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The influence of co-morbidity on health-related quality of life in asthma and COPD patients

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ABSTRACT

This study examines the association between somatic co-morbidity and both general and disease-specific health-related quality of life (HRQoL) in patients with asthma and chronic obstructive pulmonary disease (COPD). A cross-sectional analysis was done among161COPD patients and 395 asthma patients, aged 40-75 years, recruited from general practice. In the total study population,47% had no, 32% had one, and 21% had two or more somatic co-morbid conditions, with no significant differences between asthma and COPD patients. Co-morbidity appeared to be associated with poor disease-specific HRQoL in asthma [odds ratio (OR) = 2.08 (1.37-3.18)] and with poor general HRQoL in asthma [OR = 2.96 (1.93-4.53)] and COPD [1.81 (0.91-3.60)] patients. Poorest HRQoL was found in patients with more than one co-morbid condition. Cardiac disease and hypertension were associated with poor disease-specific HRQoL in asthma. Of all co-morbid conditions, musculoskeletal disorders were most strongly associated with poor general HRQoL. Cardiac disease was found to be associated with general and disease-specific HRQoL in asthma but not in COPD. In studies on patients with asthma or COPD aged 40-75 years, co-morbidity should be treated as a determinant of HRQoL.

INTRODUCTION

It is well known that older patients with asthma or chronic obstructive pulmonary disease (COPD) often suffer from other somatic diseases as well. In a study among asthma and COPD patients 40 years of age and older, 73% reported one or more other diseases (1). In a population of older male COPD patients, Ferrer et al. (2) found that 84% had at least one somatic co-morbid condition. Several studies have examined determinants of health-related quality of life (HRQoL) in patients with asthma (3-5) or COPD (6-9). However, not much is known about the impact of somatic co-morbidity on HRQoL in COPD patients. This is because in many studies, patients with significant co-morbid illness are excluded (6). The same is true for asthma patients. Examining the impact of co-morbidity on HRQoL in asthma or COPD patients is important for several reasons. First of all, the 'one-disease' approach often used in studies on asthma and COPD patients does not reflect reality, especially in older patient groups as mentioned already. Excluding patients with co-morbidity therefore decreases the external validity of a study. Secondly, it is important to know whether co-morbidity is a determinant of

HRQoL, since if it is, it should be taken into account as a covariate in clinical trials and descriptive studies among asthma and COPD patients. Finally, clinicians treating asthma and COPD patients should be aware of the influence of co-morbidity on HRQoL, because it might change patients'need for health care.

HRQoL can be measured by means of disease-specific or generic questionnaires. Disease-specific questionnaires focus on the influence of characteristics of a particular disease on functioning, while generic questionnaires focus on the influence of general health status on functioning. Therefore, it is likely that the presence of co-morbidity in patients with asthma or COPD has a greater impact on general than on disease-specific HRQoL. In this study, the association between somatic co-morbidity and both disease-specific and general HRQoL is examined in asthma and COPD patients aged 40-75 years.

MATERIALS AND METHODS

Design

The impact of somatic co-morbidity on HRQoL was examined in a cross-sectional study, using the baseline measurement of a longitudinal observational study among patients with asthma and COPD. An extensive description of the patients and methods can be found elsewhere (10).

Patients

Patients with asthma or COPD were recruited from 25 general practices in three regions of the Netherlands. The inclusion criteria were: aged16-75 years, capable of filling in a Dutch questionnaire, no specific pulmonary disease other than asthma or COPD (such as localized disease of the upper airways, bronchiectasis, and cystic fibrosis), and absence of any disease in a terminal phase. Informed consent to participate was obtained. For the purpose of this study, only patients aged 40-75 years were included.

