

# Health-related quality of life in outpatients with COPD in daily practice: the *VICE* Spanish study

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**Background:** The objective of this study was to measure health-related quality of life (HRQL) in outpatients with chronic obstructive pulmonary disease (COPD) and to assess differences in HRQL according to age, gender, and severity of COPD.

**Methods:** A total of 9405 patients (79% men, mean age 68 years) participated in a cross-sectional study. HRQL was measured with the Short Form 12 Health Survey Questionnaire (SF-12). Severity of COPD was graded into three levels according to forced expiratory volume in one second value.

**Results:** COPD severity was mild in 33.8% of cases, moderate in 49.3% and severe in 16.8%. The mean physical component summary (PCS-12) and mental component summary (MCS-12) scores were  $36.8 \pm 10.4$  and  $47.2 \pm 11.2$ , respectively. General health and physical functioning domains were those with the lowest scores. The mean MCS-12 scores were significantly higher in men ( $47.9 \pm 10.9$ ) than in women ( $44.1 \pm 11.8$ ) ( $P < 0.001$ ). Patients older than 60 years rated HRQL worse than patients aged 40–59 years. There were statistically significant differences according to severity of disease in the mean scores of all domains of the PCS-12 and MCS-12 scales.

**Conclusions:** The present findings show the influence of female gender, older age and moderate-to-severe of airflow limitation on HRQL in outpatients with COPD attended in daily practice.

**Keywords:** health status, health surveys, multicenter study, pulmonary disease, chronic obstructive/epidemiology, quality of life, questionnaires

## Introduction

Chronic obstructive pulmonary disease (COPD) is a debilitating multicomponent respiratory condition primarily affecting the airway and lung parenchyma but also inducing a variety of extrapulmonary consequences, such as systemic inflammation, nutritional abnormalities, weight loss, skeletal muscle dysfunction and additional organ effects (Decramer et al 2005). The high burden of COPD resulting from cough, sputum production and shortness of breath, is further contributed to by systemic effects, leading to a pronounced deterioration in health status and a diminished quality of life. It has been largely recognized that COPD is a public health problem worldwide and a major cause of chronic morbidity and mortality (Chan-Yeung et al 2004; Pauwels and Rabe 2004; Manino 2005). COPD is a highly prevalent disease, and it is estimated that 7%–10% of the adult population may be affected (Sobradillo-Peña 2000; Halbet et al 2003, 2006). In spite of antismoking campaigns, the prevalence and mortality rates of COPD continue to rise every year. It has been shown that COPD is the most rapidly increasing cause of death in individuals older than 65 years of age, which represents the most rapidly growing segment of the population in developed countries. Disability from COPD is expected to rise by 2020 with aging of the population and the increase in disease prevalence (Weiss et al 2003).

Health-related quality of life (HRQL) in COPD patients has received an increasing interest over the past decade. An impaired health status is a risk factor for frequent

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exacerbations and hospital admissions (Miravittles et al 2006). Previous studies using both generic and disease-specific instruments for measuring HRQL in COPD patients (Mahler 2000) have shown relationships between HRQL and disease severity, respiratory symptoms, gender, comorbidity, body weight, upper airway symptoms, and psychological status (Hajiro et al 2000; Wijnhoven et al 2003; Peruzza et al 2003; Hurst et al 2004; Katsura et al 2005; Ståhl et al 2005; de Torres et al 2006). In a recent study carried out in Spain, determinants of HRQL in patients with COPD followed in primary care included sex, forced expiratory volume in one second ( $FEV_1$ ), use of oxygen therapy, and number of visits to emergency rooms and hospital admissions (Carrasco Garrido et al 2006).

In order to provide further information on HRQL in patients with COPD, a multicenter cross-sectional study was designed, the primary objectives of which were to collect information on HRQL in a large sample of outpatients with COPD visited by family physicians and pneumologists in actual conditions of the daily practice and to determine whether there were differences in HRQL according to age, gender, and severity of COPD. Secondary objectives included to assess the correlation between quality of life perceived by COPD patients and functional status ( $FEV_1$ ) and level of dyspnea, and to determine health care resources consumption.

## Methods

### Study design

The *VICE* Study (Spanish acronym of *Living with Chronic Obstructive Pulmonary Disease*) was a 2-month (April–May 2004) cross-sectional survey of the first five consecutive patients with COPD in the outpatient setting seen by general practitioners in primary care centers and pneumologists in the outpatients clinics of the Services of Pneumology of acute care hospitals from all over Spain. A sample of 2300 general practitioners and 200 pneumologists were recruited using a stratified random sample drawn from the list of registered physicians in all autonomous communities. Physicians were eligible for inclusion if they were actively practicing in Spain, reported spending at least 50% of their time in direct patient care and had a primary specialty in family practice or pneumology. Physicians participated voluntarily in the study and did not receive any payment.

The study protocol was approved by the Ethics Committee of hospital Gregorio Marañón, Madrid (Spain), and written informed consent was obtained from all participants.

## Patients

Patients of both sexes, aged 40 years or older, with a previous diagnosis of COPD (confirmed by history and spirometry) were eligible provided that the reason of consultation was related to his/her pulmonary condition. The diagnosis of the disease was performed according to the criteria of the Spanish Society of Pneumology and Chest Surgery (SEPAR) based on the demonstration, through a forced spirometry, of a  $FEV_1$  below 80% of the reference value and a  $FEV_1$ /forced vital capacity (FVC) ratio below 0.7 after the bronchodilation test. The severity of COPD was graded according to the  $FEV_1$  value: mild ( $FEV_1$  60%–80% of the reference value), moderate ( $FEV_1$  40%–59% of the reference value) and severe ( $FEV_1$  < 40% of the reference value) following SEPAR criteria (Barberà et al 2001), which are based on the guidelines of the British Thoracic Society (BTS 1997). Spirometric measurements at the time of the study were not performed.

