these results are difficult to compare with the results of our study because in these studies different independent variables were used to predict HRQoL. Some studies used other independent variables such as other HRQoL instruments, exercise tolerance or activities of daily living. We believe these measures are all part of HRQoL rather than determinants of HRQL and do therefore not indicate which part of HRQoL is explained by patient characteristics. Instead, they provide information on the validity of a HRQoL instrument.
One final limitation of this study needs to be mentioned.
The results of our study were based on a subjective measure of co-morbidity, namely the self-report of patients. Several studies have indicated that patients' self-reports are fairly accurate (28-30). Moreover, some problems, such as insomnia, may not be detected otherwise. However, for some diseases agreement between questionnaire data and medical record data is rather poor, e.g. in the case of locomotive diseases (28,29). These diseases may reflect a symptom rather than a physician-diagnosed disease. The data on these diseases should therefore be interpreted as such. Nevertheless, these data are expected to be valid for assessing the symptom rather than the diagnosis, because patients are considered to be the best experts in reporting perceived disease symptoms.
In conclusion, co-morbidity is a better predictor of HRQoL than demographic variables and clinical variables which are routinely measured in COPD patients. The importance of co-morbidity for HRQoL is particularly relevant as co-morbid diseases frequently occur in COPD patients. The presence of three or more co-morbidities has a highly significant impact on HRQoL. Furthermore, insomnia deserves special attention, as it is one of the most frequently mentioned problems (12%) and it has an important influence on almost all aspects of HRQoL.
Asking about sleeping problems may therefore give information on the impairments COPD patients experience in daily life. However, as HRQoL is still only partly explained, co-morbidity and other patient characteristics do not clearly distinguish between COPD patients with severe impairments in HRQoL and COPD patients with minor or no impairments in HRQoL. Therefore, it remains important to ask for problems in daily functioning and wellbeing, rather than to rely on patient characteristics alone.

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TABLES

Table 1

TABLE 1. General characteristics of the study population. Data are expressed as numbers (%) or means (SD)*

	n=163
Mean age (SD)	66·8 (9·8)
Male	117 (71·8)
Low education	138 (86·3)
Mean number of pack-years (SD)	35·9 (25·3)
FEV_1 < 50% predicted	60 (36·8)
FEV_1 50–70% predicted	65 (39·9)
FEV_1 70–80% predicted	38 (23·3)
Mean % reversibility FEV_1 (SD)	5·1 (4·0)
Chronic cough	108 (67·5)
Chronic phlegm	110 (68·8)
Dyspnoea	127 (78·4)
Co-morbidity†	107 (72·3)
Number of co-morbid disease†	
0	41 (27·7)
1	46 (31·1)
2	32 (21·6)
3	16 (10·8)
4	7 (4·7)
5	5 (3·4)
6	1 (0·7)
Locomotive diseases	61 (37·9)
Hypertension	32 (20·1)
Heart diseases	25 (15·5)
Insomnia	20 (12·3)
Ulcus stomach/duodenum	16 (9·8)
Sinusitis	15 (9·2)
Cancer	14 (8·6)
Dizziness with falling	11 (6·8)
Migraine	9 (5·6)
Stroke	9 (5·6)
Depression	8 (4·9)
Diabetes	7 (4·3)
Skin diseases	6 (3·7)
Atherosclerosis	6 (3·7)
Kidney stones	6 (3·7)
Serious intestinal diseases	6 (3·7)
Thyroid diseases	4 (2·5)
Cystitis	3 (1·9)
Gallbladder diseases	3 (1·8)
Thrombosis	3 (1·8)
Liver diseases	1 (0·6)
Renal diseases	1 (0·6)
Epilepsy	1 (0·6)

*For variables with missing data, the percentages or means are based on patients without missing data.
†The presence of co-morbidity and the number of co-morbid diseases was only calculated for patients who filled in the complete questionnaire on co-morbidity.