The distinction between asthma and COPD was made by the researcher using pulmonary function measurements, following the1997 revised guidelines of the Dutch College of General Practitioners for the diagnosis of asthma and COPD(11). Among the patients selected by the general practitioner (GP), asthma was defined as: (1) a pre (before use of a bronchodilator) FEV_1 %pred $\geq$ 80%; or 2) a combination of a pre-FEV_1%pred < 80%, a reversible obstruction (increase in $FEV_1$10 min after administration of a bronchodilator $\geq$ 9% of predicted), and a post (after use of a bronchodilator) FEV_1%pred $\geq$ 80%. COPD was defined as a pre-FEV_1 %pred < 80% combined with an irreversible obstruction (variation in FEV_1 before and after bronchodilation < 9% of predicted). Patients with a mixed disease (10) were excluded.

Measurements

Spirometry

Forced expiratory volume in1s (FEV_1) was measured according to ATS criteria (12) before (pre-FEV_1) and after (post-FEV_1) administration of a bronchodilator (10). FEV_1 was expressed as a percentage of the predicted FEV_1 (FEV_1 %pred) using the adult predicted normals of the European Community for Coal and Steel (13).

Quality of life

HRQoL was measured by a disease-specific and a generic (general) questionnaire. The disease-specific instrument used was the Quality Of Life in Respiratory Illness Questionnaire (QoL-RIQ) of Maillé and Kaptein (14). This written questionnaire was especially developed and validated for patients with asthma and COPD treated primarily in general practice, who generally have mildly to moderately severe disease. It contains 55 items divided into seven subscales: (1) breathing problems; (2) physical problems; (3) emotions; (4) situations triggering or enhancing breathing problems; (5) general activities; (6) daily and domestic activities; and (7) social activities, relationships and sexuality. For every item, patients were asked to answer, on a seven-point Likert-type scale, to what degree they were troubled due to pulmonary complaints. The response categories of all items ranged

from 1 (not troubled at all) to 7 (very much troubled). Cronbach's α's varied from0.68 to 0.92 for the domain subscales, and was 0.92 for the overall score (14). In case of missing data, < 50% missing items were allowed per subscale and were substituted, and one missing subscale was allowed for the calculation of the overall score (15).

The generic instrument used was the Dutch version of the Nottingham Health Profile (NHP) (16). The NHP is a self-administered two-part questionnaire designed to measure the respondent's subjective perception of his or her health status (17). In this study, only part one of the questionnaire was used which contains 38 statements relating to six dimensions: (1) physical mobility; (2) pain; (3) sleep; (4) energy; (5) social isolation; and (6) emotional reactions. Patients were asked whether or not the item applied to them. Positive answers were given the appropriate weight, according to their relative severity (18). Each dimension score ranges from 0 (= optimal) to 100. No missing data were allowed for calculation of a dimension score. An overall score was calculated by adding all dimension scores divided by six. Although the use of an overall score for the NHP is not widely accepted (19), it was considered appropriate for the purpose of this study (2).

Co-morbidity

Patients were questioned about co-morbidity by trained interviewers administering a questionnaire during a face-to-face interview. The questionnaire included questions on the presence or absence of specific chronic diseases (yes/no): (1) diabetes mellitus; (2) hypertension; (3) cardiac disease (including cardiac arrhythmia, previous myocardial infarction, angina pectoris, and congestive heart failure); (4) cerebrovascular disease [stroke or transient ischemic attack (TIA)]; (5)musculoskeletal disorders [including arthritis (osteoarthritis or rheumatoid arthritis) and chronic back pain]; and (6) malignancies. In addition, patients were asked whether they had any other chronic disease. Compared to information obtained from GP's, self-reports of chronic diseases were found to be suffiently accurate (20).Co-morbidity was defined as: (1) presence of co-morbidity (yes/no); (2) number of co-morbid conditions (0/ 1/ $\geq$ 2); (3) presence of specific co-morbidity.

Statistical analyses

Analyses were performed using the statistical package SPSS.9.0. Patients with missing values on pulmonary function, co-morbidity or HRQoL were excluded from the analyses. All analyses were performed separately for asthma and COPD patients.

