

Perceived health status and quality of life: measurements and changes
after a short inpatient rehabilitation programme for female and male
COPD patients

Einar Haave

Glittrelinikken

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Summary

Perceived health status (HS) and quality of life (QoL) are regularly used as outcome variables to evaluate the effect of various treatments for patients with chronic obstructive pulmonary disease (COPD). Disease-specific HS questionnaires for patients with COPD quantify the impact of disease on patients' daily life, health and well-being, and they usually include items that address both physical and psychological aspects. Application of the term quality of life often seems to be inconsistent, but there is some consensus that QoL should probably be reserved for scales where the items refer to life experiences but not in the context of disease. QoL is a broader concept than HS and includes factors such as social and psychological well-being and satisfaction with life, factors that may or may not be influenced by health or treatment. Factors that are closely related to health conditions – easily captured by disease-specific instruments – do not necessarily affect general QoL very much. Conversely, factors that are not health-related, and thus missed by disease-specific instruments, can make a significant difference in the assessment of general QoL.

The first aim of the thesis was to examine the associations between HS, QoL and physical function among COPD patients. Our results indicated that in order to achieve a comprehensive assessment, both total scores and subscores of HS and QoL instruments should be included to evaluate the impact of COPD on a person's life and to measure the effects of pulmonary rehabilitation. Furthermore, it can be important to distinguish between variables related to physical functioning and variables related to psychological well-being.

COPD can have a substantial effect on the physical, emotional and social aspects of patients' lives. Activities of daily living are often considerably impeded and many COPD patients suffer from emotional problems such as anxiety and depression. HS instruments, QoL instruments and physical indicators – e.g. spirometric values or walking tests – can show how patients' lives are affected by COPD. Furthermore, they can be useful in order to evaluate effects of a pulmonary rehabilitation programme (PRP). Beneficial outcomes of PRPs are well documented and previous research has indicated that rehabilitation can enhance patients' exercise capacity, HS, QoL and well-being. The magnitude of improvements, however, has varied considerably, both for physical tests and self-reported outcome variables. Also,

improvements in emotional well-being and QoL have tended to be weaker and less consistent than improvements in HS.

The second aim of the thesis was to assess short-term and longitudinal changes in HS and QoL after a pulmonary rehabilitation programme for a sample of female and male COPD patients, as compared to a sample of asthma patients referred to the same PRP.

A short inpatient PRP was followed by immediate positive changes on HS, QoL and exercise capacity for the sample of COPD patients. Significant improvements were observed for variables related to physical functioning; emotionally related variables changed considerably less, although in a positive direction. Surprisingly, changes in exercise capacity did not co-vary with changes in physically related HS or QoL variables. The PRP appeared to have similar effects for female and male COPD patients. In contrast to an asthma sample, however, most of the gains in HS and QoL for the COPD sample had vanished at six months follow-up.

List of papers

1. Haave E, Hyland ME & Engvik H.: Physical and emotional aspects of self-reported health status. A two-factor model of the short-form Breathing Problems Questionnaire. *Chronic Respiratory disease* 2005; 2(4):21-26.
2. Haave E, Hyland ME & Skumlien S.: The relation between measures of health status and quality of life in COPD. *Chronic Respiratory disease* 2006; 3(4):195-199.
3. Haave E, Hyland ME & Engvik H.: Improvements in exercise capacity during a 4 weeks pulmonary rehabilitation program for COPD patients do not correspond with improvements in self-reported health status or quality of life. *International Journal of COPD* 2007; 2(4).
4. Haave E, Skumlien S & Hyland ME.: Gender considerations in pulmonary rehabilitation. *Journal of Cardiopulmonary Rehabilitation and Prevention* (in press)
5. Haave E & Hyland ME.: Different short-term and longitudinal results on perceived health status for asthma and COPD patients after pulmonary rehabilitation. Patients living alone have the largest improvements in perceived quality of life. *Chronic Respiratory disease* (in press)

Most important abbreviations

COPD = Chronic obstructive pulmonary disease

HS = Health status

QoL = Quality of life

PRP = Pulmonary rehabilitation programme

PCA = Principal component analysis

ES = Effect size

ANOVA = Analysis of variance

ANCOVA = Analysis of covariance

6MWD = Six minutes walking distance (in meters)

6MWD % = Six minutes walking distance; presented as percent of expected values, adjusted for age, gender, weight and height

FEV1 = Forced expiratory volume in 1 second (in litres)

FEV1 % = Forced expiratory volume in 1 second; presented as percent of expected values, adjusted for age, gender and height.

BPQ = The Breathing Problems Questionnaire (10 items short version)

PQoL = The Perceived Quality of Life Scale

STAI = Spielberger's State and Trait Anxiety Inventory

SGRQ = The St George Respiratory Questionnaire

QOLS = The Quality of Life Scale

5PF = Five Personality Factors

Introduction

Perceived health status (HS) and quality of life (QoL) are regularly used outcome variables to evaluate the effect of various treatments for patients with chronic obstructive pulmonary disease (COPD). Although there is no consensus, the terms HS and health-related quality of life (HRQoL) are commonly used for scales where the items refer to the impact of disease on various experiences (1-5). Application of the term quality of life (QoL) often seems to be inconsistent, but there is some consensus that QoL should probably be reserved for scales where the items refer to life experiences but not in the context of disease. QoL is a broader concept than HS and includes factors such as social and psychological well-being and satisfaction with life (6), factors that may or may not be influenced by health or treatment. Factors that are closely related to health conditions – easily captured by disease-specific instruments – do not necessarily affect general QoL very much. Conversely, factors that are not health-related, and thus missed by disease-specific instruments, can make a significant difference in the assessment of general QoL.

Disease-specific HS questionnaires for patients with COPD quantify the impact of disease on patients' daily life, health and well-being (5), and they usually include items that address both physical and psychological aspects. Curtis et al (3) define health status as “the impact of health on a person's ability to perform and derive fulfilment from the activities of daily life”, and they claim that a patient's self-reported HS should include both health-related quality of life (HRQoL) and functional status. In other words, a HS instrument should invite the patients to report how their disease influences what they are able to do and how they feel in daily life. The short version of the Breathing Problems Questionnaire (7) (called BPQ throughout the thesis) satisfies these criteria, and its ten items cover a relatively broad range of activities and perceptions of well-being in everyday life.

In the COPD literature, relatively low associations between self-reported HS and measures of lung function are often reported (8-10). One explanation for the low associations between HS questionnaires and lung function could be that only total scores on the HS instrument are used. If the BPQ really captures the two mentioned aspects: functional status and HRQoL, then these two parts of the instrument should be differentially related to other variables. One would expect the functional status part of the instrument to be largely associated with physical performance tests, but less associated with psychological factors. The HRQoL part of the instrument, in contrast, is hypothesized to correlate strongly with variables that measure general quality of life and psychological well-being, while the associations with physical performance tests should be considerably lower (11-13). The analyses in paper 1 were conducted to investigate whether the short version BPQ can be used to measure not only self-reported HS as a whole, but also the two subdimensions hypothesised by Curtis et al. Previously it was shown that the 33 items of the full version BPQ tended to cluster around two such dimensions – “functional problems” and “negative evaluations” (4). The 10 items version, however, had not been validated for that purpose; hence an additional feature of paper 1 was to demonstrate that this two-dimensional solution applies to the shorter version too.

For COPD patients, measures of disease-specific HS (hereafter we use the term HS to include HRQoL) can be more or less correlated with measures of general QoL, since HS scales are multi-component, and each component may have a different relationship with QoL. Furthermore, HS and QoL measures can be more or less correlated with measures of disease severity, such as lung function or exercise capacity. Engström et al (14) found that physiological, functional and psychosocial consequences of COPD was only moderately related to each other. They concluded that the impact of COPD is best assessed by a battery of instruments that not only tap disease-specific effects, but also the burden on daily functioning and emotional well-being. Stureson and Branholm (15) discovered that in a group of COPD patients, satisfaction with life as a whole was unrelated to lung function but significantly associated with two subscores (emotional function and fatigue) of a disease-specific HS instrument. Fuchs-Climent et al (16) observed that generic QoL was independent of disease severity among COPD patients, which further emphasized the value of different types of evaluation. Results such as these indicate that it can be useful to distinguish between quality of life, health status and disease severity. In paper 2, we therefore investigated associations

between two measures of self-reported QoL, two measures of self-reported HS plus clinical variables and neuroticism in a sample of COPD patients. Our aim was to investigate to what extent it is meaningful to discriminate QoL from the different components of HS.

COPD can have a substantial effect on the physical, emotional and social aspects of patients' lives (17). Activities of daily living are often considerably impeded (18) and many COPD patients suffer from emotional problems such as anxiety and depression (19). HS instruments, QoL instruments and physical indicators – e.g. spirometric values or walking tests – can show how patients' lives are affected by COPD. Furthermore, they are useful to evaluate effects of pulmonary rehabilitation programs (PRPs). Beneficial outcomes of PRPs are well documented (20-23), and previous research has indicated that pulmonary rehabilitation can enhance patients' exercise capacity, HS, QoL and well-being (24-30). The magnitude of improvements, however, has varied considerably, both for physical tests and self-reported outcome variables. Also, improvements in emotional well-being and QoL have tended to be weaker and less consistent than improvements in HS (31-35).

In paper 3, we assessed a sample of COPD patients on a set of outcome variables before and after a 4 weeks inpatient PRP. The first aim of our study was to assess whether physically related variables would improve more than emotionally related variables, since the rehabilitation program had a main focus on physical exercise. Since COPD is a chronic disease, we did not expect statistically significant changes in lung function for the sample. However, if the PRP had a positive effect, we expected that exercise capacity (walking distance) and physically oriented questionnaire scores would improve considerably. We also expected that emotionally oriented questionnaire scores such as emotional HS, general QoL and trait anxiety would improve, but to a smaller degree.

Few studies have investigated whether change in one outcome variable correlates with change in another outcome variable. The second aim of our study was therefore to assess the relations between changes in different types of outcome variables. Our main expectation was that changes in exercise capacity would be at least moderately related to changes in perceived HS and/or QoL – particularly to physically related subscores.

