

# Determinants and predictors of the cost of COPD in primary care: A Spanish perspective

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**Objectives:** 1) To estimate the annual cost of patients with stable chronic obstructive pulmonary disease (COPD) followed in primary care in Spain; 2) To analyze the possible cost predictor variables.

**Patients and methods:** A multicenter, epidemiological, observational, descriptive study. Sociodemographic data, severity of disease, associated comorbidity, treatment followed by patients, quality of life (SF-12 questionnaire), health care resource utilization in the previous 12 months and duration of working disability due to COPD were collected.

**Results:** A total of 10,711 patients (75.6% men; 24.4% women) with a mean age of  $67.1 \pm 9.66$  years were evaluated. The mean forced expiratory volume in one second ( $FEV_1$ ) value was  $57.4 \pm 13.4\%$ . The total cost per patient per year was  $\text{€}1,922.60 \pm 2,306.44$ . The largest component of this cost was hospitalization ( $\text{€}788.72 \pm 1,766.65$ ), followed by cost of drugs ( $\text{€}492.87 \pm 412.15$ ) and visits to emergency rooms ( $\text{€}134.32 \pm 195.44$ ). Linear regression analysis found associated heart disease,  $FEV_1$ , physical component of quality of life, number of medical visits (primary care physician, pneumologist and emergency room), hospital admissions (frequency and duration of stay) and duration of working disability to be significant predictors of the total annual cost.

**Conclusions:** The total annual cost of a COPD patient followed in primary care in Spain was considered high in this study. The presence of associated heart disease, severity of airflow obstruction, physical component of quality of life, health care resource utilization and duration of work disability were found to be predictor of cost.

**Keywords:** COPD, primary care, costs, predictors, Spain

## Introduction

Chronic obstructive pulmonary disease (COPD) is one of the most important respiratory problems we face today. It is the fourth leading cause of morbidity and mortality in the developed world (Pauwels et al 2001). In Spain, COPD affects 9.1% of the general population between 40 and 69 years of age (Sobradillo et al 2000), and is responsible for approximately 10%–12% of primary care visits and 35%–40% of visits to a pneumologist. It also causes 35% of permanent work disabilities and 7% of hospital admissions (Pauwels et al 2001; Álvarez-Sala et al 2001). Because of the growing morbidity and mortality associated with this disease, it causes a high utilization of health care resources and a large economic burden to society. Thus, it has been reported that the expenses caused by this disease in Spain amount by 2% of the national health annual budget and 0.25% of the gross domestic product (Álvarez-Sala et al 2001). Furthermore, it is predicted that the impact of this disease will increase in coming years as a result of the rise in the life expectancy of the population, the increase in its prevalence and the emergence of new drugs and treatment modalities. Despite this, there are few studies in Spain that have quantified the costs of COPD (Grupo DAFNE 2000; García et al 2003; Miravittles et al 2003; Izquierdo 2003;

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Izquierdo-Alonso 2004; Masa et al 2004; Sicras Mainar et al 2007), and they differ in the criteria used for sampling and for assessment of the resources consumed. As a result, they also differ in the findings obtained. In addition, most of these studies had a small sample size and included patients from different care levels.

The primary objective of this study was to estimate the annual cost generated by patients with stable COPD followed in primary care facilities in Spain. The secondary objective was to analyze the possible variables with ability to predict the cost of the disease.

## Materials and methods

### Design and study population

This analysis is part of the EPIDEPOC study, a multicenter, epidemiological, observational, descriptive study carried out in the primary care setting to estimate the use of health care resources and to assess the quality of life of patients with stable COPD (Carrasco Garrido et al 2006). The recruitment of patients and calculation of sample size corresponded to that performed in the EPIDEPOC study (Carrasco Garrido et al 2006). For calculation of sample size, a cluster design was used, considering 3 types of variables: health centers, physicians, and medical records. As the health centers were considered to be homogeneous and representative of the Spanish geographical population, the medical record was chosen as the unit of study and the prescriber as the cluster. A previous study in a large cohort of 1,510 primary care patients found that the average annual cost per patient varied widely, with an estimated standard deviation of €3,407 (Izquierdo 2003). Assuming a precision of €90, 5,505 medical records needed to be evaluated. If the effect of the cluster design is also taken into account, ie, the loss of efficacy from the use of clusters, assuming a correlation of 0.3 and a cluster size of 5, a total of 2,422 prescribers and 12,111 medical records would be required.