Since scores on both general (NHP) and disease-specific HRQoL (QoL-RIQ) were not normally distributed, they were dichotomized at the median value of the total study population. HRQoL was coded as 0 when the score was lower than or equal to the median value (good HRQoL) and1when the score was higher than the median value (poor HRQoL).The same was done for all subscale scores. The association between co-morbidity and HRQoL was examined using logistic regression analyses with HRQoL (the dichotomized total scores and subscale scores of both the QoL-RIQ and the NHP) as the dependent variable and co-morbidity as the independent variable. The association between HRQoL and specific chronic diseases was studied multivariately only when the prevalence of the specific chronic disease was 10% or higher. For specific chronic diseases with a prevalence lower than 10% a variable 'remaining chronic diseases' was computed (yes or no). All regression models were adjusted for age and gender, since these variables are likely to be associated with both HRQoL and co-morbidity. Interaction was tested between disease group (asthma or COPD) and co-morbidity in order to examine whether or not the impact of co-morbidity differed between the asthma and COPD groups.

RESULTS

A total of1254 patients with asthma or COPD, aged 40- 75 [mean age = 57±11 (SD); 47% male], was selected by the GP to be included in the study. Of those, 505 refused to participate, leaving 749 patients [mean age = 57±11 (SD); 45% male; 65.2% asthma, 27.4% COPD, and 7.5% mixed disease]. After excluding patients with missing data on co-morbidity or HRQoL, 603 patients [mean age = 56±11 (SD); 46% male; 65.5% asthma, 26.7% COPD, and 7.8% mixed disease] were left. Only patients with asthma (n =395) or COPD(n = 161)were included in this study.

Table1presents the characteristics of the study population separately for asthma and COPD patients. COPD patients were generally older than asthma patients and reported poorer HRQoL. In both the asthma and COPD group approximately 55% of the patients reported at least one somatic co-morbid condition. The most common co-morbid conditions were musculoskeletal disorders (32.2% in asthma and 27.3% in COPD), hypertension (17.0% in asthma and 17.4% in COPD), and cardiac disease (12.7% in asthma and19.3% in COPD).

[TABLE 1]

The age- and gender-adjusted associations between co-morbidity and HRQoL are presented in Table 2. Although not all associations were statistically significant, overall, co-morbidity appeared to be negatively associated with HRQoL. When more than one co-morbid condition was present, HRQoL was even poorer. This was most apparent for general HRQoL in asthma patients; compared to no co-morbid conditions, one comorbid condition gave an odds ratio (OR) of 2.00, more than one co-morbid condition an OR of 6.91. In asthma patients, co-morbidity was associated with disease-specific HRQoL, while in COPD patients no statistically significant association was observed. The ORs were statistically significantly different between the two disease groups. Associations were stronger for general than for disease-specific HRQoL.

[TABLE 2]

Multivariate associations between specific chronic diseases and HRQoL can be found in Table 2 (total scores of HRQoL) and Table 3 (subscales of HRQoL).The presence of hypertension was statistically significantly associated with poor disease specific HRQoL in asthma patients only. Especially the more 'general' subscales of the QoLRIQ were affected ('physical problems','general activities', 'daily and domestic activities', 'social activities, relationships and sexuality').Cardiac disease was associated both with poor disease-specific and poor general HRQoL in asthma patients. No associations were found in COPD patients. Differences between the two disease groups were statistically significant. For cardiac disease, almost all subscales of both questionnaires were affected, including 'breathing problems' of the QoL-RIQ. Musculoskeletal disorders were associated with poor general HRQoL in both asthma and COPD patients. Especially the subscales 'physical mobility','sleep','energy', and 'pain' were affected. Although the total score of the QoL-RIQ was not statistically significantly associated with musculoskeletal disorders, in COPD, some subscales of the QoL-RIQ were influenced by musculoskeletal disorders.