COPD represents a growing health problem among women (36;37). Whether women are more susceptible than men to development of this disease remains controversial (38-40), but results have indicated that physicians under-diagnose COPD in females (41) and a recent study suggested that women with COPD develop symptoms that reduce perceived health status at a younger age than men (42). Also, it has been shown that with equal predicted lung function values, female COPD patients tend to have lower exercise capacity and worse HS scores than their male counterparts (43). In other words, there may be gender differences in the clinical manifestations of this disease.

A recent review (44) stated that the impact of COPD in women is significantly understudied, and it was speculated that female and male COPD patients may show different responses to various forms of treatment. Therefore, in paper 4, we addressed two central research questions: Did the four weeks PRP have different effects for men and women? Were there any differences between female and male COPD patients referred to an inpatient PRP? HS, QoL, anxiety, lung function and exercise capacity were compared cross-sectionally and longitudinally. Additionally, we analyzed associations between different outcome measures, which could be important for the interpretation of eventual gender differences.

Several studies have addressed the questions of short-term versus long-term effects of PRP (27;28;34;45-56). The majority of PRP studies, however, have been conducted for samples of patients with COPD, and only a few reports have used asthma samples (57) or combined samples of COPD and asthma patients (47;58). Therefore, although both these diagnoses represent obstructive lung disease, it is still an open question whether patients in the two groups react similarly to PRPs on an immediate or long-term basis. In paper 5, we compared the short and long-term changes in HS, QoL and anxiety scores for COPD patients versus asthma patients. This was the main purpose of the study.

To summarize, there were two main aims of this thesis: The first aim was to examine closer the relations between HS, QoL and physical function among COPD patients. Secondly, we wanted to assess short-term and longitudinal changes in HS and QoL after a short inpatient PRP for a sample of female and male COPD patients, as compared to a sample of asthma patients referred to the same PRP.

Subjects and Methods

All papers include lung patients referred to a 4 weeks inpatient pulmonary rehabilitation programme (PRP) at a small hospital in the south-east of Norway.

Two separate samples/studies

The thesis is based on data from two different samples of patients.

The first sample provided the data for papers 1 and 2. This was a cross-sectional study, in which a sample of COPD patients was assessed on several variables once; immediately before the start of a rehabilitation programme.

The second sample – a combined sample of COPD and asthma patients – was assessed immediately before and after the rehabilitation programme and at follow-up six months later. Data from this longitudinal study were analysed in papers 3 – 5. Since the main focus of the thesis is COPD, results for asthma patients are represented only in one paper (paper 5), in order to illustrate longitudinal differences between COPD and asthma patients after a PRP. Due to different degrees of completion of tests and questionnaires, N will vary between different analyses conducted on the same sample.

Ethics

All patients in both samples were informed that participation in the research projects was voluntary and that information would be treated confidentially. Those who wanted to participate gave their written consent.

The regional ethical committee had approved both studies in advance.

Rehabilitation programme

Patients participated in a four weeks inpatient, multidisciplinary PRP. All patients were exposed to the same 4 weeks activity plan, which comprised physical exercise, educational lectures, lifestyle change support and social sharing with other COPD patients. The programme consisted of three to four 45 min educational or exercise group sessions all weekdays. Physical exercise was conducted individually and in groups; outdoors, in a gymnasium and in a warm swimming pool. Educational lectures were given by physicians, nurses, physiotherapists, psychologists, occupational workers and social workers. The lectures covered topics such as: Causes, mechanisms and treatment of COPD, living with chronic disease, optimal physical exercise and social rights for pulmonary patients. Patients were seen at least weekly by their attending physician, and issues such as medication or nutrition were followed up regularly by nurses. All patients were given individual appointments with physiotherapist. Individual appointments with social worker or psychologist were given as needed. While still at the hospital, patients were encouraged to continue with physical exercise after discharge, but no maintenance program was applied in the follow-up period six months after discharge.

Sample 1

- ✓ COPD patients
- ✓ Asked for participation: N = 160
- ✘ Did not want to participate: N = 40
- ✘ Reduced vision prevented tests: N = 2
- ✓ Enrolled in the study: COPD patients: N = 118
- ✘ Excluded due to change of diagnosis during the stay at the hospital: N = 8
- ✓ COPD patients with diagnosis confirmed: N = 110

✘ Reduced N due to insufficient completion of tests and questionnaires lead to:

Paper 1

- ◆ A total of N = 97 were suitable for most data analyses
- ✓ N = 93 in the analyses entailing 6MWD

Paper 2

- ◆ A total of N = 105 were suitable for most data analyses
- ✓ N = 102 in the analyses entailing 5PF
- ✓ N = 90 in the analyses entailing SGRQ

Sample 2

- ✓ COPD and asthma patients
- ✓ Asked for participation: N = 354; COPD (N = 249), asthma (N = 105).
- ✘ Did not return envelopes: N = 133
- ✓ Enrolled in the study: N = 221; COPD (N = 155) and asthma (N = 66) patients.

COPD patients:

Enrolled: N = 155

Completed questionnaires at t1; 2 weeks before the PRP: N = 155

Completed questionnaires at t2; 2 weeks after the PRP: N = 110

Completed questionnaires at t3; 6 months after the PRP: N = 96

Performed walking test at T1; first week of the PRP: N = 118

Performed walking test at T2; last week of the PRP: N = 104

Completed questionnaires at t1, t2 and also walking tests at T1 and T2: N = 95

Completed questionnaires at t1, t2, t3 and also walking tests at T1 and T2: N = 81

Asthma patients:

Enrolled: N = 66

Completed questionnaires at t1; 2 weeks before the PRP: N = 66

Completed questionnaires at t2; 2 weeks after the PRP: N = 45

Completed questionnaires at t3; 6 months after the PRP: N = 40

Performed walking test at T1; first week of the PRP: N = 39

Performed walking test at T2; last week of the PRP: N = 33

- ✘ N was reduced due to drop-out, change of diagnosis during the PRP or insufficient completion of tests and questionnaires at different point in time. This provided the following sample sizes for the papers:

Paper 3

- ✓ COPD patients only; measured before and immediately after the PRP. N = 95 were considered suitable for data analyses; only patients with all actual variables (lung function, walking tests and questionnaires) measured immediately pre and post rehabilitation intact were included in these analyses.
- ✘ Of these 95, N = 3 were excluded due to change of diagnosis during the PRP
- ◆ N = 92 COPD patients analysed

Paper 4

- ✓ COPD patients only, questionnaires completed at all points in time (t1 – t3), N = 96. For walking tests (T1 and T2), N = 81.
- ✘ Excluded N = 4 due to change of diagnosis during the PRP
- ◆ N = 92 patients – 46 females and 46 males – included in the data analyses.

Paper 5

- ✓ COPD and asthma patients, measured at all points in time (t1 – t3): N = 136
- ✘ Excluded N = 4 due to change of diagnosis during the PRP
- ◆ N = 132 patients (COPD N = 92, asthma N = 40) included in the data analyses.

Please notice that the samples in papers 3 and 4 are not identical.

The five papers; subjects and methods

Paper 1

Analyses in paper 1 were conducted on a sample of 97 COPD patients. First, we used a principal component analysis (PCA) to examine the internal structure of the BPQ. Then, based on the results of the PCA, we constructed two subscores of the BPQ. Finally, we correlated the BPQ total scores and subscores to a set of other variables; personality traits, general perceived quality of life, happiness, exercise capacity and lung function.

Perceived health status (HS) was measured by the short version of the Breathing Problems Questionnaire (7). The BPQ short version was developed as a purpose-specific and disease-specific instrument for measuring changes in perceived health status among COPD patients. It has 10 items, each with a scoring range 0 – 3, which can be added to a total score that ranges from 0 to 30. Higher BPQ scores mean worse health status.

Perceived quality of life (QoL) and happiness were measured by the Perceived Quality of Life Scale (59), which measures people's satisfaction with life over several different domains. QoL was calculated as the mean of the first 19 items of the PQoL, in which the participants rate their satisfaction on an 11-point end-anchored scale from 0 ("extremely dissatisfied") to 10 ("extremely satisfied"). (Higher PQoL scores mean better quality of life.) Happiness was measured by one item (PQoL20) that measures happiness ("How happy are you?") on an 11-point scale from 0 ("extremely unhappy") to 10 ("extremely happy").

Personality traits were measured by the Five Factor Model of personality by 20 selected adjective scales from 5PFa (60). The five factors are: Surgency, agreeableness, conscientiousness, emotional stability/neuroticism and openness to experience.

Exercise capacity was measured by 6-minute walking tests (6MWD) according to ATS guidelines (61). All tests were conducted indoors, along flat, straight corridors with 30 meters marked walking courses. Patients were instructed to walk as far as possible for 6 minutes, but permitted to slow down, to stop, and to rest as necessary.

Lung function was measured as forced expiratory volume in 1 s (FEV1) recorded from the better of two flow-volume curves (Jaeger, Masterlab) and presented as percent of expected values, adjusted for age, gender and height (FEV1 %) (62).

Paper 2

Analyses in paper 2 were conducted on a sample of 105 COPD patients.

First, we calculated correlation coefficients and ran a PCA in order to investigate associations between two instruments measuring disease-specific HS, two instruments measuring general QoL, personality trait emotional stability/neuroticism, exercise capacity and lung function.

HS was measured by two disease-specific questionnaires; the short version of the BPQ and the St George Respiratory Questionnaire (SGRQ).

In addition to the total score of the BPQ, a BPQ physical subscore (BPQ phys) was calculated by adding items 1 – 4 and a BPQ emotional subscore (BPQ emo) was calculated by adding items 7 – 10. The SGRQ is a 76-item questionnaire for self-completion (63). Responses are given partly on scales, partly as “right”/”wrong”. The SGRQ gives a total score (SGRQ tot) as well as sub-scores for the degree of respiratory symptoms (SGRQ symp), the level of activity restriction (SGRQ act) and the impact of the pulmonary disease (SGRQ imp). For both instruments, higher scores mean worse health status.

QoL was measured by the PQoL and the Quality of Life Scale (QOLS) (64;65); only total scores were used for these instruments.

Personality trait emotional stability/neuroticism, exercise capacity and lung function were measured as in paper 1.