Patients with an acute worsening of their COPD in the previous month were excluded as were those suffering from any physical and/or psychiatric disease precluding to complete the HRQL questionnaire. Patients with more than 80% of missing data for the study variables in their medical records were also excluded.

## Data collection

Interviews were carried out by the participating physician during the course of the patient's consultation in routine daily practice. All data were collected in a single visit using a questionnaire in which the following variables were recorded: age; sex; height; weight; smoking habit (current smoker, never smoker, ex-smoker); year of COPD diagnosis; data of the last spirometric measurement and  $FEV_1$  and  $FEV_1$ /FVC values; severity of COPD; current COPD therapy including nonpharmacological management (smoking cessation counseling, stop smoking treatment, oxygen therapy, rehabilitation, others) and pharmacological treatment (short-acting  $\beta_2$ -agonists, long-acting  $\beta_2$ -agonists, short-acting anticholinergics, long-acting anticholinergics, inhaled steroids, oral steroids, a fixed combination of anticholinergics and short-acting  $\beta_2$ -agonists, a fixed combination of long-acting  $\beta_2$ -agonists and inhaled steroids, antibiotics, others); disability; and health resources utilization in the previous 12 months (number of outpatient visits to either the primary care physician and the pneumologist, emergency department visits, hospitalizations, and days on sick leave).

Disability was classified according to the Medical Research Council (MRS) dyspnea scale (Bestall et al 1999). The MRC dyspnea scale concerns perceived breathlessness

and consists of five degrees: 1, "shortness of breath with strenuous exercise"; 2, "shortness of breath when hurrying"; 3, "walking slower than people of the same age on the level ground or stop for breath while walking at own pace on the level ground"; 4, "needing to stop after 100 yards on the level ground"; 5, "too breathless to leave the house". A Spanish translation of MRC dyspnea scale was administered to the subjects (Gallego et al 2002).

## Health status

All patients were administered the Short Form 12 Health Survey Questionnaire (SF-12), an abbreviated version of the SF-36 health questionnaire that contains 12 items (Ware et al 1996). These 12 items explain more than 90% of the variance of the physical and mental component scales of the SF-36. From them two scores can be calculated, the physical (PCS-12) and the mental (MCS-12) component summary, using a value of 50 with a standard deviation of 10 as reference population. In this study, the general Spanish adult population has been used as reference (Alonso et al 1998a; Vilagut et al 2005). Scores range from 0 to 100, with higher scores representing better HRQL. A score  $>60$  has been regarded as high HRQL, 40–60 as normal HRQL, and  $<40$  as impaired (low) HRQL. A translated version of the questionnaire validated for Spain has been used (Alonso et al 1998b).

## Statistical analysis

In order to detect a clinically relevant differences of 5 points in the mean PCS-12 and MCS-12 scores among the subgroups of men and women stratified by the three severity levels of COPD with a statistical power of 95% and a level of statistical significance (alpha) of 0.05, using a two-tailed Student's *t* test for the comparison of two groups (considering a standard deviation of 12 for the mean SF-12 scores of each group), a total number of patients required in each stratum was 165. According to data of the IBERPOC study (Sobradillo et al 1999; Villasante Fernandez-Montes et al 1999), women showed the lowest prevalence of COPD (22%) with the subset of women with severe disease accounting for 1.653% of the total number of patients with COPD. Therefore, the total number of patients required was 9981 ( $165/0.01653$ ). This number was increased to 12,477 assuming losses of patients due to nonevaluable cases of 20%.

The Statistical Package for the Social Sciences (version 12.0; SPSS Inc., Chicago, IL) was used for the analysis of data. Double data entry was carried out with a subsequent validation to guarantee the quality and consistency of the data. Continuous variables are expressed as mean and

standard deviation (SD) or median and ranges (25th–75th percentiles). Qualitative variables are described as frequency and percentages. Confidence intervals (CIs) were calculated at the 95% level. Differences of HRQL in the subgroups of patients according to gender and severity of COPD were analyzed with the paired Student's *t* test. The Spearman's rank-order correlation coefficient ( $\rho$ ) was calculated to assess the relationship between HRQL and FEV<sub>1</sub> and level of dyspnea. The chi-square ( $\chi^2$ ) test was used to assess differences in health resources utilization among the study groups. Statistical significance was set at  $P \leq 0.05$ .

## Results

The number of physicians participating in the study was 2144 (general practitioners,  $n = 1826$ ; pneumologists,  $n = 240$ ), which enabled a recruitment total of 10,782 patients. However, 1377 patients (12.8%) were excluded due to missing data in the patient's medical history ( $n = 831$ ) and lack of fulfillment of the selection criteria ( $n = 546$ ).

The study population included 9405 patients (79.7% men, 20.3% women) with a mean ( $\pm$ SD) age of  $67.8 \pm 9.8$  years. Sociodemographic and clinical characteristics of the patients are shown in Table 1. Salient features were as follows: 69% of patients were found in the 60–79 year stratum, 77% had a body mass index (BMI)  $\geq 25$  kg/m<sup>2</sup>, 61% were ex-smokers (median of 10 years since smoking cessation) and 22.6% were current smokers (median pack-years 40) and had been smoking for a mean of  $36.7 \pm 13.6$  years. Patients had a long-standing COPD, with a mean time since diagnosis of 10 years.