[TABLE 3]

DISCUSSION

As far as we know, this is the first study examining in detail the impact of co-morbidity on general and disease-specific HRQoL in both asthma and COPD patients. The influence of somatic co-morbidity on both disease-specific and general HRQoL is examined using three operational definitions of co-morbidity: (1) presence of co-morbidity; (2) number of co-morbid conditions; and (3) presence of specific co-morbidity. The reason for using three operational definitions of comorbidity is that we want to get a complete picture of the influence of co-morbidity on HRQoL. By using only one definition, relevant information might be missed. Furthermore, the first two definitions might be interesting for the purpose of epidemiological studies, while the clinician might be more interested in the third. It appears that co-morbidity is an important determinant of disease- specific HRQoL in asthma and of general HRQoL in asthma and COPD. Especially, the presence of more than one co-morbid condition increases the risk of poor HRQoL. Cardiac disease and hypertension are associated with poor disease-specific HRQoL in asthma. Of all comorbid conditions, musculoskeletal disorders

have the greatest impact on a patient's general HRQoL. Cardiac disease is associated with HRQoL in asthma but not in COPD.

The finding that co-morbidity is a determinant of HRQoL in patients with asthma and COPD is supported by others. In patients with COPD, co-morbidity was found to be associated with general HRQoL (2,21) and, less strongly, with disease-specific HRQoL (2). Smeele et al. (15) studied patients with chronic airway disease and found that the presence of co-morbidity was associated with both poor disease-specific HRQoL and poor general health status. The influence of co-morbidity on HRQoL in asthma patients was not studied before.

The finding that the influence of co-morbidity on HRQoL is more pronounced in asthma than in COPD patients, might be explained by differences in disease characteristics. Contrary to COPD, asthma patients usually are not continuously confronted with complaints due to pulmonary obstruction, but only during exacerbations. Therefore, the influence of a co-morbid condition on HRQoL in asthma patients is likely to be stronger than the influence in COPD patients who already experience chronic complaints and a poorer HRQoL. Furthermore, comparable to other studies examining the impact of co-morbidity on health outcomes such as depression (22) or disability (23), there appears to be a dose -response relation between co-morbidity and HRQoL.

We found that the presence of hypertension is not associated with poor disease-specific HRQoL in COPD patients and only weakly (not statistically significant) with poor general HRQoL in both asthma and COPD patients, which is not really surprising since hypertension does not cause direct physical complaints. Surprising, however, is that in asthma patients, the presence of hypertension is associated with poor disease-specific HRQoL. In a study done by Lawrence et al. (24), the presence of hypertension appeared to be associated with reduced HRQoL when compared to a group without hypertension. It is possible that asthma patients are more affected by the presence of hypertension than COPD patients because of the differences in disease characteristics as mentioned before. A possible explanation for the finding that disease-specific HRQoL is more affected than general HRQoL may be that dyspnea is one of the adverse effects of commonly used antihypertensive drugs. However, the association between hypertension and disease-specific HRQoL was not modified by adjusting for dyspnea (data not shown). Also body mass index, as a proxy measure for obstructive sleep apnea, did not modify the association (data not shown).

Another remarkable finding, since cardiac disease is one of the most frequent causes of death in COPD (25,26), is the association between cardiac disease and HRQoL in asthma, but not in COPD patients. Apparently, although co-morbid cardiac disease is a risk factor for mortality in COPD patients (27), it does not affect patients' HRQoL. This theory is supported by Patrick et al. (28), who found that adults with musculoskeletal disorders report poorer general HRQoL than adults with cardiac disease. So even though the prognosis for survival may differ, patients with non-life-threatening conditions may have poorer HRQoL than patients with potentially life-threatening conditions. The finding that in asthma the presence of cardiac disease is associated with HRQoL, while in COPD it is not, might also be explained by differences in disease characteristics. It is possible that asthma patients are, more than COPD patients, troubled by a potentially life-threatening and socially limiting disease. However, subscale analyses in asthma only partly support this hypothesis; the presence of cardiac disease is associated with reduced disease-specific HRQoL for the subscale 'social activities, relationships and sexuality', but no association is found with general HRQoL according to the subscale 'social isolation'. Another explanation might be that patients with angina pectoris (present in 64% of asthma patients with cardiac disease) experience periodical chest pain and dyspnea, especially with effort, resembling dyspnea due to asthma. In line with this theory, COPD patients might avoid physical effort because of continuous dyspnea due to COPD, resulting in less complaints due to angina pectoris and thus less additional effect on HRQoL. However, adjusting for dyspnea did not modify the association between co-morbid cardiac disease and HRQoL (data not shown).