Paper 3

In paper 3, a sample of 92 COPD patients was assessed on a set of different questionnaire-based indicators immediately before and after the 4 weeks pulmonary rehabilitation programme. We measured disease-specific HS, general perceived QoL and trait anxiety.

HS was measured by the BPQ; both the total score and the two subscores emotional HS and physical HS were included in the analyses.

QoL was measured by the PQoL; in addition to total scores two subscores were included in the analyses; a physical score (PQoL phys) and a social score (PQoL social).

Anxiety was measured by the trait part of Spielberger's state/trait anxiety inventory (STAI) (66). The scale consists of 20 questions, each with a scoring range 1 – 4, some of them in reversed order, which can be added to calculate a trait anxiety total score that ranges from 20 to 80.

Exercise capacity and lung function were measured at the start and near the end of the rehabilitation programme, by the same methods as in papers 1 and 2.

T-tests for paired samples were used to analyze changes in scores over time. To evaluate the magnitude of changes from before to after the PRP, Cohen's *d* was used as an estimate of effect size (ES). It was calculated by dividing the mean change score for a variable with the pooled standard deviation of raw scores on the same variable, from before to after rehabilitation. Values of *d* were interpreted as follows: $d < 0.2$ = small effects, $0.2 \leq d < 0.5$ = medium effects, $d \geq 0.5$ = large effects. For the purpose of analyzing associations between variable *changes*, we did as follows. Using the criterion of change in walking tests ($\Delta 6\text{MWD}$), patients were allocated into one of three groups: Group 1 = worsening or no improvement ($\Delta 6\text{MWD} \leq 0$ meters), $N = 29$; Group 2 = small or moderate improvement ($0 \text{ meters} < \Delta 6\text{MWD} \leq 40$ meters), $N = 32$; Group 3 = large improvement ($\Delta 6\text{MWD} > 40$ meters), $N = 31$. Then, these three groups of patients were tested for changes over time on other variables by repeated measures ANCOVAs. Age and gender were used as covariates in these analyses.

Paper 4

A sample of 92 COPD patients – 46 females and 46 males – was assessed on a set of different questionnaire-based indicators immediately before and after the 4 weeks pulmonary rehabilitation programme and at six months follow-up. (As noted earlier, this sample was not identical to the sample in paper 3, although there was considerable overlap.)

As in paper 3, we measured total scores and subscores of disease-specific *HS* and general perceived *QoL* plus *trait anxiety*. *Exercise capacity and lung function* were measured at the start and near the end of the rehabilitation programme, by the same methods as in papers 1 and 2.

In this paper, exercise capacity values were presented both as unadjusted values (6MWD) in meters and as percent of expected values, adjusted for age, gender, weight and height (6MWD %) (67).

Lung function was presented as unadjusted values in litres (FEV1) and as percent of expected values, adjusted for age, gender and height (FEV1 %) (62).

ANOVAs and multiple regression analyses were used to check for gender differences on all variables at the different times of measurement. The multiple regression analyses were used in order to assess gender differences in exercise capacity and self-reported variables, after controlling for differences in lung function, since there was a statistically significant gender difference in FEV1 %. Repeated measures ANOVAs were first used to test changes over time for the whole sample and secondly for interaction effects gender x time. Gender x time ANCOVAs were also conducted with FEV1 % at T1 as a covariate, to test gender differences in self-report variables and walking distance while controlling for lung function. Pearson correlation coefficients were calculated to test associations between variables.

Paper 5

A combined sample of 132 COPD patients – 92 COPD patients and 40 asthma patients – was assessed on a set of questionnaire-based indicators immediately before and after the 4 weeks pulmonary rehabilitation programme and at six months follow-up.

We measured total scores of disease-specific *HS* (BPQ), general perceived *QoL* (PQoL) and *trait anxiety* (STAI). Also, *cohabitation status* was registered as a dichotomous variable defined by asking patients to answer yes or no to the question: “Are you living alone?” These scores were used in paper 5.

We used Pearson Chi-square test to check for difference in female percentage and t-test for independent samples to analyse age difference between the two diagnostic groups. ANCOVAs for repeated measures assessed changes in BPQ, PQoL and STAI for the whole sample plus group x time effects. In the group x time analyses for asthma versus COPD patients, gender and cohabitation were used as covariates. We also tested whether rehabilitation effects were different for patients with different cohabitation status. In these analyses, gender and diagnosis were used as covariates. Cohen’s *d* was used as an estimate of effect size (ES).

Additionally, for analyses purposes in this thesis, patients with different cohabitation status were also tested for rehabilitation effects on three different PQoL subscores; PQoL physical = mean of items 1, 2, 4, 5 and 19, PQoL social = mean of items 8 –18 and PQoL cognitive = mean of items 3 and 6.

Results

Paper 1

The analyses in paper 1 were conducted to investigate whether the BPQ can be used to measure not only self-reported HS as a whole, but also two subdimensions – “functional status” and “health-related quality of life” – that had previously been hypothesised in the COPD literature (68). Results in paper 1 indicated a two-component solution for the short-version BPQ, which was consistent with previous data using the longer version (4). In our PCA the three first eigenvalues were 3.91, 1.43 and 0.87, and the ten different items of the short-version BPQ loaded in a meaningful way on the two components. However, we found that self-reported “physical health status” and “emotional health status” would be the most appropriate labels to describe what is measured in the two dimensions of the BPQ. Both of the BPQ subscores correlated statistically significantly with general perceived QoL, but QoL was more closely associated with the emotional subscore than with the physical subscore. As expected, physical HS was highly associated with exercise capacity while emotional HS was highly associated with emotional stability and happiness. Lung function (FEV1 %) was more highly associated with physical HS than with emotional HS, but none of these associations were strong.

To check that our interpretations regarding a two-factor solution would be similar across factoring methods, we ran exploratory factor analyses with alternative methods for factor extractions and rotations in addition to the PCA. Overall, these analyses gave very similar results.

For example, a factor analysis with principal axis factoring as extraction method and direct oblimin rotation resulted in the pattern matrix (table 1) and the structure matrix (table 2) presented below. This analysis indicated a two factor solution with correlated factors, in which the two factors correlated 0.48. SPSS 12.0.1 was used for these analyses.

Table 1. Pattern matrix

Variables	Factors	
	1	2
Speed on the flat (item 1)	0.87	- 0.12
Distance on the flat (item 2)	0.64	- 0.09
Bath or shower (item 3)	0.61	0.08
Light gardening or DIY (item 4)	0.55	0.12
Family or friends (item 6)	0.42	0.39
Energy (item 5)	0.37	0.21
Anxiety (item 10)	- 0.10	0.84
Depression (item 9)	0.13	0.65
Sleep (item 8)	- 0.05	0.57
Social gatherings (item 7)	0.16	0.42

Table 2. Structure matrix

Variables	Factors	
	1	2
Speed on the flat (item 1)	0.82	0.30
Distance on the flat (item 2)	0.60	0.22
Bath or shower (item 3)	0.65	0.38
Light gardening or DIY (item 4)	0.61	0.38
Family or friends (item 6)	0.61	0.59
Energy (item 5)	0.47	0.39
Anxiety (item 10)	0.30	0.79
Depression (item 9)	0.44	0.71
Sleep (item 8)	0.22	0.54
Social gatherings (item 7)	0.36	0.49

In paper 1 – based on the PCA results – we suggested a simple scoring procedure to calculate two subscores of the BPQ: Adding items 1-4 gives a physical HS subscore and adding items 7-10 gives an emotional HS subscore. The item scales (0-3) of the BPQ may be considered dubious as to having the properties of real interval scales; hence this represents a weakness of the study when conducting PCAs and factor analyses with these variables. However, the conceptual meaningfulness of item groupings and the associations between the two component scores and other variables supported our suggestions and conclusions.

A confirmatory factor analysis (CFA) using AMOS 7.0 showed that our scoring model – with items 1-4 loading on a physical factor while items 7-10 loading on an emotional factor – was acceptable (the two factors correlated 0.48, uncorrelated error terms for the observed variables, chi-square = 26.8, df = 19, p = 0.109, CFI (comparative fit index) = 0.958, RMSEA (root mean square error of approximation) = 0.065). CFA also showed that a two-factor model with items 1-3 loading on a physical factor while items 8-10 loading on an emotional factor might have been an even better solution (chi-square = 7.8, df = 8, p = 0.450, CFI = 1.000, RMSEA = 0.000, the two factors correlated 0.45). However, since ours was a small sample in CFA terms, and due to the limitations of item scales mentioned above, CFA results should be interpreted with caution.

Paper 2

Our main aim in this paper was to investigate to what extent it is meaningful to discriminate QoL from the different components of HS. We found that two QoL scales were highly correlated ($r = 0.73$) as were the two HS scales ($r = 0.83$), but the correlations between HS and QoL scales were lower (from $r = 0.55$ to $r = 0.60$). The results provided support for the assertion that QoL scales and HS scales measure something different and so it is worth including both types of scale in outcome assessment. However, when the subscales of the HS scales were considered, a somewhat different picture emerged. The PCA (table 3, below), supported by the table of correlations between variables (table 4, below), showed that the physical problems subscale of the BPQ and the activity subscale of the SGRQ measure the same concept, namely the effect of COPD on physical activities, and that these two subscales are highly correlated with both exercise capacity and to a lesser extent, lung function. The data also indicated that the emotional subscale of the BPQ and the symptoms subscale of the SGRQ measure the same latent variable as QoL, and that this latent variable is associated with trait emotional stability/neuroticism. As in paper 1, our results indicated that it can be important to distinguish two different components of HS, and that these two components have different associations to other, physically or emotionally oriented variables.

Table 3. Rotated matrix from the PCA

Variables	Components	
	1	2
QOLS tot	- 0.82	- 0.20
BPQ emo	0.80	0.29
PQoL tot	- 0.79	- 0.20
Neuroticism	- 0.74	0.04
SGRQ symp	0.71	0.20
SGRQ imp	0.60	0.56
6 min wd	0.02	- 0.88
BPQ phys	0.27	0.86
SGRQ act	0.26	0.79

Extraction method: Principal components.
Rotation method: Varimax.

Table 4. Correlations coefficients.