With regard to the last spirometric measurement, the mean FEV<sub>1</sub> value was  $55.1 \pm 14.3\%$ . The severity of disease was mild in 33.8% of cases, moderate in 49.3% and severe in 16.8%. There were differences in COPD severity according to gender, with significantly higher percentages of men compared to women with moderate (50.4% vs 45.4%) and severe (18.0% vs 10.7%) disease ( $P < 0.001$ ). 40.8% of patients aged 40–50 years suffered from moderate or severe COPD as opposed to 76.1% of patients of 80 years of age or older ( $P < 0.001$ ). Most patients (46%) had a moderate degree of dyspnea (MRC category 2). However, 14.5% of men showed a moderately severe degree of dyspnea (MRC categories 4 and 5) compared with 13.7% of women. The degree of dyspnea also increased with age, with 3.4% of patients aged 40–50 years in the MRC categories 4 and 5 compared with 29.2% of patients aged 80 years or older ( $P < 0.001$ ).

The mean PCS-12 and MCS-12 scores were  $36.8 \pm 10.4$  and  $47.2 \pm 11.2$ , respectively. General health and physical functioning domains were those with the lowest scores,

**Table 1** Sociodemographic and clinical characteristics of patients

Characteristic	Number (%)	Mean $\pm$ SD (range)*
Total no of patients	9405	
Age, years (n = 9095)		67.8 $\pm$ 9.8 (61–75)
Age groups (n = 8744)		
40–49 years	405 (4.6)	
50–59 years	1324 (15.1)	
60–69 years	2932 (33.5)	
70–79 years	3120 (35.7)	
$\geq 80$ years	963 (11.1)	
Sex (n = 8808)		
Men	7022 (79.7)	
Women	1786 (20.3)	
Height cm mean (SD) (n = 9124)		166.1 $\pm$ 7.7 (161–171)
Weight kg, mean (SD) (n = 9017)		76.3 $\pm$ 12.1 (69–84)
Body mass index (BMI) (n = 8930)		
<25 kg/m <sup>2</sup>	2090 (23.4)	
25–29 kg/m <sup>2</sup>	4677 (52.4)	
30–34 kg/m <sup>2</sup>	1735 (19.4)	
35–39 kg/m <sup>2</sup>	341 (3.8)	
$\geq 40$ kg/m <sup>2</sup>	87 (1.0)	
Smoking (n = 9347)		
Never	1500 (16.0)	
Ex-smoker	5737 (61.4)	
Current smoker	2110 (22.6)	
Years since COPD diagnosis (n = 7157)		9.7 $\pm$ 7.9
FEV <sub>1</sub> % predicted (n = 7214)		55.1 $\pm$ 14.3 (45–66)
FEV <sub>1</sub> /FVC % (n = 5850)		61.6 $\pm$ 14.4 (52–70)
Severity of COPD (n = 9049)		
Mild	3062 (33.8)	
Moderate	4464 (49.3)	
Severe	1523 (16.8)	
MRC dyspnea scale (n = 9211)		
1	1353 (14.7)	
2	4237 (46.0)	
3	2293 (24.9)	
4	1018 (11.1)	
5	310 (3.4)	

**Abbreviations:** COPD, chronic obstructive pulmonary disease; FEV<sub>1</sub>, forced expiratory volume in one second; FVC, forced vital capacity; MRC, Medical Research Council; SD, standard deviation.

**Note:** \*25th–75th percentile.

whereas role emotional and social functioning domains were those with the highest scores (Table 2). According to results of the SF-12 questionnaire, HRQL was graded as normal (40–60 points) by 61% of patients and low (<40 points) by 39% of patients. However, a higher percentage of patients scored less than 40 points in the physical health

domain compared with the mental health domain (60.2% vs 25.7%) (Table 2). As compared to the reference population, patients with COPD had a reduction of HRQL, with a mean of  $-1.32 \pm 1.04$  for PCS-12 and  $-0.28 \pm 1.12$  for MCS-12.

When HRQL in men and women was compared, there were no significant differences in the mean PCS-12 scores

**Table 2** Quality of life in patients with COPD

SF-12 questionnaire	Mean $\pm$ SD	No patients (%)
Physical component summary (PCS-12)	36.8 $\pm$ 10.4	
Mental component summary (MCS-12)	47.2 $\pm$ 11.2	
SF-12 scales		
Physical functioning	38.6 $\pm$ 32.1	
Role physical	44.8 $\pm$ 46.1	
Bodily pain	64.3 $\pm$ 29.4	
General health	30.9 $\pm$ 19.5	
Vitality	43.4 $\pm$ 26.7	
Social functioning	65.9 $\pm$ 27.1	
Emotional role	73.1 $\pm$ 41.5	
Mental health	63.1 $\pm$ 20.8	
Physical domain (n = 9,405)		
High (>60 points)		26 (0.3)
Normal (40–60 points)		3714 (39.5)
Low (<40 points)		5665 (60.2)
Mental domain (n = 9,405)		
High (>60 points)		613 (6.5)
Normal (40–60 points)		6373 (67.8)
Low (<40 points)		2419 (25.7)

**Abbreviations:** COPD, chronic obstructive pulmonary disease; SD, standard deviation; SF-12, Medical Outcomes Study Short Form 12 Health Survey Questionnaire.

(36.9  $\pm$  10.4 vs 36.5  $\pm$  10.3) but the mean MCS-12 scores were significantly higher in men (47.9  $\pm$  10.9) than in women (44.1  $\pm$  11.8) ( $P < 0.001$ ). Scores for the different domains of PCS-12 and MSC-12 according to gender are shown in Figure 1. As compared with the reference population, the mean reduction of HRQL for the mental domain was significantly higher in women ( $-0.59 \pm 1.18$ ) than in men ( $-0.20 \pm 1.09$ ) ( $P < 0.001$ ).