The fact that musculoskeletal disorders appear to have such a great impact on a patients' general HRQoL in both asthma and COPD, is in line with Patrick et al. (28) as mentioned before. Additional support can be found in Fried et al. (29), who found that, in older women, the presence of lung disease

and arthritis were synergistically associated with disability. Xuan et al. (30) found, among asthma patients, musculoskeletal disorders (arthritis or back pain)was the only co-morbid condition associated with both general and disease-specific HRQoL.

It can be argued that patients with co-morbidity may have more severe asthma, thus explaining the impact of co-morbidity on disease-specific HRQoL. However, all associations remained statistically significant after adjusting for pulmonary function and dyspnea (data not shown), which does not support this theory.

Some methodological limitations of the study should be mentioned. Regarding the external validity of the study, one has to keep in mind that patients were recruited from general practice, which is likely to result in a patient group with a relatively mild disease severity. Especially in COPD patients, co-morbid conditions might therefore also be relatively mild or less frequent, compared to, patients from outpatient clinics or hospitals. As a result, associations between HRQoL and co-morbidity might be underestimated, since the more extreme end of the spectrum is missed. However, it is also possible that, in COPD patients, a more severe disease would have masked the influence of co-morbidity. Regarding the internal validity, self-report of co-morbid conditions may have resulted in stronger associations between comorbidity and HRQoL, since over-reporting of co-morbid conditions (especially more subjective complaints such as back pain) may be related to reporting of poorer HRQoL, while under-reporting may be related to better HRQoL. Although a substantial proportion of the initial study population refused to participate or was excluded due to missing data, we do not suspect a selection bias, since no selective exclusion was observed with respect to gender, age, and disease group (the latter could only be examined for participating patients).

Concluding, in patients with asthma and COPD aged 40-75 years somatic co-morbidity is an important determinant of HRQoL. Since co-morbidity is common in patients over 40 years of age, excluding patients with co-morbidity in clinical and descriptive studies does not seem to be the right approach. Co-morbidity should be taken into account as an important covariate in studies with subjective health outcomes. Depending on the research question, several ways of expressing co-morbidity might be considered.

TABLES

TABLE 2. Results from logistic regression analyses with HRQoL as the dependent variable and co-morbid conditions as the independent variables

	QoL-RIQ total score OR (95% CI)[a]		NHP total score OR (95% CI)[a]	
Independent variables	Asthma (*n*=395)	COPD (*n* = 161)	Asthma (*n* = 395)	COPD (*n* = 161)
Presence of co-morbidity				
Yes	**2.08 (1.37–3.18)**	1.09 (0.55–2.17)[b]	**2.96 (1.93–4.53)**	1.81 (0.91–3.60)
Number of co-morbid conditions[c]				
1 condition	1.37 (0.86–2.20)	0.87 (0.41–1.87)	**2.00 (1.26–3.20)**	1.35 (0.63–2.87)
> 1 condition	**4.77 (2.62–8.69)**	1.61 (0.64–4.07)[b]	**6.91 (3.64–13.12)**	**3.22 (1.23–8.45)**
Specific co-morbid conditions[d]				
Hypertension	**2.47 (1.37–4.43)**	0.60 (0.25–1.44)[b]	1.79 (0.99–3.27)	2.05 (0.79–5.31)
Cardiac disease	**3.72 (1.82–7.62)**	0.99 (0.41–2.39)[b]	**2.28 (1.11–4.70)**	0.61 (0.25–1.53)[b]
Musculoskeletal disorders	1.52 (0.96–2.40)	2.17 (0.95–4.98)	**3.12 (1.95–4.99)**	**2.52 (1.10–5.78)**
Remaining chronic diseases[e]	1.62 (0.91–2.86)	1.58 (0.63–3.97)	**2.14 (1.18–3.90)**	2.22 (0.84–5.85)

[a]Odds ratios (OR) + 95% confidence intervals (C.I.) are presented. An OR > 1 indicates a higher risk on poor HRQoL. The OR is printed bold when the association is statistically significant. All associations are adjusted for age and gender.