	6MWD	PQoL	QOLS	BPQ phys	BPQ emo	SGRQ symp	SGRQ act	SGRQ imp	Neuroti cism
FEV1 %	0.41	0.14	0.15	- 0.34	- 0.24	0.02	- 0.41	- 0.18	0.13
6MWD		0.17	0.21	- 0.68	- 0.25	- 0.14	- 0.52	- 0.41	0.05
PQoL			0.73	- 0.36	- 0.62	- 0.54	- 0.37	- 0.49	0.38
QOLS				- 0.39	- 0.60	- 0.53	- 0.33	- 0.50	0.41
BPQ phys					0.42	0.36	0.68	0.57	- 0.26
BPQ emo						0.53	0.38	0.67	- 0.58
SGRQ symp							0.41	0.48	- 0.41
SGRQ act								0.54	- 0.21
SGRQ imp									- 0.42

Correlation coefficients ≥ 0.50 in bold

Paper 3

The first aim in paper 3 was to assess whether physically related variables would improve more than emotionally related variables, since the rehabilitation program was focused primarily on physical exercise. Results confirmed these expectations (see table 5, below), as statistically significant improvements were observed for exercise capacity and for the total scores and the physically related subscores of HS and QoL, while no statistically significant improvements were observed for the emotional HS component, the social QoL component or for trait anxiety. We also observed a statistically significant improvement in lung function for the sample, which was unexpected, since other rehabilitation studies do not tend to find such effects (16;69). Adjustment of medications and/or better medical compliance might possibly be an explanation for the improvements of lung function among patients in our study.

Table 5. Scores before and after the rehabilitation programme. N = 92

Variables	Scores before rehabilitation: Means (SD)	Scores after rehabilitation: Means (SD)	p-values	Effect size Cohen's d
FEV1 %	50.78 (18.92)	53.23 (19.41)	p = 0.001	0.13
6MWD	500.54 (114.61)	528.42 (123.85)	p < 0.001	0.23
BPQ total	10.83 (5.39)	9.99 (5.71)	p = 0.006	0.15
BPQ phys	4.30 (2.35)	3.88 (2.40)	p = 0.001	0.18
BPQ emo	3.60 (2.49)	3.39 (2.57)	p = 0.236	0.08
PQoL total	5.06 (1.67)	5.36 (1.70)	p = 0.014	0.18
PQoL phys	4.62 (1.94)	5.15 (1.88)	p = 0.001	0.28
PQoL social	5.10 (1.76)	5.31 (1.79)	p = 0.072	0.12
STAI	42.73 (10.77)	42.38 (11.61)	p = 0.610	0.03

The second aim in paper 3 was to assess the relations between changes in different outcome variables. We expected that changes in exercise capacity would be related to changes in perceived HS and QoL – especially to the physically related subscores. If patients responded well to the PRP by increasing their 6 minutes walking distance, this should be reflected by

corresponding improvements in physical HS and possibly also in physically related QoL. Surprisingly, these expectations were disconfirmed, since longitudinal associations between exercise capacity and other outcome variables were missing. While the 6MWD was significantly correlated to other variables cross-sectionally, changes in walking distance were unrelated to changes in the other outcome variables (see table 6, below). Our results suggest that COPD patients do not respond uniformly to a PRP, or to different parts of a PRP. Furthermore, they indicate that it is important to use a set of different instruments and tests for evaluation purposes, since both subjective and objective improvements can be important for the patients.

Table 6. Changes in walking distance related to changes in the other main variables

Variables		Group 1: Worsening or no improvement on the 6MWD	Group 2: Small or moderate improvement on the 6MWD	Group 3: Large improvement on the 6MWD	Group x Time
		N = 29	N = 32	N = 31	p Value
BPQ tot	t1	11.8 (5.3)	10.2 (6.2)	10.5 (4.6)	p = 0.650
	t2	10.5 (5.6)	9.5 (6.6)	10.0 (4.9)	
BPQ phys	t1	4.7 (2.4)	4.1 (2.5)	4.2 (2.1)	p = 0.900
	t2	4.1 (2.4)	3.7 (2.7)	3.9 (2.1)	
PQoL tot	t1	4.7 (1.6)	5.2 (1.7)	5.2 (1.7)	p = 0.586
	t2	5.2 (1.7)	5.4 (1.9)	5.5 (1.6)	
PQoL phys	t1	4.1 (1.9)	4.9 (1.9)	4.9 (1.9)	p = 0.507
	t2	4.8 (1.7)	5.2 (2.2)	5.4 (1.6)	
STAI	t1	44.4 (12.2)	42.2 (9.5)	41.6 (10.8)	p = 0.366
	t2	44.0 (12.8)	43.1 (12.3)	40.2 (9.6)	
FEV1 %	t1	51.1 (21.2)	48.7 (16.9)	52.7 (19.0)	p = 0.925
	t2	53.4 (22.2)	50.8 (17.7)	55.6 (18.7)	

Group1: ($\Delta 6MWD \leq 0$ meters), Group 2 : ($0 < \Delta 6MWD \leq 40$ meters), Group 3 : ($\Delta 6MWD > 40$ meters).

Paper 4

Paper 4 addressed two central research questions: Did the four weeks PRP have different effects for men and women? Were there any differences between female and male COPD patients referred to inpatient pulmonary rehabilitation? Additionally, we analyzed associations between different outcome measures, which could be important for the interpretation and discussion of gender differences, if any such differences were discovered.

Table 7. Longitudinal Results for Women and Men

Variables		Mean (SD)	Mean (SD)	Mean (SD)	Gender x Time
		t1	t2	t3	p Value
BPQ tot	women	10.3 (5.2)	9.4 (5.1)	10.3 (5.7)	p = 0.677
	men	10.4 (4.6)	9.6 (5.4)	10.0 (5.8)	
PQoL tot	women	5.2 (1.5)	5.3 (1.5)	5.3 (1.4)	p = 0.521
	men	5.1 (1.6)	5.5 (1.7)	5.3 (1.7)	
STAI	women	44.1 (11.6)	43.5 (11.4)	43.7 (11.5)	p = 0.656
	men	41.4 (10.0)	41.3 (10.5)	42.3 (11.1)	
		T1	T2		
6MWD	women	506.1 (105.6)	530.1 (122.0)	p = 0.346	
	men	509.5 (127.9)	544.0 (131.1)		
6MWD %	women	98.1 (19.0)	102.5 (21.3)	p = 0.484	
	men	88.6 (22.4)	94.4 (22.5)		
FEV1	women	1.4 (0.4)	1.5 (0.5)	p = 0.773	
	men	1.5 (0.7)	1.6 (0.7)		
FEV1 %	women	57.9 (17.9)	61.2 (20.1)	p = 0.562	
	men	45.5 (19.0)	47.9 (18.0)		

For 6MWD, N(women) = 41 and N(men) = 40. For FEV1 % and STAI, N(women) = 45 and N(men) = 46. For all other measures, N = 46 for both genders.

The results in table 7 (above) illustrate our findings that female and male COPD patients tended to respond similarly to a four weeks inpatient PRP as no significant gender x time effect was discovered for any variable, over any period of time, including all subscores on the HS and QoL instruments. During their stay at the clinic, both women ($p = 0.004$, $ES = 0.21$) and men ($p < 0.001$, $ES = 0.26$) had statistically significant improvements with moderate effect sizes on the 6MWD. In both gender groups, HS scores improved from immediately before to immediately after the PRP, but reverted at follow-up. The male group had somewhat larger improvements in QoL scores than females immediately after the PRP, but this difference was smaller at follow-up. Anxiety scores changed very little; however with no substantial gender differences.

For self-report measures, no statistically significant gender difference in average scores were observed for any variable, at any time of measurement with or without controlling for FEV1 %. Females had statistically significant higher mean FEV1 % than males. 6MWD values were similar for the two gender groups. Females had larger 6MWD % values than males, but this difference disappeared after controlling for FEV1 %. One odd observation deserves a little attention: Both gender groups in our study had mean scores close to 100 on the 6MWD %, which was interesting for two reasons. First, COPD patients are not expected to have normal values on a walking test (6MWD %) which was standardized for healthy persons (67). Secondly, de Torres et al (70) observed the same phenomenon and concluded that there is probably a need to develop predictive values for 6MWD in different areas of the world. We agree to this.

Walking distance was highly associated to lung function while QoL (total score PQoL) was highly associated to anxiety. HS (total score BPQ) was moderately associated to all the other variables. Very low associations were observed between QoL/anxiety versus exercise capacity/lung function.

In paper 5, we compared our COPD sample to a sample of asthma patients for short and long-term changes in HS, QoL and anxiety scores after the PRP. The asthma group had significantly more females and a lower mean age than the COPD group.

Asthma and COPD patients had different longitudinal development on HS, while less such differences on QoL and trait anxiety levels. The development in scores for the two groups is depicted in table 8, below.

Table 8. Mean scores at t1, t2 and t3 for the COPD (N = 92) and Asthma (N = 40) group

Variable	Diagnosis	t1	t2	t3	Group x Time
BPQ	COPD	10.3 (4.9)	9.5 (5.2)	10.2 (5.7)	p = 0.013
	Asthma	9.8 (5.0)	9.6 (5.3)	8.7 (5.1)	
PQoL	COPD	5.2 (1.5)	5.4 (1.6)	5.3 (1.5)	p = 0.491
	Asthma	5.5 (1.8)	5.8 (1.7)	5.8 (1.8)	
STAI	COPD	42.8 (10.8)	42.4 (10.9)	43.0 (11.3)	p = 0.350
	Asthma	42.2 (10.8)	40.9 (10.8)	40.2 (11.6)	

The COPD group had improved on HS ($p = 0.005$) and QoL ($p = 0.042$) scores immediately after the PRP but then relapsed at follow-up, while trait anxiety scores changed very little. In contrast, the asthma patients had less immediate HS improvement but made progress in the follow-up period and actually achieved a significant positive change in BPQ scores from t1 to t3 ($p = 0.040$). Asthma patients also had a somewhat better long-term development than COPD patients on QoL and anxiety, but the improvements from t1 to t3 on the PQoL ($p = 0.122$) and the STAI ($p = 0.134$) did not quite reach levels of significance for the asthma group. The positive PQoL development from t1 to t2 was significant for the COPD group while not for the asthma patients. The reason for this was probably the difference in sample sizes; effect sizes in the two groups (COPD = 0.16, asthma = 0.17) were similar. Overall, changes in HS, QoL and anxiety for the two groups were not large; effect sizes were small or moderate only.