As shown in Table 3, the physical domain was scored <40 points by a significantly higher percentage of patients compared with the mental domain for all age strata. On the other hand, the percentage of patients considering that their HRQL in the physical domain was normal or high was also significantly lower than for the mental domain. Patients older than 60 years of age rated HRQL worse than patients in the 40–59 year age group.

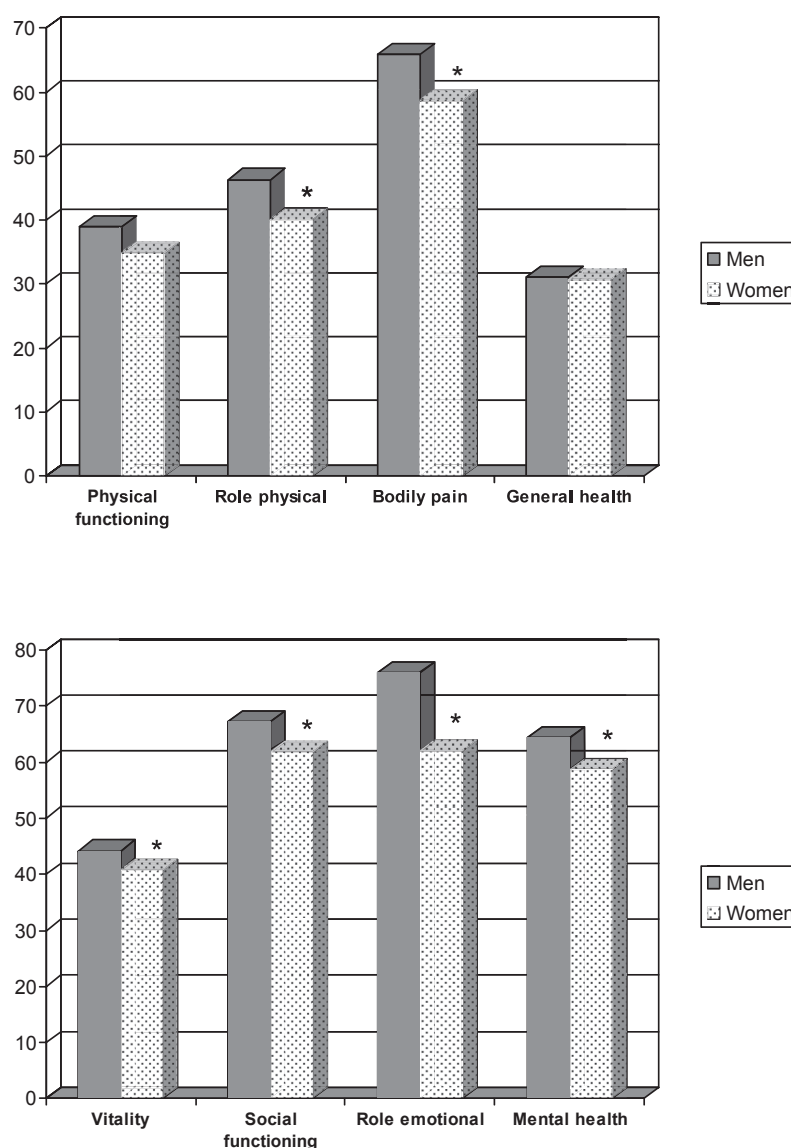
In relation to COPD severity, a significantly higher percentage of patients with mild disease rated HRQL as normal compared with patients with severe disease (physical domain 61.3% vs 18.5%; mental domain 75.9% vs 53.5%;  $P < 0.001$ ) (Table 3). The mean PCS-12 scores were 42.4  $\pm$  9.5 in patients with mild disease, 35.2  $\pm$  9.5 in those with moderate COPD and 30.6  $\pm$  9.5 in those with severe

disease ( $P < 0.001$ ); the corresponding figures for the mean MCS-12 scores were 49.1  $\pm$  10.1, 47.0  $\pm$  11.1 and 43.9  $\pm$  13.0 in the groups of mild, moderate and severe COPD, respectively. There were statistically significant differences according to severity of disease in the mean scores of all domains of the PCS-12 and MCS-12 scales (Figure 2). Moreover, patients with severe COPD showed a significantly higher reduction of HRQL for both the physical ( $-1.94 \pm 0.95$ ) and mental domains ( $-0.61 \pm 1.30$ ) than patients with moderate or mild COPD as compared with the reference population.

HRQL correlated significantly with FEV<sub>1</sub> in both PCS-12 ( $\rho = 0.313$ ,  $P < 0.001$ ) and MCS-12 ( $\rho = 0.101$ ,  $P < 0.001$ ) scales. As expected, an inverse significant correlation between HRQL and degree of dyspnea in the PCS-12 ( $\rho = -0.599$ ,  $P < 0.001$ ) and the MCS-12 ( $\rho = -0.237$ ,  $P < 0.001$ ) scales was observed.

In relation to utilization of health resources, patients with severe COPD had more visits to the primary care center in the previous 12 months than those with mild to moderate COPD (5.8, 4.6 and 3.2, respectively,  $P < 0.001$ ). They were also in the emergency department more often (2.5, 1.6 and 0.9, respectively,  $P < 0.001$ ). Patients with severe COPD had longer hospital stays (16.7 days) when compared to





**Figure 1** Mean scores of the physical component summary (PCS-12) (upper panel) and the mental component summary (MCS-12) (lower panel) in COPD patients according to gender (\*statistically significant differences,  $P < 0.001$ ).

those with moderate (10.9 days) or mild disease (8.8 days) ( $P < 0.001$ ) as well as a more days on sick leave (51.2, 29.4 and 18.9, respectively,  $P < 0.001$ ).