Patients were selected consecutively by primary care physicians from all Spanish autonomous communities, whose distribution was weighted based on the population of each community. Patients were recruited during a period of 3 months (from January 1 to March 31, 2003). Subjects of both sexes, aged 40 years or older, and diagnosed with COPD at least 12 months before the start of the study, were included. The diagnosis of COPD was performed according to the criteria of the Spanish Society of Pneumology and Chest Surgery (SEPAR) and was based on demonstration by means of forced spirometry of a forced expiratory volume in 1 second ( $FEV_1$ ) less than 80% of the predicted value and a

$FEV_1$ /forced vital capacity (FVC) ratio less than 0.7 after the bronchodilation test. The severity of the disease was classified into three levels based on the  $FEV_1$  value: mild ( $FEV_1$  60%–80% of predicted value), moderate ( $FEV_1$  40%–59% of predicted value) and severe ( $FEV_1$  less than 40% of predicted value), in accordance with the SEPAR criteria (Barberà et al 2001). Patients with a neurological or psychiatric illness that would preclude their assessment during the study were excluded. Patients with an acute exacerbation of COPD in the previous month were also excluded. An acute exacerbation was considered to be the occurrence of an impairment of the clinical condition of the patient characterized by increased baseline dyspnea, purulent sputum, increased volume of sputum or any combination of these symptoms.

The study was approved by the Ethics Committee of the Alcorcón Hospital Foundation, and all patients gave their oral consent to participate in it.

### Assessment of patients

A single visit was completed in which sociodemographic data, year of COPD diagnosis, severity of the disease, comorbidity, and utilization of health care resources in the previous 12 months was collected. All patients were administered the short form 12-item (SF-12) quality of life questionnaire, an abbreviated version of the SF-36 health questionnaire (Ware et al 1996). These 12 items explain more than 90% of the variance of the physical and mental component scores of the SF-36. The physical (PCS-12) and mental component summary (MCS-12) scores are then calculated, using a value of 50 with a standard deviation of 10 as the reference population. The SF-12 is scored from 0 to 100 with higher scores indicating better health status.

Direct costs were calculated from the information on the different procedures provided by the managements of Madrid Health Area 8 and the Alcorcón and Móstoles Hospitals. Indirect costs were calculated using the human capital method. This method is based on the assumption that the value of the lost production is equal to the wages associated with obtaining this production. In other words, a day missed from work implies a loss of production equal to the wages that would have been earned on that day. The information on employment and wages was obtained from the Spanish Statistical Office.

### Statistical analysis

Statistical analysis of the data was carried out using the SPSS 12.0 for Windows statistical package (SPSS Inc., Chicago, IL). Qualitative variables were described by

frequency and percentage and quantitative variables by mean, standard deviation, minimum and maximum. The Pearson  $\chi^2$  test was used to analyze the relationship between qualitative variables. Student's *t* test for independent measurements was used to calculate the differences in the means of the two groups and the ANOVA test to study the differences between more than two groups of patients. Finally, a multiple linear regression analysis was performed using the total annual cost per COPD patient as the dependent variable. Variables significant in the bivariate analysis or deemed clinically relevant were included in the model. All statistical tests were two-tailed and a value of  $p < 0.05$  was considered significant.