An additional finding in this paper was that QoL changes were small for patients living together with someone, while patients living alone improved their QoL immediately after the PRP and the improvement was sustained in the follow-up period (shown in table 9, below).

Table 9. Mean PQoL total scores at t1, t2 and t3 for patients living alone (N = 35) and patients not living alone (N = 97)

Cohabitation	t1	t2	t3	Group x time
Alone	4.8 (1.6)	5.4 (1.7)	5.4 (1.7)	p = 0.039
Not alone	5.4 (1.6)	5.6 (1.6)	5.5 (1.6)	

For all patients living alone (COPD plus asthma patients), there was a statistically significant QoL improvement from before rehabilitation to follow-up six months after the PRP ($p = 0.017$), and this tendency existed within both groups of patients since there was no statistically significant interaction effect diagnosis x cohabitation x time. Effect sizes for PQoL change from t1 to t3 were 0.37 for COPD patients living alone and 0.31 for asthma patients living alone, which indicate that these changes tended to be relatively large, at least as compared to the other analysed changes in our study.

Analyses performed on *subscores* of the PQoL showed that the differences in longitudinal QoL score development between the two cohabitation groups were mainly due to the PQoL social subscores (shown in table 10, below).

Table 10. Mean PQoL subscores at t1, t2 and t3 for patients living alone (N = 35) and patients not living alone (N = 97)

Variable	Cohabitation	t1	t2	t3	Group x time
PQoL social	Alone	4.7 (1.8)	5.3 (1.8)	5.3 (1.8)	p = 0.007
	Not alone	5.6 (1.7)	5.6 (1.7)	5.5 (1.7)	
PQoL physical	Alone	4.8 (1.9)	5.4 (2.0)	5.3 (2.0)	p = 0.704
	Not alone	4.8 (1.8)	5.3 (1.8)	5.3 (1.9)	
PQoL cognitive	Alone	6.0 (2.0)	5.9 (2.2)	6.3 (2.0)	p = 0.577
	Not alone	6.1 (2.3)	6.1 (2.1)	6.1 (2.1)	

No statistically significant cohabitation x time effect was observed for HS or trait anxiety.

General discussion

Data from our first sample indicated that it can be important to distinguish two different components in a disease-specific health status instrument (BPQ) for pulmonary patients. One of these components appears to reflect psychological well-being, whereas the other component measures levels of activity and physical performance.

The manifestation of two different HS components illustrates a clinically important feature of COPD; an imbalance often exists between physical and emotional manifestations of the disease. In the clinic, one sometimes meet patients with severe, disabling COPD who are surprisingly calm about their condition – at other times patients who are deeply bothered by their breathing problems, however with spirometric values far better than expected from their clinical appearance. COPD is a somatic disease, predominantly characterized by a reduction of lung function, dyspnoea, lack of energy and an ensuing reduction of physical functioning as compared to healthy persons. A physical HS component captures these symptoms. In addition to the physical manifestations, COPD samples also tend to score higher than normal on negative affect variables such as anxiety and depression (19;71), which is likely to be reflected in an emotional HS component. However, in the COPD literature, associations between levels of lung function and emotional problems have generally been very low (14;72-74). Apparently, COPD *may* have a negative influence on perceived emotional status, but this is less obvious than the negative impact COPD has on perceived physical status. While perceived physical health status tend to be closely associated with pulmonary function, perceived emotional health status obviously depends on a more complex set of psychological, social and physiological processes; hence our results were not entirely surprising. However, they underscore the importance of evaluating both physical and emotional health status in COPD.

In our first sample, subscores of the BPQ and another disease-specific instrument (SGRQ) loaded differently on a physical versus an emotional HS component. BPQ physical subscore and the activity subscale of the SGRQ loaded on the physical factor. BPQ emotional subscore and the symptom subscale of the SGRQ loaded on the emotional factor, consistent with research showing that reporting of respiratory symptoms has an emotional basis (75;76). However, the impact factor of the SGRQ cross-loaded, showing that items in this subscale

were influenced by both latent variables. These results suggested that if the intention is to use the total score of an HS scale in addition to a QoL scale, then it makes little difference which scale is used. However, if the intention is to use a HS scale only, then the BPQ may be better as it provides a clearer separation between the underlying physical problem and the emotional latent variable compared with the SGRQ.

As was shown in paper 2, total scores on the two different HS instruments (BPQ and SGRQ) were highly correlated, as were total scores on two different QoL instruments (PQoL and QOLS). Correlations between HS and QoL scales were also statistically significant, but considerably lower. Thus, to a certain extent, these data supported the assertion that QoL scales and HS scales measure something different and so it is worth including both types of scale in outcome assessment.

However, our data also indicated that while physical HS loaded together with exercise capacity on a latent variable related to physical functioning, emotional HS loaded together with variables such as QoL and emotional stability/neuroticism on a latent variable characterised by psychological well-being. On the basis of these results, we stated that an HS scale may be adequate as a measure of outcome without the need to introduce a QoL measure, so long as the subscales of the HS measures are considered independently.

This statement was contradicted by our subsequent, longitudinal data, since results in paper 3 – changes in outcome variables from before to after rehabilitation – provided a more complicated picture. As expected, the physically related outcome variables generally improved more than variables related to well-being and emotional status. Physical HS improved more than emotional HS and there was no statistically significant improvement in either emotional HS or anxiety after the rehabilitation programme. Still, emotional HS was not an adequate outcome measure to replace QoL scores as we postulated in paper 2, since in contrast to emotional HS, total scores on the PQoL improved significantly.

Overall, the observation of statistically significant improvements in exercise capacity, HS total scores and QoL total scores – from immediately before to immediately after the PRP – was in line with a number of previous studies (25;28;32;35;46;47;49;51;77-83). Effect sizes have varied a lot across such reports; ours were in the middle or lower region. One reason for the modest results may be the relatively short duration of the PRP in our study. A recent meta-analysis of respiratory rehabilitation for COPD patients (84) reported a total of 31 randomised controlled trials (RCTs). Four of them were based on inpatient PRPs, with durations of 24, 8,

8 and 6 weeks. Only one of the 31 RCTs reported had a program as short as 4 weeks. In the light of this, large effect sizes could probably not be expected in our case.

The fact that we discovered no significant changes in anxiety levels for our sample was in line with Engstrøm et al (34) but contrary to the results of Garuti et al (26) who found significant reductions of anxiety and depression levels from before to after an inpatient PRP – and contrary to Withers et al (85) who observed significant improvements in anxiety and depression both immediately after a PRP and at 6 months follow-up. Also, a recent review showed that comprehensive PRPs for COPD patients tend to have significantly better short-term effects than standard care on anxiety and depression levels, although education alone or exercise alone had no effect. Two recent studies using cognitive therapy (86) and cognitive behavioural therapy (87) showed anxiety reduction among COPD patients. Such elements, however, were not systematically included in our PR program.

One possible reason for the discrepancy between the results mentioned above and ours may be the choice of measurement scales; we measured STAI trait anxiety – asking how one usually feels – while both Garuti and Withers, for example, used the hospital anxiety and depression scale (HADs) which assesses perceptions of anxiety and depression symptoms experienced during the last week. Another reason may be that PRPs tend to vary, both in content and duration, hence the relatively short duration and the large emphasize on exercise and education in our PRP may have made anxiety improvements less likely. Finally, the different COPD samples studied will vary as to anxiety levels pre rehabilitation, and the likelihood of significant anxiety reductions after a PRP is certainly less in a non-anxious sample. However, the average STAI scores in our sample (42.7) before the PRP was relatively high – both as compared to scores on reference groups in the STAI manual (66) and to a COPD sample (39.4) in a previous study (88) – hence an anxiety reduction after the PRP was probably not impossible for our sample.

Another interesting result from paper 3 was that when analyses were conducted for subscores of the PQoL, we found that a physically related QoL subscore improved more than a social QoL subscore – which was much in line with the HS subscores (see table 5). However, when running a PCA for the data in paper 3 (see table 11, below) – including the subscores of HS and QoL plus anxiety, exercise capacity and lung function – both of the QoL subscores loaded highest on the well-being component while the HS subscores split and loaded differently on the two components.

Table 11. Rotated matrix from the principal component analysis.

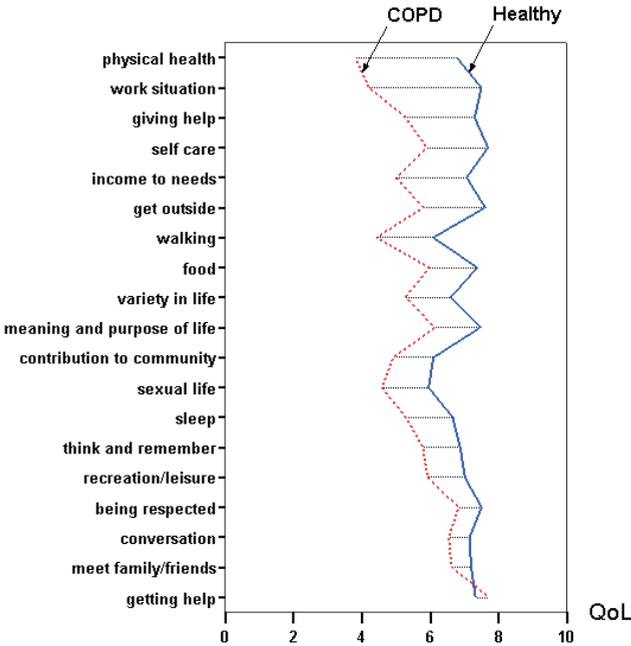
Variables	Components	
	1	2
PQoL social	- 0.88	0.18
STAI	0.87	0.07
PQoL physical	- 0.81	0.20
BPQ emo	0.75	- 0.33
6MWD	- 0.09	0.88
FEV1 %	- 0.04	0.82
BPQ phys	0.38	- 0.79

Extraction method: Principal components
 Rotation method: Varimax.