Details of nonpharmacological and pharmacological treatment according to HRQL and severity of COPD are summarized in Table 4. Anti-smoking treatment was recorded in only 4% of patients, and even in a lower percentage of patients (3.6%) with severe COPD. More than 80% of patients were receiving pharmacological treatment (bronchodilators in 73.7%, fixed combinations in 57.5% and steroids in 19.8%). Long-acting  $\beta_2$ -agonists were given to 42% of patients. When patients were stratified according to normal or low HRQL, a significantly higher percentage of patients with low HRQL received any modality of pharmacological treatment except

for long-acting anticholinergics. In addition, a significantly higher percentage of patients with severe COPD received any of medication as compared with those with mild and moderate severity of disease.

## Discussion

The use of HRQL measures in COPD has currently achieved widespread acceptance (Domingo-Salvany et al 2002). However, HRQL measures have shown an inconsistent relationship with clinical and functional components of the disease. The objective of this study was to assess HRQL in a large population of COPD patients during the patients' routine care in the outpatient setting. A generic quality of life questionnaire, the SF-12 that enables to calculate the

**Table 3** Differences in HRQL according to age and severity of COPD

Variable	Physical domain			Mental domain		
	High >60 points	Normal 40–60 points	Low <40 points	High >60 points	Normal 40–60 points	Low <40 points
Age groups, years						
40–49 (n = 2193)	10 (0.5)	1112 (50.7)	1071 (48.8)	145 (6.6)	1546 (70.5)	502 (22.9)
50–59 (n = 1990)	3 (0.2)	742 (37.3)	1245 (62.6)	131 (6.6)	1384 (69.5)	475 (23.9)
60–69 (n = 1382)	2 (0.1)	439 (31.8)	941 (68.1)	80 (5.8)	914 (66.1)	388 (28.1)
70–79 (n = 519)	2 (0.4)	139 (26.8)	378 (72.8)	25 (4.8)	330 (63.6)	164 (31.6)
≥80 (n = 1073)	2 (0.2)	344 (32.1)	727 (67.8)	79 (7.4)	678 (63.2)	316 (25.9)
COPD severity						
Mild (n = 3062)	16 (0.5)	1876 (61.3)	1170 (38.2)	179 (5.8)	2323 (75.9)	560 (18.3)
Moderate (n = 4464)	9 (0.2)	1425 (31.9)	3030 (67.9)	284 (6.4)	3000 (67.2)	1180 (26.4)
Severe (n = 1523)	1 (0.1)	282 (18.5)	1240 (81.4)	130 (8.5)	815 (53.5)	578 (38.0)

**Abbreviations:** COPD, chronic obstructive pulmonary disease; HRQOL, health-related quality of life.

**Note:** Percentages in parenthesis.

physical well-being and the mental-well being components of HRQL was administered to all patients. This instrument has been shown to be a valid evaluation tool with excellent measurement properties in patients with chronic respiratory conditions, such as COPD and asthma (Katz et al 2000; Garratt et al 2000; Miravittles et al 2002, 2004).

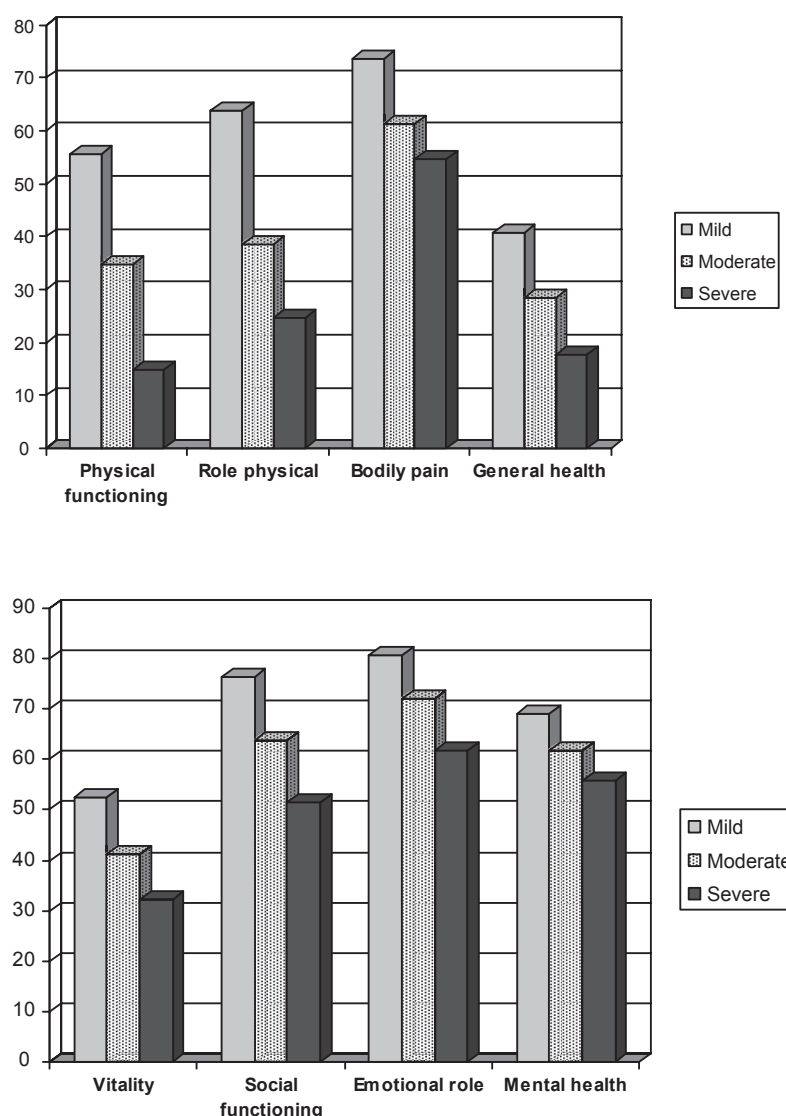
In general, most patients perceived that their HRQL was not impaired by COPD, although the physical health domain was rated poorly than the mental health domain, with general health, physical functioning, role physical and vitality showing lowers scores than the domains of mental health, emotional role, social functioning and bodily pain. Lower scores for the PCS-12 component than for the MSC-12 component in patients with COPD have been also reported by others (Ståhl et al 2005; Carrasco Garrido et al 2006).