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Table 2

TABLE 2. Influence of co-morbidity on HRQoL. Univariate analysis, mean scores (SD)

	n	Physical functioning	Role function physical	Social functioning	Mental health	Role function emotional	Vitality	Bodily pain	General health
No co-morbidity	41	60·0 (20·4)	68·2 (32·7)	83·2 (21·4)	79·3 (13·0)	87·8 (26·6)	61·1 (14·4)	88·8 (18·5)	49·1 (15·9)
≥1 diseases†	107	50·0 (26·8)*	48·1 (43·6)*	72·0 (28·7)*	71·2 (20·8)*	67·9 (42·8)*	55·9 (23·4)	83·6 (23·2)	45·8 (20·4)
1–2 diseases†	78	54·6 (26·6)	55·4 (43·3)	77·2 (28·1)	74·9 (18·9)	74·7 (39·8)	60·5 (22·6)	87·0 (21·1)	49·5 (19·8)
≥3 diseases†	29	37·5 (23·5)*	27·7 (38·1)*	57·8 (25·8)*	61·4 (22·7)*	50·6 (46·0)*	43·6 (21·1)*	74·4 (26·2)*	35·8 (18·8)*
Locomotive diseases	61	45·5 (25·9)*	41·3 (43·4)*	70·9 (27·6)*	70·8 (19·7)*	64·4 (43·3)*	52·4 (21·5)*	81·9 (24·6)	43·0 (19·0)
Hypertension	32	53·2 (29·9)	54·8 (46·7)	72·6 (29·5)	74·2 (18·1)	74·2 (41·0)	59·0 (22·1)	87·4 (18·1)	49·3 (16·4)
Heart diseases	25	45·2 (24·8)*	53·3 (46·7)	73·0 (28·3)	72·6 (20·5)	68·1 (42·3)*	56·6 (21·7)	82·0 (25·0)	40·8 (14·3)*
Insomnia	20	41·4 (29·0)*	31·3 (39·6)*	56·3 (29·7)*	54·4 (25·6)*	53·3 (43·8)*	41·0 (21·1)*	70·8 (26·5)*	32·7 (22·3)*
Ulcus duodenum /stomach	16	50·9 (28·5)	46·7 (46·2)	75·8 (31·8)	73·8 (19·2)	66·7 (43·9)	55·6 (23·9)	85·6 (23·1)	49·4 (22·1)
Sinusitis	15	41·8 (24·9)*	23·1 (40·1)*	72·3 (24·1)	68·6 (23·1)	51·3 (42·2)*	46·1 (18·8)*	67·6 (31·2)*	36·0 (21·2)*
Cancer	14	48·1 (36·0)	44·6 (42·9)*	69·6 (34·6)	71·7 (25·8)	51·3 (46·4)*	61·4 (26·7)	85·4 (23·4)	50·7 (21·2)
Dizziness with falling	11	33·4 (29·7)*	31·8 (37·2)*	63·6 (33·3)	66·9 (27·0)	60·6 (44·3)	48·6 (23·2)*	80·1 (24·6)	40·0 (18·2)
Migraine	9	55·0 (29·5)	40·6 (46·2)	72·2 (29·8)	67·6 (29·0)	58·3 (42·7)	51·7 (19·5)	67·6 (25·8)*	44·4 (12·4)
Stroke	9	32·8 (27·6)*	41·7 (43·3)*	69·4 (33·7)	76·0 (25·6)*	81·5 (33·8)	53·9 (24·0)	87·5 (19·8)	43·9 (17·6)

*$P<0·05$, reference group is patients without co-morbidity (*t*-test).
†The number of co-morbid diseases was only calculated for those patients who filled in the complete questionnaire on co-morbidity.