[b]The OR is statistically significantly different between asthma and COPD patients ($P < 0.05$).

[c]Reference category = no co-morbid condition.

[d]All co-morbid conditions are entered in a multivariate model.

[e]Includes: diabetes mellitus, cerebrovascular disease, malignancies, and other chronic diseases.

TABLE I. Characteristics of the study populations

	Asthma (n=395)	COPD (n=161)	P-value[a]
Age (mean ± SD)	54.0 ± 10.0	61.0 ± 10.3	< 0.01
Gender (%male)	41.0	55.3	< 0.01
FEV_1 %predicted (mean ± SD)	96.3 ± 16.1	60.7 ± 15.0	< 0.01
Health-related quality of life[b]			
QoL-RIQ [median (range)]	13.2 (7.1–36.7)	16.1 (7.1–35.9)	< 0.01
NHP [median (range)]	10.1 (0.0–81.5)	12.4 (0.0–73.0)	< 0.1
Number of co-morbid conditions			
No co-morbidity (%)	47.3	46.6	> 0.1
One co-morbid condition (%)	32.2	30.4	
More than one co-morbid condition (%)	20.5	23.0	
Specific co-morbid conditions			
Hypertension (%yes)	17.0	17.4	> 0.1
Cardiac disease (%yes)	12.7	19.3	< 0.1
Cardiac arrhythmia (%yes)	2.0	1.2	> 0.1
Myocardial infarction (%yes)	4.3	10.6	< 0.01
Angina pectoris (%yes)	8.1	9.9	> 0.1
Congestive heart failure	1.8	3.7	> 0.1
Musculoskeletal disorders (%yes)	32.2	27.3	> 0.1
Arthritis (%yes)	25.1	23.0	> 0.1
Other (%yes)	8.4	6.2	> 0.1
Diabetes mellitus (%yes)	5.3	5.0	> 0.1
Cerebrovascular disease (%yes)	3.5	2.5	> 0.1
Malignancies (%yes)	4.8	6.8	> 0.1
Other chronic diseases (%yes)	5.1	5.0	> 0.1
Remaining chronic diseases[c] (%yes)	16.7	17.4	> 0.1

[a]Differences between asthma and COPD are tested using the appropriate statistics.
[b]A higher score indicates poorer HRQoL.
[c]Includes: diabetes mellitus, cerebrovascular disease, malignancies, and other chronic diseases

TABLE 3. Results from logistic regression analyses with HRQoL (subscales) as the dependent variable and co-morbid conditions as the independent variables.