## Results

The number of physicians participating in the study was 2,377, which allowed a total of 10,711 patients (75.6% men) to be recruited, with a mean age of  $67.1 \pm 9.66$  years. Table 1 show the sociodemographic and clinical characteristics of the sample studied. The mean FEV<sub>1</sub> value was  $57.4 \pm 13.4\%$ . The severity of the disease was mild in 35.5% of cases, moderate in 53.4% and severe in 11.2%. The most frequent observed comorbidities were hypertension (47.7%), hypercholesterolemia (41.3%), anxiety (22.2%), heart disease (18.8%), gastroduodenal ulcer (17.4%), diabetes (16.9%), and depression (12.8%). The mean PCS-12 and MCS-12 scores on the SF-12 quality of life questionnaire were  $35.9 \pm 10.3$  and  $48.2 \pm 11.4$ , respectively. The mean number of drugs prescribed to the patients was  $2.28 \pm 1.03$ . The most frequently prescribed drugs were anti-cholinergics (84.8%), followed by short-acting  $\beta_2$ -agonists (38.9%), inhaled corticoids (22.1%), theophyllines (11.8%), long-acting  $\beta_2$ -agonists (9.5%), mucolytics (8.9%), and oral corticoids (4.6%).

With regard to the use of health care resources in the previous year, the mean values were: visits to primary care physicians;  $6.66 \pm 5.71$ , visits to pneumologists;  $1.43 \pm 1.52$ , visits to emergency rooms;  $1.60 \pm 2.71$  and hospital admissions;  $0.50 \pm 1.17$  (Table 2). When the possible factors related to the use of health care resources were analyzed, a significant association was found with sex, with a significantly higher number of hospital admissions in men than in women ( $0.53 \pm 1.24$  versus  $0.33 \pm 0.93$ ,  $p < 0.001$ ), although there were no differences in the number of visits to primary care or specialist physicians or in the duration of disability leaves. As expected, a statistically significant association was found between the use of health care resources and the age of the patients; the older the patient, the more frequent was the use of health care resources (Table 3). Finally, a clear association

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

Characteristic (no of patients)	
Total no of patients	10711
Age (years)* (8865)	$64.1 \pm 9.7$ (40; 98)
Age groups (8862)	
40–54 years	963 (10.9)
55–64 years	2249 (25.4)
65–74 years	3669 (41.4)
>75 years	1981 (22.4)
Sex (men) (10,620)	8030 (75.6)
Smoking (10,649)	
Never smoked	2468 (23.2)
Ex-smoker	6153 (57.8)
Active smoker	2028 (19.0)
FEV <sub>1</sub> * (9963)	$57.4 \pm 13.4$
COPD severity (9963)	
Mild	3634 (35.5)
Moderate	5471 (53.4)
Severe	1146 (11.2)
Comorbidities	
Hypertension (9876)	4706 (47.7)
Diabetes (9453)	1598 (16.9)
Heart disease (9390)	1770 (18.8)
Ulcer (9425)	1637 (17.4)
Depression (9333)	1196 (12.8)
Anxiety (9397)	2084 (19.5)
Treatment	
Short-acting $\beta_2$ -adrenergic agonists (10,706)	4165 (38.9)
Long-acting $\beta_2$ -adrenergic agonists (10,610)	1008 (9.5)
Anticholinergics (10,615)	9002 (84.8)
Theophyllines (10,703)	1263 (11.8)
Inhaled corticoids (10,711)	2369 (22.1)
Oral corticoids (10,711)	498 (4.6)
Mucolytics (10,674)	950 (8.9)
Oxygen therapy (10,007)	1351 (13.5)

**Notes:** \* Values expressed as mean  $\pm$  standard deviation (minimum; maximum) or frequencies (percentages).

**Abbreviations:** COPD, chronic obstructive pulmonary disease; FEV<sub>1</sub>, forced expiratory volume in one second.

was found between the use of health care resources and the severity of COPD: patients with a more severe disease consumed more health care resources in terms of the number of visits to primary care, pneumologist and emergency rooms, the number of hospital admissions and duration of work disability (Table 4).