In agreement with previous reports (Peruzza et al 2003; de Torres et al 2006; Carrasco Garrido et al 2006), the present findings confirm the effect of age, gender and stage of disease on HRQL in patients with COPD. It has been shown that COPD is a main cause of severe deterioration of quality of life in elderly subjects and that the degree of this impairment mainly depends on the severity of airway obstruction (Peruzza et al 2003). In our study, patients older than 60 years of age, particularly those in the 70–79-year-old group, perceived that their HRQL was more affected by COPD than younger patients. However, in the age stratum of very old patients (≥80 years), a lower percentage of subjects considered that their quality of life for the physical and mental health domains was low as compared with patients aged 70 to 79 years. This observation may be related to that

fact that the oldest elderly population tend to restrict their own daily activities and expectations.

Compared with men, women had worse scores in all domains of mental health and in the role of physical and bodily pain of the physical health domain. Taking into account that a significantly percentage of men had moderate and severe COPD, this observation is clinically relevant as indicating that women with COPD develop symptoms influencing HRQL with less degree of obstruction than men. Unfortunately, a better characterization of our female population is not feasible given that other factors, such as socioeconomic status, education level, working status or co-morbidity were not evaluated. However, our results are in-line with those reported by de Torres and colleagues (2006) in a FEV<sub>1</sub>-matched case series study of 73 consecutive women and 73 men. These authors speculate that the factors affecting HRQL differ by gender at least in early stages of the disease and that the perceived expression of the disease is different between genders. In the study of Antonelli-Incalzi and colleagues (2003) in which differences in health status according to the Global Initiative for Chronic Obstructive Lung Disease (GOLD) criteria was evaluated, female sex was also associated with a greater impact of COPD on the health status.

In our study, like others (Ferrer et al 1997; Hajiro et al 2000) disease severity (based on FEV<sub>1</sub>) influenced significantly HRQL among subjects with COPD. Therefore, staging criteria for COPD based on percentage of predicted FEV<sub>1</sub> separated groups of patients with varying degrees of impairment in HRQL. Contrary to expectations, even patients with



**Figure 2** Mean scores of the physical component summary (PCS-12) (upper panel) and the mental component summary (MCS-12) (lower panel) in COPD patients according to severity of disease ( $P < 0.001$  in all domains of both components).

mild disease showed substantially compromised HRQL. Additionally, the importance of dyspnea causing patients with COPD to reduce their activities of daily living (Reardon et al 2006) is also demonstrated in our study, with dyspnea showing a stronger correlation with HRQL than  $FEV_1$ .

A remarkable finding was that 22.6% of COPD patients were current smokers but only 4% of the total population was receiving smoking cessation treatment. In a survey of 11,973 COPD patients carried out in Spain, 35% of them continued smoking (Viejo-Bañuelos et al 2006). Our patients had been smoking for about 40 years and the median pack-years was 40. Effective intervention strategies directed to quit smoking in COPD patients are mandatory. With regard to pharmacological treatment, bronchodilators,

fixed combinations and steroids were the most frequently used medications. Anticholinergics were used by 58.5% of the patients followed by  $\beta_2$ -agonists (50%), theophylline (21.4%), inhaled steroids (15.9%) and oral steroids (7.5%). High dose inhaled corticosteroids in patients with moderate to severe chronic obstructive pulmonary disease has been associated with a reduced rate of decline in health status (Burge et al 2000). Finally, we also found a strong relationship between health-care resource utilization and severity of disease (Hilleman et al 2000).

Our study had some limitations. A generic questionnaire was used to measure HRQL, which is less sensitive than the specific tools. The cross-sectional design of the study limits our ability to describe how progression of disease