	QoL-RIQ subscales OR (95% C.I.)[a]			NHP subscales OR (95% C.I.)[a]	
	Asthma (n = 395)[b]	COPD (n = 161)[b]		Asthma (n = 395)	COPD (n = 161)
	Hypertension			Hypertension	
Physical problems	**2.72 (1.52–4.88)**	0.60 (0.25–1.46)	Physical mobility	**2.74 (1.42–5.29)**	2.23 (0.82–6.05)
General activities	**1.92 (1.06–3.46)**	0.63 (0.25–1.54)	Sleep	1.01 (0.58–1.78)	0.87 (0.36–2.11)
Daily and domestic activities	**1.92 (1.06–3.48)**	1.44 (0.57–3.64)	Energy	1.64 (0.92–2.94)	0.79 (0.33–1.90)
Emotions	1.78 (0.99–3.20)	2.02 (0.85–4.80)	Emotional reactions	1.15 (0.65–2.02)	1.69 (0.71–4.03)
Social activities, relationships and sexuality	**2.25 (1.20–4.21)**	0.62 (0.23–1.68)	Social isolation	0.83 (0.40–1.73)	1.06 (0.40–2.83)
Breathing problems (BPs)	1.46 (0.79–2.70)	0.89 (0.37–2.17)	Pain	1.63 (0.86–3.01)	0.77 (0.29–2.06)
Situations triggering or enhancing BP	1.32 (0.75–2.33)	**0.17 (0.06–0.46)**			
	Cardiac disease			Cardiac disease	
Physical problems	**2.85 (1.43–5.68)**	1.17 (0.48–2.87)	Physical mobility	**3.30 (1.45–7.51)**	1.35 (0.51–3.52)
General activities	**2.70 (1.38–5.31)**	0.87 (0.36–2.12)	Sleep	**2.31 (1.16–4.56)**	0.53 (0.22–1.30)
Daily and domestic activities	**4.67 (2.21–9.89)**	1.33 (0.54–3.27)	Energy	**2.00 (1.00–4.00)**	0.68 (0.28–1.64)
Emotions	1.88 (0.96–3.66)	1.12 (0.44–2.82)	Emotional reactions	**2.11 (1.09–4.09)**	0.62 (0.26–1.47)
Social activities, relationships and sexuality	**3.21 (1.51–6.84)**	0.85 (0.32–2.25)	Social isolation	1.37 (0.62–3.01)	0.67 (0.24–1.91)
(BPs)	**2.49 (1.13–5.50)**	0.80 (0.34–1.90)	Pain	**2.96 (1.44–6.09)**	0.80 (0.31–2.09)
Situations triggering or enhancing BP	1.29 (0.67–2.49)	1.28 (0.50–3.26)			
	Musculoskeletal disorders			Musculoskeletal disorders	
Physical problems	1.42 (0.90–2.25)	**2.39 (1.08–5.31)**	Physical mobility	**4.34 (2.63–7.18)**	**3.88 (1.58–9.50)**
General activities	1.49 (0.91–2.45)	**2.26 (1.05–4.89)**	Sleep	**1.78 (1.14–2.79)**	**3.78 (1.64–8.74)**
Daily and domestic activities	**1.87 (1.17–2.97)**	1.29 (0.58–2.89)	Energy	**2.51 (1.59–3.97)**	**2.80 (1.26–6.20)**
Emotions	0.83 (0.50–1.40)	**2.43 (1.11–5.30)**	Emotional reactions	**2.02 (1.29–3.15)**	1.76 (0.82–3.78)
Social activities, relationships and sexuality	1.47 (0.87–2.46)	2.07 (0.85–5.06)	Social isolation	1.65 (0.93–2.92)	2.26 (0.98–5.23)
(BPs)	1.53 (0.95–2.47)	0.99 (0.44–2.22)	Pain	**5.03 (3.07–8.24)**	**5.26 (2.34–11.83)**
Situations triggering or enhancing BP	**1.65 (1.05–2.58)**	2.14 (0.88–5.20)			
	Sum score 'other chronic diseases'			Sum score 'other chronic diseases'	
Physical problems	**1.90 (1.07–3.35)**	1.63 (0.67–3.98)	Physical mobility	1.83 (0.97–3.45)	**2.81 (1.00–7.88)**
General activities	**2.68 (1.51–4.78)**	**2.81 (1.16–6.78)**	Sleep	1.60 (0.91–2.81)	1.94 (0.77–4.87)
Daily and domestic activities	1.66 (0.92–2.30)	1.64 (0.65–4.17)	Energy	**2.11 (1.18–3.79)**	1.75 (0.71–4.29)
Emotions	**1.83 (1.02–3.30)**	1.06 (0.43–2.64)	Emotional reactions	0.91 (0.52–1.60)	2.09 (0.86–5.10)
Social activities, relationships and sexuality	1.21 (0.63–2.29)	0.49 (0.19–1.29)	Social isolation	**2.58 (1.37–4.84)**	1.67 (0.66–4.26)
(BPs)	1.36 (0.74–2.48)	1.26 (0.50–3.17)	Pain	1.33 (0.71–2.49)	2.26 (0.89–5.72)
Situations triggering or enhancing BP	1.68 (0.94–2.95)	0.78 (0.30–2.04)			

[a]OR + 95% CI are presented. An OR > 1 indicates a higher risk on poor HRQoL. The OR is printed bold when the association is statistically significant. All associations are adjusted for age, gender and all other reported chronic diseases. [b]For the subscale 'Social activities, relationships and sexuality', the number of patients is 356 (asthma) and 135 (COPD).

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