Taken together, results from our two samples showed the importance of assumptions and conclusions from cross-sectional data analyses being tested and eventually reconsidered by longitudinal results and measurement of change. Two variables with fairly comparable loadings on components/factors are not necessarily very highly correlated with each other. Also, even in the case when two such variables do correlate highly, their sensitivity to change can be different. In our samples, variables such as emotional stability/neuroticism and trait anxiety were very likely to have high loadings on a latent variable labelled “well-being”, but it may have been too optimistic to expect a significant improvement in e.g. trait anxiety after a 4 weeks PRP. Both emotional HS (BPQ emo) and general perceived QoL (PQoL total) would also be expected to load considerably on the well-being component, but such variables are more likely to improve significantly after rehabilitation. Only one of them (PQoL total), however, did.

We have shown in a previous paper (89) (see figure 1, below) that the largest gaps between COPD patients and healthy persons tend to be observed on items related to physical functioning. Since PQoL physical scores were lower than PQoL social scores at t1 (table 5) the potential for improvement may have been somewhat greater for PQoL physical. Also, since the PRP had a main focus on physical exercise, it was no surprise that the physical subscore showed the largest improvement after rehabilitation.

Figure 1



Estimated marginal means of the PQoL scores were calculated by using a general linear model with PQoL scores as dependent variables, group as fixed factor, and age, gender and personality factors as covariates.

A surprising observation, based on results from the sample in paper 3, was the fact that changes in exercise capacity was virtually unrelated to changes in HS and QoL – no matter whether total scores or subscores were considered. Although some earlier studies have reported low or moderate correlation coefficients between changes in exercise tolerance and changes in HRQoL (90), our observations were truly surprising; especially as regards the lack of correspondence between changes in walking distance and changes in physical HS. In fact, the group that worsened or had no improvement on the 6MWD actually showed slightly larger improvements on the physical HS scores than the group with large 6MWD improvement. Thus, an evaluation of results for a sample of COPD patient after rehabilitation can be very different based on whether a self-reported outcome measure or a test of physical performance is used. In our case, the patients evidently did not respond uniformly to the rehabilitation programme. Some patients managed to increase their exercise capacity considerably, while others appeared to think and feel better about their daily functioning or general satisfaction with life immediately after the PRP. Again, this shows the importance of evaluating both physical and emotional health status in COPD.

In paper 4, we compared female and male COPD patients immediately before and immediately after the PRP and at follow-up six months later. There was no statistically significant gender x time effect for any variable over any period of time; indicating that rehabilitation had relatively similar short and long term effects on female and male patients. Very few previous studies have tested for gender differences within treatment or rehabilitation for COPD patients. In one study (83), only the male COPD group improved on 6MWD, and the male group also tended to have the largest HS improvements. Another study (91) reported that long-term exercise therapy gave additional benefit in HS scores over short-term therapy, but only for males. Hence, although these reports suggested therapeutic interventions to be more effective for male than for female COPD patients, our data did not support such a conclusion. In fact, our results were more in line with a recent study from Canada (92). Although in this sample women improved more than men on one HS subscore (dyspnoea) immediately after rehabilitation, overall HS scores and 6MWD scores improved equivalently and significantly for both sexes. From a treatment perspective, this should be considered satisfactory. On the one hand, it could mean that a structured PRP has the same effects on female and male COPD patients. On the other hand, it could indicate that the program was flexible enough to suit patients of both sexes.

Additionally, in paper 4, we found that the female group had similar levels of self-reported HS, QoL and anxiety as the male group, but better lung function. This could mean that COPD hits women harder, which is bad. On the other hand, it could imply that women report more symptoms and hence are referred to PRPs at an earlier stage of the disease, which might actually be beneficial for the female sex. It has been pointed out that cultural factors may influence symptom reporting among COPD patients (93). For example, it may be more acceptable for women than for men to report shortness of breath.

It is important, however, to notice the low associations between physical test and self-reported variables in this study, which is similar to earlier reports (14;94;95). The correlation coefficients clearly indicated independence between “emotional” and “physical” variables. Thus, when comparing men and women across such variables, interpretations of results can be difficult. For example, since there was little connection between QoL and lung function in the sample, the fact that the female group had better lung function but equal QoL to the male group does not automatically mean that COPD has greater negative consequences for women. Previous studies analyzing gender differences on similar variables (42;96) seem to have largely overlooked this problem.

In paper 5, we evaluated to what degree the improvement from immediately before to immediately after rehabilitation was sustained after six months for the COPD sample, and the COPD patients (N = 92) were also compared to a smaller sample of asthma patients (N = 40) referred to the same PRP. HS and QoL had improved immediately after rehabilitation for the COPD group, but then relapsed at follow-up. Trait anxiety did scores for the sample remained stable over time. This development in scores was somewhat in contrast to the results of the asthma patients who, overall, had a better long-term development.

For our COPD sample, a significant positive short-term effect and subsequent relapse of HS and QoL scores during the follow-up period was comparable to previous research. In one study (97), outcome variables had improved 2 weeks after a PRP but deteriorated during the subsequent 6 months; another study found no improvements in HS one year after the programme (34). Follow-up regimes may produce better longitudinal results. For example, a COPD study with monthly follow-up sessions after the PRP found HS improvements to be present after six months but not after one year (46), while a procedure of weekly telephone calls and monthly reinforcement visits after rehabilitation produced only modest improvements (54). More comprehensive after-care procedures probably produce better results, since a weekly community-based maintenance exercise class, combined with a home exercise programme, proved to be an effective intervention for long term maintenance of improvements in HS and walking distance following pulmonary rehabilitation (98). Also, previous studies showing good long-term results after PRPs (49-51) all tended to comprise some form of aftercare, and results have even indicated that COPD patients require a differentiated aftercare program following rehabilitation (27). Since no systematic after-care was applied for our sample of patients, however, it was no great surprise that the COPD group had lost their gains in HS and QoL at six months follow-up.

Our results indicated that a short rehabilitation programme for COPD patients tended to have transient effects only, and effective follow-up procedures should be implemented if possible since modification of behavioural patterns, coping styles and emotional function probably requires longer periods of time for COPD patients (99). However, the best interventions to achieve this goal are not known today, and additional research is needed to supply knowledge about how different factors can have an impact on long-term results of short-term PRPs (48).

There were obvious limitations to our study. The design was quasi-experimental, many patients did not want to participate and – as expected – there was a considerable dropout from the project since patients were informed that they could withdraw from the study at any time without any consequences. Additionally, improvements in scores were only small or moderate, as shown by the effect sizes, which also tend to weaken our conclusions. In spite of these limitations, the study provided some implications for future studies to explore further.

A recent qualitative study of “what really matters” for patients with COPD showed that engagement in specific activities and social participation were considered to be of great importance (100). Interestingly, an additional observation in our study was that the main part of QoL improvements was discovered among patients living alone – a consistent finding in both the COPD and asthma sample. Also, on the social subscale of the QoL instrument, improvements were observed only for the subsample of patients living alone.

Because of distressing symptoms, pulmonary disease can reduce social activities for patients with or without a partner. The negative effect of this on QoL is probably larger among patients living alone, an assumption that was supported by the fact that single patients had lower average QoL before entering the PRP. A four weeks inpatient PRP may have counteracted feelings of isolation and recreated feelings of participation, and our results suggest that social sharing can be an important aspect of a PRP. However, there are other possible explanations. For example, patients living alone may have been more unconcerned about self-care and healthy lifestyle before PRP, making them more receptive for the programme interventions. Also, since patients living alone had lower baseline QoL scores, there was probably a larger potential for improvement in this group. Nevertheless, a QoL improvement sustained over 6 months for this subgroup of patients was a surprising observation; hopefully there will be possibilities in the future to further explore the importance of social factors for perceived health status and quality of life in pulmonary rehabilitation.

Conclusions

Our results indicated that it is meaningful to use both total scores and subscores of HS and QoL instruments to evaluate the impact of COPD on a person's life and the effects of pulmonary rehabilitation. Furthermore, it can be important to distinguish between variables related to physical functioning and variables related to psychological well-being.

A short inpatient PRP was followed by immediate positive changes on HS, QoL and exercise capacity for a sample of COPD patients. Significant improvements were observed for variables related to physical functioning; emotionally related variables changed considerably less, although in a positive direction. The PRP appeared to have similar effects for female and male COPD patients. In contrast to an asthma sample, however, most of the gains in HS and QoL for the COPD sample had vanished at six months follow-up.

References

- (1) Carone M, Jones PW. Health status "quality of life". [13], 22-35. 2000. European Respiratory Monograph.
Ref Type: Serial (Book,Monograph)
- (2) Carone M, Donner CF, Jones PW. Health Status measurement: an increasingly important outcome evaluation in COPD patients. *Monaldi Arch Chest Dis* 2001 August;56(4):297-8.
- (3) Curtis JR, Patrick DL. The assessment of health status among patients with COPD. *Eur Respir J Suppl* 2003 June;41:36s-45s.
- (4) Hyland ME, Bott J, Singh S, Kenyon CA. Domains, constructs and the development of the breathing problems questionnaire. *Qual Life Res* 1994 August;3(4):245-56.
- (5) Jones PW. Health status measurement in chronic obstructive pulmonary disease. *Thorax* 2001 November;56(11):880-7.
- (6) Bowling A. The conceptualization of functioning, health and quality of life. *Measuring health*. 2 ed. Buckingham: Open University Press; 1991. p. 1-8.
- (7) Hyland ME, Singh SJ, Sodergren SC, Morgan MP. Development of a shortened version of the Breathing Problems Questionnaire suitable for use in a pulmonary rehabilitation clinic: a purpose-specific, disease-specific questionnaire. *Qual Life Res* 1998 April;7(3):227-33.
- (8) Antonelli-Inc, Imperiale C, Bellia V, Catalano F, Scichilone N, Pistelli R, Rengo F. Do GOLD stages of COPD severity really correspond to differences in health status? *Eur Respir J* 2003 September;22(3):444-9.
- (9) Carone M, Donner CF, Jones PW. Health Status measurement: an increasingly important outcome evaluation in COPD patients. *Monaldi Arch Chest Dis* 2001 August;56(4):297-8.