Table 3

TABLE 3. Influence of number of co-morbid diseases and other determinants on HRQoL. Linear regression analysis with domain as dependent variable in two steps: model without co-morbidity (only adjusted R^2 is shown) and model with co-morbidity (standardized β as well as adjusted R^2 are shown)

	Physical functioning	Role function physical	Social functioning	Mental health	Role function emotional	Vitality	Bodily pain	General health
Standardized β								
Age (years)	−0·16	0·04	<0·01	0·18	0·11	0·05	0·09	0·07
Male gender	0·20*	0·05	0·20*	0·10	0·23*	0·11	0·12	0·08
Low education	−0·06	−0·05	0·03	−0·08	−0·01	0·08	0·05	0·02
Number of pack-years	0·12	0·04	0·04	0·02	<0·01	0·07	0·11	0·09
FEV_1 % predicted	0·32*	0·09	0·21*	0·09	0·01	0·20*	0·07	0·30*
Chronic cough	−0·02	−0·04	−0·07	−0·03	0·01	−0·09	−0·07	−0·13
Chronic phlegm	0·02	−0·05	0·02	0·06	<0·01	−0·05	0·14	−0·05
Dyspnoea	−0·32*	−0·37*	−0·11	−0·19*	−0·17	−0·24*	−0·12	−0·10
1–2 diseases	−0·10	−0·24*	−0·12	−0·22*	−0·26	<0·01	−0·07	−0·04
≥3 diseases	−0·34*	−0·39*	−0·40*	−0·44*	−0·43*	−0·29*	−0·30*	−0·35*
Adjusted $R^2_{\text{without co-morbidity}}$	0·30	0·16	0·07	0·04	0·06	0·14	0·02	0·09
Adjusted $R^2_{\text{with co-morbidity}}$	0·37	0·24	0·16	0·15	0·17	0·20	0·07	0·18
ΔR^2	0·07	0·08	0·09	0·11	0·11	0·06	0·05	0·09

*$P<0·05$.

Table 4

TABLE 4. Influence of eight most common co-morbid diseases[†] and other determinants on health-related quality of life among COPD patients. Linear regression analysis with domain as dependent variable in two steps: model without co-morbidity (only adjusted R^2 is shown) and model with co-morbidity (standardized β as well as adjusted R^2 are shown). In the model with co-morbidity, co-morbid diseases were added step-wise forward (only added diseases are presented)

	Physical functioning	Role function physical	Social functioning	Mental health	Role function emotional	Vitality	Bodily pain	General health
Standardized β								
Age (years)	−0·16*	−0·03	−0·04	0·11	0·06	0·01	0·06	0·06
Male gender	0·21*	0·08	0·25*	0·16	0·26*	0·15	0·16	0·15
Low education	−0·08	−0·05	−0·01	−0·10	−0·02	0·05	0·03	< −0·01
Number of pack-years	0·10	0·02	−0·04	−0·06	−0·02	< −0·01	0·04	0·02
FEV_1 % predicted	0·26*	0·05	0·13*	< −0·01	−0·02	0·12	0·01	0·18*
Chronic cough	−0·02	−0·05	−0·09	−0·04	−0·04	−0·10	−0·09	−0·14
Chronic phlegm	0·03	−0·08	−0·03	0·01	−0·03	−0·06	0·10	−0·05
Dyspnoea	−0·39*	−0·44*	−0·19*	−0·25*	−0·20*	−0·32*	−0·17	−0·22*
Heart diseases								−0·19*
Insomnia	−0·18*		−0·22*	−0·34*	−0·20*	−0·27*	−0·18*	−0·24*
Cancer					−0·20*			
Dizziness with falling	−0·20*							
Adjusted $R^2_{\text{without co-morbidity}}$	0·32	0·19	0·08	0·06	0·06	0·21	0·03	0·11
Adjusted $R^2_{\text{with co-morbidity}}$	0·39	—	0·12	0·17	0·13	0·28	0·05	0·17
ΔR^2	0·07	—	0·04	0·11	0·07	0·07	0·02	0·06

*$P < 0·05$.

[†]Eight most common diseases: locomotive diseases, hypertension, heart diseases, insomnia, gastric ulcus, sinusitis, cancer and dizziness with falling.