The total annual cost per COPD patient was  $\text{€}1,922.60 \pm 2,306.44$ , with the largest component for

**Table 2** Health care resource utilization and disability days at work during the year previous to the study

Health care resources and disability at work	N	Median	Mean	95% CI	
Primary care physician visits (#)	10,242	5	6.66	6.55	6.77
Pneumologist visits (#)	9897	1	1.43	1.40	1.46
Emergency room visits (#)	9574	1	1.60	1.54	1.65
Hospital admissions (#)	8677	0	0.50	0.48	0.52
Duration of stay (days)	4744	5.6	7.24	6.91	7.57
Duration of disability leave (days)	4984	5.1	8.86	8.21	9.52

**Abbreviation:** CI, confidence interval.

hospital admissions ( $\text{€}788.72 \pm 1,766.65$ ), followed by cost of drugs ( $\text{€}492.87 \pm 412.15$ ) and cost of visits to emergency rooms ( $\text{€}134.32 \pm 195.44$ , Figure 1). Significant higher total annual costs were found in men than in women (Table 5), and in smokers and ex-smokers than in nonsmoker subjects (Table 6). Age and severity of disease was also shown to be associated with total costs, with differences according

to gender at different levels of age and severity of disease. In men, both factors were found to be independently significant without interaction. In women, only severity of COPD was found to be statistically significant (Figure 2). As expected, patients with hospital admissions showed higher total annual costs than subjects without admissions (Table 7).

**Table 3** Health care resource utilization by age group

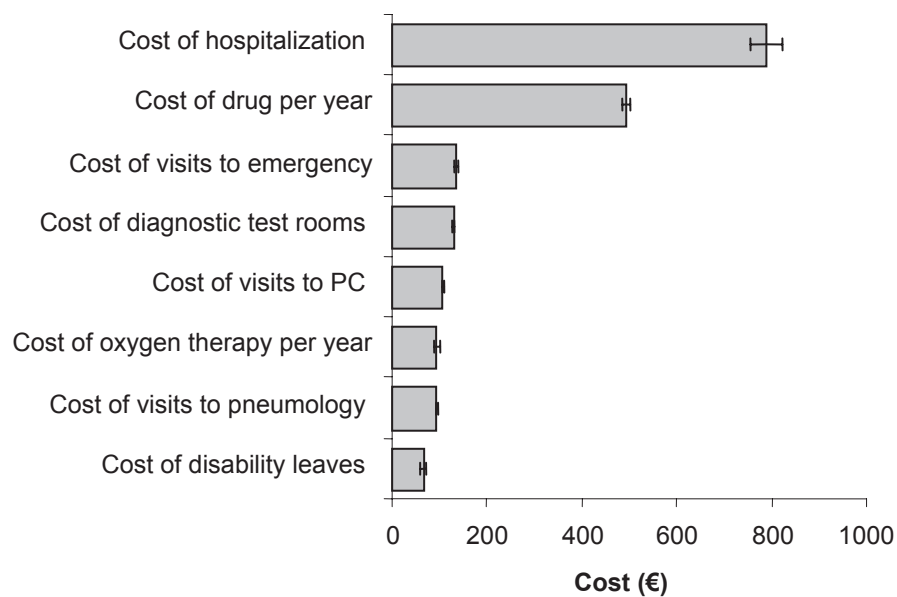
	N	Median	Mean	95% CI	p
Primary care physicians visits (#):					
– 40–54 years	921	4.00	5.73	(5.42–6.03)	<0.001
– 55–64 years	2180	5.00	6.44	(6.20–6.68)	
– 65–74 years	3525	5.00	6.84	(6.64–7.02)	
– >75 years	1900	6.00	7.35	(7.06–7.63)	
Pneumologist visits (#):					
– 40–54 years	887	1.00	1.28	(1.18–1.36)	<0.001
– 55–64 years	2106	1.00	1.39	(1.33–1.46)	
– 65–74 years	3418	1.00	1.45	(1.41–1.50)	
– >75 years	1840	1.00	1.57	(1.48–1.65)	
Emergency room visits (#):					
– 40–54 years	865	1.00	1.37	(1.20–1.54)	<0.001
– 55–64 years	2039	1.00	1.59	(1.47–1.71)	
– 65–74 years	3311	1.00	1.62	(1.53–1.71)	
– >75 years	1783	1.00	1.79	(1.65–1.93)	
Hospital admissions (#):					
– 40–54 years	769	0.00	0.30	(0.24–0.36)	<0.001
– 55–64 years	1828	0.00	0.40	(0.36–0.44)	
– 65–74 years	3007	0.00	0.52	(0.47–0.57)	
– >75 years	1670	0.00	0.68	(0.62–0.74)	
Duration of disability leave (days):					
– 40–54 years	693	8.00	15.60	(13.40–17.81)	<0.001
– 55–64 years	1391	7.00	16.44	(14.73–18.14)	
– 65–74 years	1402	0.34	2.10	(1.62–2.58)	
– >75 years	677	0.00	0.42	(0.22–0.62)	