- (10) Engstrom CP, Persson LO, Larsson S, Sullivan M. Health-related quality of life in COPD: why both disease-specific and generic measures should be used. *Eur Respir J* 2001 July;18(1):69-76.
- (11) Anderson KL. The effect of chronic obstructive pulmonary disease on quality of life. *Res Nurs Health* 1995 December;18(6):547-56.
- (12) Costa PT, Jr., McCrae RR. Neuroticism, somatic complaints, and disease: is the bark worse than the bite? *J Pers* 1987 June;55(2):299-316.
- (13) Engstrom CP, Persson LO, Larsson S, Sullivan M. Health-related quality of life in COPD: why both disease-specific and generic measures should be used. *Eur Respir J* 2001 July;18(1):69-76.
- (14) Engstrom CP, Persson LO, Larsson S, Sullivan M. Health-related quality of life in COPD: why both disease-specific and generic measures should be used. *Eur Respir J* 2001 July;18(1):69-76.
- (15) Stureson M, Branholm I. Life satisfaction in subjects with chronic obstructive pulmonary disease. *Work* 2000;14(2):77-82.
- (16) Fuchs-Climent D, Le Gallais D, Varray A, Desplan J, Cadopi M, Prefaut CG. Factor analysis of quality of life, dyspnea, and physiologic variables in patients with chronic obstructive pulmonary disease before and after rehabilitation. *Am J Phys Med Rehabil* 2001 February;80(2):113-20.
- (17) Guthrie SJ, Hill KM, Muers ME. Living with severe COPD. A qualitative exploration of the experience of patients in Leeds. *Respir Med* 2001 March;95(3):196-204.
- (18) McSweeney AJ, Grant I, Heaton RK, Adams KM, Timms RM. Life quality of patients with chronic obstructive pulmonary disease. *Arch Intern Med* 1982 March;142(3):473-8.
- (19) Kunik ME, Roundy K, Veazey C, Soucek J, Richardson P, Wray NP, Stanley MA. Surprisingly high prevalence of anxiety and depression in chronic breathing disorders. *Chest* 2005 April;127(4):1205-11.

- (20) Ambrosino N. Pulmonary Rehabilitation Programs; Outcomes in patients with chronic obstructive pulmonary disease. *Dis Manage Health Outcomes* 2002;10(9):535-42.
- (21) Celli BR. Pulmonary rehabilitation in patients with COPD. *Am J Respir Crit Care Med* 1995 September;152(3):861-4.
- (22) Lacasse Y, Wong E, Guyatt GH, King D, Cook DJ, Goldstein RS. Meta-analysis of respiratory rehabilitation in chronic obstructive pulmonary disease. *Lancet* 1996 October 26;348(9035):1115-9.
- (23) Lacasse Y, Brosseau L, Milne S, Martin S, Wong E, Guyatt GH, Goldstein RS. Pulmonary rehabilitation for chronic obstructive pulmonary disease. *Cochrane Database Syst Rev* 2002;(3):CD003793.
- (24) Buchi S, Villiger B, Sensky T, Schwarz F, Wolf C, Buddeberg C. Psychosocial predictors of long-term success of in-patient pulmonary rehabilitation of patients with COPD. *Eur Respir J* 1997 June;10(6):1272-7.
- (25) Finnerty JP, Keeping I, Bullough I, Jones J. The effectiveness of outpatient pulmonary rehabilitation in chronic lung disease: a randomized controlled trial. *Chest* 2001 June;119(6):1705-10.
- (26) Garuti G, Cilione C, Dell'Orso D, Gorini P, Lorenzi MC, Totaro L, Cirelli G, Clini E. Impact of comprehensive pulmonary rehabilitation on anxiety and depression in hospitalized COPD patients. *Monaldi Arch Chest Dis* 2003 January;59(1):56-61.
- (27) Ketelaars CA, bu-Saad HH, Schlosser MA, Mostert R, Wouters EF. Long-term outcome of pulmonary rehabilitation in patients with COPD. *Chest* 1997 August;112(2):363-9.
- (28) Singh SJ, Smith DL, Hyland ME, Morgan MD. A short outpatient pulmonary rehabilitation programme: immediate and longer-term effects on exercise performance and quality of life. *Respir Med* 1998 September;92(9):1146-54.
- (29) van Stel HF, Maille AR, Colland VT, Everaerd W. Interpretation of change and longitudinal validity of the quality of life for respiratory illness questionnaire

- (QoLRIQ) in inpatient pulmonary rehabilitation. *Qual Life Res* 2003 March;12(2):133-45.
- (30) Wijkstra PJ, van AR, Kraan J, Otten V, Postma DS, Koeter GH. Quality of life in patients with chronic obstructive pulmonary disease improves after rehabilitation at home. *Eur Respir J* 1994 February;7(2):269-73.
- (31) Arnold R, Ranchor AV, Koeter GH, de Jongste MJ, Wempe JB, ten Hacken NH, Otten V, Sanderman R. Changes in personal control as a predictor of quality of life after pulmonary rehabilitation. *Patient Educ Couns* 2006 April;61(1):99-108.
- (32) Benzo R, Flume PA, Turner D, Tempest M. Effect of pulmonary rehabilitation on quality of life in patients with COPD: the use of SF-36 summary scores as outcomes measures. *J Cardiopulm Rehabil* 2000 July;20(4):231-4.
- (33) de Torres JP, Pinto-Plata V, Ingenito E, Bagley P, Gray A, Berger R, Celli B. Power of outcome measurements to detect clinically significant changes in pulmonary rehabilitation of patients with COPD. *Chest* 2002 April;121(4):1092-8.
- (34) Engstrom CP, Persson LO, Larsson S, Sullivan M. Long-term effects of a pulmonary rehabilitation programme in outpatients with chronic obstructive pulmonary disease: a randomized controlled study. *Scand J Rehabil Med* 1999 December;31(4):207-13.
- (35) Ries AL, Kaplan RM, Limberg TM, Prewitt LM. Effects of pulmonary rehabilitation on physiologic and psychosocial outcomes in patients with chronic obstructive pulmonary disease. *Ann Intern Med* 1995 June 1;122(11):823-32.
- (36) Soriano JB, Maier WC, Egger P, Visick G, Thakrar B, Sykes J, Pride NB. Recent trends in physician diagnosed COPD in women and men in the UK. *Thorax* 2000 September;55(9):789-94.
- (37) Tanoue LT. Cigarette smoking and women's respiratory health. *Clin Chest Med* 2000 March;21(1):47-65, viii.
- (38) de Torres JP, Campo A, Casanova C, guirre-Jaime A, Zulueta J. Gender and chronic obstructive pulmonary disease in high-risk smokers. *Respiration* 2006;73(3):306-10.

- (39) Ringbaek T, Seersholm N, Viskum K. Standardised mortality rates in females and males with COPD and asthma. *Eur Respir J* 2005 May;25(5):891-5.
- (40) Silverman EK, Weiss ST, Drazen JM, Chapman HA, Carey V, Campbell EJ, Denish P, Silverman RA, Celedon JC, Reilly JJ, Ginns LC, Speizer FE. Gender-related differences in severe, early-onset chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 2000 December;162(6):2152-8.
- (41) Chapman KR, Tashkin DP, Pye DJ. Gender bias in the diagnosis of COPD. *Chest* 2001 June;119(6):1691-5.
- (42) de Torres JP, Casanova C, Hernandez C, Abreu J, Montejo de GA, guirre-Jaime A, Celli BR. Gender associated differences in determinants of quality of life in patients with COPD: a case series study. *Health Qual Life Outcomes* 2006;4:72.
- (43) de Torres JP, Casanova C, Hernandez C, Abreu J, guirre-Jaime A, Celli BR. Gender and COPD in patients attending a pulmonary clinic. *Chest* 2005 October;128(4):2012-6.
- (44) Varkey AB. Chronic obstructive pulmonary disease in women: exploring gender differences. *Curr Opin Pulm Med* 2004 March;10(2):98-103.
- (45) Behnke M, Taube C, Kirsten D, Lehnigk B, Jorres RA, Magnussen H. Home-based exercise is capable of preserving hospital-based improvements in severe chronic obstructive pulmonary disease. *Respir Med* 2000 December;94(12):1184-91.
- (46) Bestall JC, Paul EA, Garrod R, Garnham R, Jones RW, Wedzicha AJ. Longitudinal trends in exercise capacity and health status after pulmonary rehabilitation in patients with COPD. *Respir Med* 2003 February;97(2):173-80.
- (47) Cambach W, Wagenaar RC, Koelman TW, van Keimpema AR, Kemper HC. The long-term effects of pulmonary rehabilitation in patients with asthma and chronic obstructive pulmonary disease: a research synthesis. *Arch Phys Med Rehabil* 1999 January;80(1):103-11.

- (48) Foglio K, Ambrosino N, Agati S. Maintaining the benefits of pulmonary rehabilitation for patients with chronic obstructive pulmonary disease: where are we now? *Chron Respir Dis* 2007;4(3):131-3.
- (49) Goldstein RS, Gort EH, Stubbing D, Avendano MA, Guyatt GH. Randomised controlled trial of respiratory rehabilitation. *Lancet* 1994 November 19;344(8934):1394-7.
- (50) Griffiths TL, Burr ML, Campbell IA, Lewis-Jenkins V, Mullins J, Shiels K, Turner-Lawlor PJ, Payne N, Newcombe RG, Ionescu AA, Thomas J, Tunbridge J. Results at 1 year of outpatient multidisciplinary pulmonary rehabilitation: a randomised controlled trial. *Lancet* 2000 January 29;355(9201):362-8.
- (51) Guell R, Casan P, Belda J, Sengenis M, Morante F, Guyatt GH, Sanchis J. Long-term effects of outpatient rehabilitation of COPD: A randomized trial. *Chest* 2000 April;117(4):976-83.
- (52) Guyatt GH, Berman LB, Townsend M. Long-term outcome after respiratory rehabilitation. *CMAJ* 1987 December 15;137(12):1089-95.
- (53) Heppner PS, Morgan C, Kaplan RM, Ries AL. Regular walking and long-term maintenance of outcomes after pulmonary rehabilitation. *J Cardiopulm Rehabil* 2006 January;26(1):44-53.
- (54) Ries AL, Kaplan RM, Myers R, Prewitt LM. Maintenance after pulmonary rehabilitation in chronic lung disease: a randomized trial. *Am J Respir Crit Care Med* 2003 March 15;167(6):880-8.
- (55) Romagnoli M, Dell'Orso D, Lorenzi C, Crisafulli E, Costi S, Lugli D, Clini EM. Repeated pulmonary rehabilitation in severe and disabled COPD patients. *Respiration* 2006;73(6):769-76.
- (56) Wempe JB, Wijkstra PJ. The influence of rehabilitation on behaviour modification in COPD. *Patient Educ Couns* 2004 March;52(3):237-41.