**Table 4** Management of patients with COPD: nonpharmacological and pharmacological treatment in the previous 12 months

Management	Total population (n = 9405)	Health-related quality of life			Severity of COPD			
		Normal (n = 5747)	Low (n = 3658)	P value	Mild (n = 3062)	Moderate (n = 4464)	Severe (n = 1523)	P value
Nonpharmacological therapy	4479 (47.6)	2568 (44.7)	1911 (52.2)	0.001	1313 (42.9)	2134 (47.8)	892 (58.6)	0.001
Smoking cessation counseling	2263 (24.1)	1450 (25.2)	813 (22.2)	0.001	811 (26.5)	1032 (23.1)	355 (23.3)	0.002
Stop smoking treatment	385 (4.1)	239 (4.2)	146 (4.0)	0.689	136 (4.4)	184 (4.1)	55 (3.6)	0.411
Oxygen therapy	813 (8.6)	235 (4.1)	578 (15.8)	0.001	47 (1.5)	305 (6.8)	434 (28.5)	0.001
Rehabilitation	947 (10.1)	457 (8.0)	490 (13.4)	0.001	194 (6.3)	500 (11.2)	233 (15.3)	0.001
Pharmacological treatment	7980 (84.8)	4727 (82.3)	3253 (88.9)	0.001	2416 (78.9)	3872 (86.7)	1391 (91.3)	0.001
Bronchodilators	6935 (73.7)	4176 (72.7)	2759 (75.4)	0.003	2123 (69.3)	3319 (74.4)	1232 (80.9)	0.001
Short-acting $\beta_2$ -agonists	2539 (27.0)	1449 (25.2)	1090 (29.8)	0.001	747 (24.4)	1181 (26.5)	510 (33.5)	0.001
Long-acting $\beta_2$ -agonists	2167 (23.0)	1283 (22.3)	884 (24.2)	0.038	589 (19.2)	1059 (23.7)	424 (27.8)	0.001
Short-acting anticholinergics	1552 (16.5)	900 (15.7)	652 (17.8)	0.005	414 (13.5)	765 (17.1)	316 (20.7)	0.001
Long-acting anticholinergics	3953 (42.0)	2408 (41.9)	1545 (42.2)	0.747	1154 (37.7)	1951 (43.7)	710 (46.6)	0.001
Fixed combinations	5410 (57.5)	3176 (55.3)	2234 (61.1)	0.001	1585 (51.8)	2657 (59.5)	986 (64.7)	0.001
Anticholinergics and short-acting $\beta_2$ -agonists	687 (7.3)	395 (6.9)	292 (8.0)	0.043	197 (6.4)	332 (7.4)	134 (8.8)	0.014
Inhaled steroids and long-acting $\beta_2$ -agonists	5155 (54.8)	3022 (52.6)	2133 (58.3)	0.001	1510 (49.3)	2525 (56.6)	950 (62.4)	0.001
Steroids	1865 (19.8)	899 (15.6)	966 (26.4)	0.001	359 (11.7)	949 (21.3)	479 (31.5)	0.001
Oral	701 (7.5)	226 (3.9)	465 (13.0)	0.001	99 (3.2)	318 (7.1)	251 (16.5)	0.001
Inhaled	1492 (15.9)	773 (13.5)	719 (19.7)	0.001	304 (9.9)	775 (17.4)	351 (23.0)	0.001
Antibiotics	4671 (49.7)	2752 (47.9)	1919 (52.5)	0.001	1462 (47.7)	2210 (49.5)	807 (53.0)	0.003

**Abbreviations:** COPD, chronic obstructive pulmonary disease.

**Note:** Percentages in parenthesis.

stage relates to changes in HRQL. Patients were recruited from those visited in the outpatient setting, mostly in primary care centers, and therefore may not represent the COPD population at large. It should be noted that 16% of our population were never smokers. These patients were not excluded because the objective of the study was to assess HRQL in outpatients with COPD attended by family physicians and pneumologists in actual conditions of the daily practice. However, a diagnosis other than COPD cannot be excluded. In a recent multicenter study carried out in 9425 subjects with COPD recruited at 12 different sites worldwide, the percentage of never smokers varied between 3.1% and 9.4% in men and between 2.9% and 11.2% in women (Buist et al 2007). On the other hand,

other factors that may affect HRQL (eg, co-morbidity) were not evaluated. However, the large sample size strengthens the findings of our study.

In summary, this study shows the influence of female gender, older age and moderate-to-severe of airflow limitation on HRQL, particularly on the physical component of the SF-12 instrument, in patients with COPD attended in the outpatient setting in daily practice conditions.

## Disclosure

A Martín is employed by Pfizer, Madrid, Spain. E Gobartt is employed by Boehringer Ingelheim España, Madrid, Spain. JM Rodríguez, JL Izquierdo, and P de Lucas have no conflicts of interest.