**Abbreviation:** CI, confidence interval.

**Table 4** Health care resource utilization by COPD severity

	N	Median	Mean	95% CI	P
Primary care physician visits (#):					
– Mild COPD	3529	4.00	5.15	(5.00–5.30)	<0.001
– Moderate COPD	5246	6.00	7.08	(6.92–7.25)	
– Severe COPD	1096	7.50	9.54	(9.09–9.99)	
Pneumologist visits (#):					
– Mild COPD	3369	1.00	1.01	(0.97–1.04)	<0.001
– Moderate COPD	5090	1.00	1.52	(1.48–1.56)	
– Severe COPD	1084	2.00	2.32	(2.19–2.46)	
Emergency room visits (#):					
– Mild COPD	3255	0.00	1.01	(0.94–1.08)	<0.001
– Moderate COPD	4623	1.00	1.71	(1.63–1.79)	
– Severe COPD	1057	2.00	2.88	(2.68–3.08)	
Hospital admissions (#):					
– Mild COPD	2975	0.00	0.24	(0.20–0.28)	<0.001
– Moderate COPD	4406	0.00	0.50	(0.47–0.52)	
– Severe COPD	1001	1.00	1.33	(1.22–1.44)	
Duration of disability leave (days):					
– Mild COPD	1967	4.38	7.22	(6.39–8.05)	<0.001
– Moderate COPD	2495	5.69	9.75	(8.77–10.73)	
– Severe COPD	348	4.48	11.02	(7.27–14.77)	

**Abbreviations:** CI, confidence interval; COPD, chronic obstructive pulmonary disease.

**Figure 1** Comparison of different components of cost.

**Table 5** Comparison of different component of total costs by gender

	Gender	N	Mean	Median	95% CI
Cost of hospitalization	Men	8030	828.28*	563.75	(788.75–867.81)
	Women	2590	673.62	430.28	(610.77–736.47)
Cost of drugs per year	Men	8030	500.30*	529.25	(491.24–509.36)
	Women	2590	467.13	365.00	(451.60–482.67)
Cost of visits to emergency rooms	Men	8030	136.80*	104.52	(132.49–141.11)
	Women	2590	126.59	104.52	(119.30–133.88)
Cost of diagnostic tests	Men	8030	131.88*	97.32	(128.61–135.16)
	Women	2590	120.35	97.32	(114.89–125.81)
Cost of visits to primary care	Men	8030	107.69	83.85	(105.57–109.81)
	Women	2590	104.37	83.85	(100.72–108.01)
Cost of oxygen therapy per year	Men	8030	101.87*	50.72	(95.17–108.59)
	Women	2590	68.20	15.41	(58.32–78.09)
Cost of visits to pneumologists	Men	8030	95.58*	70.53	(93.21–97.95)
	Women	2590	87.22	70.53	(83.26–91.18)
Cost of disability leave	Men	8030	69.02	21.90	(62.67–75.38)
	Women	2590	60.18	19.22	(50.33–70.03)
Cost of pneumococcal vaccine	Men	8030	4.65	4.36	(4.50–4.80)
	Women	2590	4.38	4.05	(4.12–4.64)
Cost of influenza vaccine	Men	8030	0.20*	0.00	(0.18–0.21)
	Women	2590	0.23	0.00	(0.21–0.25)
Total annual cost per COPD patient	Men	8030	1989.20*	1112.20	(1937.48–2040.93)
	Women	2590	1724.53	984.23	(1643.35–1805.71)