- (57) Emtner M, Finne M, Stalenheim G. A 3-year follow-up of asthmatic patients participating in a 10-week rehabilitation program with emphasis on physical training. *Arch Phys Med Rehabil* 1998 May;79(5):539-44.
- (58) Cox NJ, Hendricks JC, Binkhorst RA, van Herwaarden CL. A pulmonary rehabilitation program for patients with asthma and mild chronic obstructive pulmonary diseases (COPD). *Lung* 1993;171(4):235-44.
- (59) Patrick DL. Information Sheet on the Perceived Quality of Life Scale (PQoL). http://depts.washington.edu/yqol/docs/PQOL_Info.pdf 2004 January 13;
- (60) Engvik, H. "Big Five" på norsk. *Tidsskrift for Norsk Psykologforening* 1993;30:884-96.
- (61) Nici L. ATS statement: guidelines for the six-minute walk test. *Am J Respir Crit Care Med* 2002 July 1;166(1):111-7.
- (62) Quanjer PH, Tammeling GJ, Cotes JE, Pedersen OF, Peslin R, Yernault JC. Lung volumes and forced ventilatory flows. Report Working Party Standardization of Lung Function Tests, European Community for Steel and Coal. Official Statement of the European Respiratory Society. *Eur Respir J Suppl* 1993 March;16:5-40.
- (63) Jones PW, Quirk FH, Baveystock CM. The St George's Respiratory Questionnaire. *Respiratory Medicine* 1991 September;85 Suppl B:25-31.
- (64) Burckhardt CS, Woods SL, Schultz AA, Ziebarth DM. Quality of life of adults with chronic illness: a psychometric study. *Res Nurs Health* 1989 December;12(6):347-54.
- (65) Wahl A, Burckhardt C, Wiklund I, Hanestad BR. The Norwegian version of the Quality of Life Scale (QOLS-N). A validation and reliability study in patients suffering from psoriasis. *Scand J Caring Sci* 1998;12(4):215-22.
- (66) Håseth K, Hagtvedt K, Spielberger C. Manual for Norwegian State-Trait Anxiety Inventory. 1993.
- (67) Enright PL, Sherrill DL. Reference equations for the six-minute walk in healthy adults. *Am J Respir Crit Care Med* 1998 November;158(5 Pt 1):1384-7.

- (68) Curtis JR, Patrick DL. The assessment of health status among patients with COPD. *Eur Respir J Suppl* 2003 June;41:36s-45s.
- (69) Trappenburg JC, Troosters T, Spruit MA, Vandebrouck N, Decramer M, Gosselink R. Psychosocial conditions do not affect short-term outcome of multidisciplinary rehabilitation in chronic obstructive pulmonary disease. *Arch Phys Med Rehabil* 2005 September;86(9):1788-92.
- (70) de Torres JP, Casanova C, Hernandez C, Abreu J, guirre-Jaime A, Celli BR. Gender and COPD in patients attending a pulmonary clinic. *Chest* 2005 October;128(4):2012-6.
- (71) Brenes GA. Anxiety and chronic obstructive pulmonary disease: prevalence, impact, and treatment. *Psychosom Med* 2003 November;65(6):963-70.
- (72) Di Marco F, Verga M, Reggente M, Maria CF, Santus P, Blasi F, Allegra L, Centanni S. Anxiety and depression in COPD patients: The roles of gender and disease severity. *Respir Med* 2006 October;100(10):1767-74.
- (73) Gudmundsson G, Gislason T, Janson C, Lindberg E, Suppli UC, Brondum E, Nieminen MM, Aine T, Hallin R, Bakke P. Depression, anxiety and health status after hospitalisation for COPD: a multicentre study in the Nordic countries. *Respir Med* 2006 January;100(1):87-93.
- (74) Okubadejo AA, Jones PW, Wedzicha JA. Quality of life in patients with chronic obstructive pulmonary disease and severe hypoxaemia. *Thorax* 1996 January;51(1):44-7.
- (75) Dales RE, Spitzer WO, Schechter MT, Suissa S. The influence of psychological status on respiratory symptom reporting. *Am Rev Respir Dis* 1989 June;139(6):1459-63.
- (76) Put C, Demedts M, Van Den BO, Demyttenaere K, Verleden G. Asthma symptoms: influence of personality versus clinical status. *Eur Respir J* 1999 April;13(4):751-6.

- (77) Ambrosino N. Pulmonary Rehabilitation Programs; Outcomes in patients with chronic obstructive pulmonary disease. *Dis Manage Health Outcomes* 2002;10(9):535-42.
- (78) Hill NS. Pulmonary rehabilitation. *Proc Am Thorac Soc* 2006;3(1):66-74.
- (79) Hui KP, Hewitt AB. A simple pulmonary rehabilitation program improves health outcomes and reduces hospital utilization in patients with COPD. *Chest* 2003 July;124(1):94-7.
- (80) Lacasse Y, Goldstein R, Lasserson TJ, Martin S. Pulmonary rehabilitation for chronic obstructive pulmonary disease. *Cochrane Database Syst Rev* 2006;(4):CD003793.
- (81) Ong KC, Wong WP, Jailani AR, Sew S, Ong YY. Effects of a pulmonary rehabilitation programme on physiologic and psychosocial outcomes in patients with chronic respiratory disorders. *Ann Acad Med Singapore* 2001 January;30(1):15-21.
- (82) Salman GF, Mosier MC, Beasley BW, Calkins DR. Rehabilitation for patients with chronic obstructive pulmonary disease: meta-analysis of randomized controlled trials. *J Gen Intern Med* 2003 March;18(3):213-21.
- (83) Skumlien S, Skogedal E, Bjortuft O, Ryg MS. Four weeks' intensive rehabilitation generates significant health effects in COPD patients. *Chron Respir Dis* 2007;4(4):5-13.
- (84) Lacasse Y, Martin S, Lasserson TJ, Goldstein RS. Meta-analysis of respiratory rehabilitation in chronic obstructive pulmonary disease. *A Cochrane systematic review*. *Eura Medicophys* 2007 November 8.
- (85) Withers NJ, Rudkin ST, White RJ. Anxiety and depression in severe chronic obstructive pulmonary disease: the effects of pulmonary rehabilitation. *J Cardiopulm Rehabil* 1999 November;19(6):362-5.
- (86) de Godoy DV, de Godoy RF. A randomized controlled trial of the effect of psychotherapy on anxiety and depression in chronic obstructive pulmonary disease. *Arch Phys Med Rehabil* 2003 August;84(8):1154-7.

- (87) Kunik ME, Braun U, Stanley MA, Wristers K, Molinari V, Stoebner D, Orengo CA. One session cognitive behavioural therapy for elderly patients with chronic obstructive pulmonary disease. *Psychol Med* 2001 May;31(4):717-23.
- (88) Di Marco F, Verga M, Reggente M, Maria CF, Santus P, Blasi F, Allegra L, Centanni S. Anxiety and depression in COPD patients: The roles of gender and disease severity. *Respir Med* 2006 October;100(10):1767-74.
- (89) Haave E, Skumlien S, Engvik H. Norwegian version of The Perceived Quality of Life Scale (PQoL), tested on a sample of patients with serious chronic obstructive pulmonary disease (COPD) and a sample of healthy adults. *Journal of the Norwegian Psychological Association* 2007;44:735-40.
- (90) Berry MJ. The relationship between exercise tolerance and other outcomes in COPD. *COPD* 2007 September;4(3):205-16.
- (91) Foy CG, Rejeski WJ, Berry MJ, Zaccaro D, Woodard CM. Gender moderates the effects of exercise therapy on health-related quality of life among COPD patients. *Chest* 2001 January;119(1):70-6.
- (92) Laviolette L, Lacasse Y, Doucet M, Lacasse M, Marquis K, Saey D, Leblanc P, Maltais F. Chronic obstructive pulmonary disease in women. *Can Respir J* 2007 March;14(2):93-8.
- (93) Becklake MR, Kauffmann F. Gender differences in airway behaviour over the human life span. *Thorax* 1999 December;54(12):1119-38.
- (94) Ketelaars CA, Schlosser MA, Mostert R, Huyer Abu-Saad H, Halfens RJ, Wouters EF. Determinants of health-related quality of life in patients with chronic obstructive pulmonary disease. *Thorax* 1996 January;51(1):39-43.
- (95) Monso E, Fiz JM, Izquierdo J, Alonso J, Coll R, Rosell A, Morera J. Quality of life in severe chronic obstructive pulmonary disease: correlation with lung and muscle function. *Respir Med* 1998 February;92(2):221-7.

- (96) de Torres JP, Casanova C, Hernandez C, Abreu J, guirre-Jaime A, Celli BR. Gender and COPD in patients attending a pulmonary clinic. *Chest* 2005 October;128(4):2012-6.
- (97) Guyatt GH, Berman LB, Townsend M. Long-term outcome after respiratory rehabilitation. *CMAJ* 1987 December 15;137(12):1089-95.
- (98) Cockram J, Cecins N, Jenkins S. Maintaining exercise capacity and quality of life following pulmonary rehabilitation. *Respirology* 2006 January;11(1):98-104.
- (99) Wempe JB, Wijkstra PJ. The influence of rehabilitation on behaviour modification in COPD. *Patient Educ Couns* 2004 March;52(3):237-41.
- (100) Williams V, Bruton A, Ellis-Hill C, McPherson K. What really matters to patients living with chronic obstructive pulmonary disease? An exploratory study. *Chron Respir Dis* 2007;4(2):77-85.