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# References

- Alonso J, Prieto L, Ferrer M, et al. 1998a. Testing the measurement properties of the Spanish version of the SF-36 Health Survey among male patients with chronic obstructive pulmonary disease. Quality of Life in COPD Study Group. *J Clin Epidemiol*, 51:1087–94.
- Alonso J, Regidor E, Barrio G, et al. 1998b. [Population reference values of the Spanish version of the Health Questionnaire SF-36.] *Med Clin (Barc)*, 111:410–6.
- Antonelli-Incalzi R, Imperiale C, Bellia V, et al; the SaRA investigators. 2003. Do GOLD stages of COPD severity really correspond to differences in health status? *Eur Respir J*, 22:444–9.
- Barberà JA, Peces-Barba G, Agustí AGN, et al. 2001. Sociedad Española de Neumología y Cirugía Torácica (SEPAR): Guía para el diagnóstico y tratamiento de la enfermedad pulmonar obstructiva crónica. *Arch Bronconeumol*, 37:297–316.
- Bestall JC, Paul EA, Garrod R, et al. 1999. Usefulness of the Medical Research Council (MRC) dyspnoea scale as a measure of disability in patients with chronic obstructive pulmonary disease. *Thorax*, 54:581–6.
- [BTS] British Thoracic Society. 1997. BTS guidelines for the management of chronic obstructive pulmonary disease. The COPD Guidelines Group of the Standards of Care Committee of the BTS. *Thorax*, 52(Suppl 5): S1–S28.
- Buist AS, McBurnie MA, Vollmer WM, et al; on behalf of the BOLD Collaborative Research Group. 2007. International variation in the prevalence of COPD (the BOLD Study): a population-based prevalence study. *Lancet*, 370:741–50.
- Burge PS, Calverley PM, Jones PW, et al. 2000. Randomised, double blind, placebo controlled study of fluticasone propionate in patients with moderate to severe chronic obstructive pulmonary disease: the ISOLDE trial. *BMJ*, 320:1297–303.
- Carrasco Garrido P, de Miguel Díez J, Rejas Gutiérrez J, et al. 2006. Negative impact of chronic obstructive pulmonary disease on the health-related quality of life of patients. Results of the EPIDEPOC study. *Health Qual Life Outcomes*, 4:31.
- Chan-Yeung M, Ait-Khaled N, White N, et al. 2004. The burden and impact of COPD in Asia and Africa. *Int J Tuberc Lung Dis*, 8:2–14.
- de Torres JP, Casanova C, Hernández C, et al. 2006. Gender associated differences in determinants of quality of life in patients with COPD: a case series study. *Health Qual Life Outcomes*, 4:72.
- Decramer M, De Benedetto F, Del Ponte A, et al. 2005. Systemic effects of COPD. *Respir Med*, 99:S3–S10.
- Domingo-Salvany A, Lamarca R, Ferrer M, et al. 2002. Health-related quality of life and mortality in male patients with chronic obstructive pulmonary disease. *Am J Respir Crit Care Med*, 166:680–5.
- Ferrer M, Alonso J, Morera J, et al. 1997. Chronic obstructive pulmonary disease stage and health-related quality of life. *Ann Intern Med*, 127:1072–9.
- Gallego MC, Samaniego J, Alonso J, et al. 2002. [Dyspnea in COPD: relation to the MRC scale with dyspnea induced by walking and cardiopulmonary stress testing.] *Arch Bronconeumol*, 38:112–6.
- Garratt AM, Hutchinson A, Russell I. 2000. Patient-assessed measures of health outcome in asthma: A comparison of four approaches. *Respir Med*, 94:597–606.
- Hajiro T, Nishimura K, Tsukino M, et al. 2000. Stages of disease severity and factors that affect the health status of patients with chronic obstructive pulmonary disease. *Respir Med*, 94:841–6.
- Halbert RJ, Isonaka S, George D, et al. 2003. Interpreting COPD prevalence estimates: what is the true burden of disease? *Chest*, 123:1684–92.
- Halbert RJ, Natoli JL, Gano A, et al. 2006. Global burden of COPD: systematic review and meta-analysis. *Eur Respir J*, 28:523–32.
- Hilleman DE, Dewan N, Malesker M, et al. 2000. Pharmacoeconomic evaluation of COPD. *Chest*, 118:1278–85.
- Hurst JR, Wilkinson TMA, Donaldson GC, et al. 2004. Upper airway symptoms and quality of life in chronic obstructive pulmonary disease (COPD). *Respir Med*, 98:767–70.
- Katsura H, Yamada K, Kida K. 2005. Both generic and disease specific health-related quality of life are deteriorated in patients with underweight COPD. *Respir Med*, 99:624–30.
- Katz PP, Eisner MD, Yelin EH, et al. 2005. Functioning and psychological status among individuals with COPD. *Qual Life Res*, 14:1835–43.
- Mahler DA. 2000. How should health-related quality of life be assessed in patients with COPD? *Chest*, 117:54S–57S.
- Manino DM. 2005. Epidemiology and global impact of chronic obstructive pulmonary disease. *Semin Respir Crit Care Med*, 26:204–10.
- Miravittles M, Alvarez-Sala JL, Lamarca R, et al; IMPAC Study Group. 2002. Treatment and quality of life in patients with chronic obstructive pulmonary disease. *Qual Life Res*, 11:329–38.
- Miravittles M, Calle M, Alvarez-Gutiérrez F, et al. 2006. Exacerbations, hospital admissions and impaired health status in chronic obstructive pulmonary disease. *Qual Life Res*, 15:471–80.
- Miravittles M, Ferrer M, Pont A, et al; IMPAC Study Group. 2004. Effect of exacerbations on quality of life in patients with chronic obstructive pulmonary disease: a 2 year follow up study. *Thorax*, 59:387–95.
- Pauwels RA, Rabe KF. 2004. Burden and clinical features of chronic obstructive pulmonary disease (COPD). *Lancet*, 364:613–20.
- Peruzza S, Sergi G, Vianello A, et al. 2003. Chronic obstructive pulmonary disease (COPD) in elderly subjects: impact on functional status and quality of life. *Respir Med*, 97:612–7.
- Reardon JZ, Lareau SC, ZuWallack R. 2006. Functional status and quality of life in chronic obstructive pulmonary disease. *Am J Med*, 119(10 Suppl 1):32–7.
- Sobradillo V, Miravittles M, Jimenez CA, et al. 1999. [Epidemiological study of chronic obstructive pulmonary disease in Spain (IBERPOC): prevalence of chronic respiratory symptoms and airflow limitation.] *Arch Bronconeumol*, 35:159–66.
- Sobradillo-Peña S, Miravittles M, Gabriel R, et al. 2000. Geographic variations in prevalence and underdiagnosis of COPD. Results of the IBERPOC multicentre epidemiological study. *Chest*, 118:981–9.
- Ståhl E, Lindberg A, Jansson SA, et al. 2005. Health-related quality of life is related to COPD disease severity. *Health Qual Life Outcomes*, 3:56.
- Viejo-Bañuelos JL, Pueyo-Bastida A, Fueyo-Rodríguez A. 2006. Characteristics of outpatients with CPD in daily practice: The E4 Spanish Project. *Respir Med*, 100:2137–43.
- Vilagut G, Ferrer M, Rajmil L, et al. 2005. [The Spanish version of the Short Form 36 Health Survey: a decade of experience and new developments.] *Gac Sanit*, 19:135–50.
- Villasante Fernandez-Montes C. 1999. [IBERPOC: an evaluation of the results. The Scientific Committee of the IBERPOC Study.] *Arch Bronconeumol*, 35(Suppl 3):40–3.
- Ware J Jr, Kosinski M, Keller SD. 1996. A 12-item Short-Form Health Survey: construction of scales and preliminary tests of reliability and validity. *Med Care*, 34:220–33.
- Weiss ST, DeMeo DL, Postma DS. 2003. COPD: problems in diagnosis and measurement. *Eur Respir J*, 21(Suppl 41):4s–12s.
- Wijnhoven HAH, Kriegsman DMW, Hesselink AE, et al. 2003. The influence of co-morbidity on health-related quality of life in asthma and COPD patients. *Respir Med*, 97:468–75.