**Note:** \* $p < 0.05$  between sexes, differences between means not significant when not stated.

**Abbreviations:** CI, confidence interval; COPD, chronic obstructive pulmonary disease.

On the other hand, a significant association between total costs and quality of life, as assessed with SF-12 questionnaire, was found with physical and mental components of quality of life. Subjects with worse quality of life showed higher costs, independently of gender (Figure 3). This figure shows the impact of poorer quality of life on total costs by quartiles of physical and mental components according to sex: The mental component showed a significant interaction with sex.

Linear regression analysis found associated heart disease, FEV<sub>1</sub>, physical component of quality of life, number of medical visits (primary care physician, pneumologist and emergency room), hospital admissions (frequency and duration of stay) and duration of working disability to be significant predictors of the total annual cost (Table 8).

## Discussion

This study showed that the total cost per COPD patient was near €2,000 per year when primary care physicians take care on these subjects. Concomitant heart disease, reduced

FEV<sub>1</sub>, poor physical component of quality of life, increased number of medical visits, hospital admissions and incapacitating days for work were found to be explanatory variables associated with increased costs. The strength of this study lies in the elevated number of patients with stable COPD recruited in primary care clinics in Spain, including patients with multiple comorbidities, which are usually excluded from clinical trials. The study thus reflects real-world data. It should be taken into account that most Spanish patients with COPD are treated by general practitioners and that the proportion of patients referred to specialists is lower than in other West European countries (Esteban et al 2003).

Previous studies have shown health care total annual cost per COPD patient to vary between €1,100 and €3,400, with a median cost of about €2,000, a figure that is similar to that obtained in our study (Garcia et al 2003; Izquierdo 2003; Miravittles et al 2003; Izquierdo-Alongo et al 2004; Masa et al 2004). The distribution of costs found in this study also shows considerable agreement with data provided by other authors: approximately 40% of the cost is produced by the



**Table 6** Comparison of different component of costs by tobacco use

	Tobacco user	N	Mean	Median	95% CI
Cost of hospitalization	No	2468	654.79	419.15	(592.56–717.03)
	Yes	8181	827.73*	561.51	(788.39–867.06)
Cost of drugs per year	No	2468	476.91	529.25	(460.85–492.98)
	Yes	8181	497.00*	529.25	(488.05–505.95)
Cost of visits to emergency rooms	No	2468	119.42	52.26	(112.51–126.34)
	Yes	8181	138.69*	104.52	(134.34–143.04)
Cost of diagnostic tests	No	2468	120.30	97.32	(114.81–125.80)
	Yes	8181	131.54*	97.32	(128.29–134.79)
Cost of visits to primary care	No	2468	104.37	83.85	(100.55–108.18)
	Yes	8181	107.79*	83.85	(105.70–109.88)
Cost of oxygen therapy per year	No	2468	71.04	18.67	(60.79–81.28)
	Yes	8181	100.260*	48.87	(93.64–106.87)
Cost of visits to pneumology	No	2468	87.19	70.53	(83.21–91.17)
	Yes	8181	95.33*	70.53	(92.97–97.68)
Cost of disability leave	No	2468	41.07	6.04	(32.08–50.06)
	Yes	8181	74.48*	26.36	(68.06–80.89)
Cost of pneumococcal vaccine	No	2468	4.96	4.69	(4.68–5.23)
	Yes	8181	4.48*	4.17	(4.34–4.63)
Cost of influenza vaccine	No	2468	0.17	0.09	(0.15–0.19)
	Yes	8181	0.22*	0.14	(0.21–0.23)
Total annual cost per COPD patient	No	2468	1693.64	966.82	(1611.71–1775.57)
	Yes	8181	1990.09*	1113.66	(1938.84–2041.33)

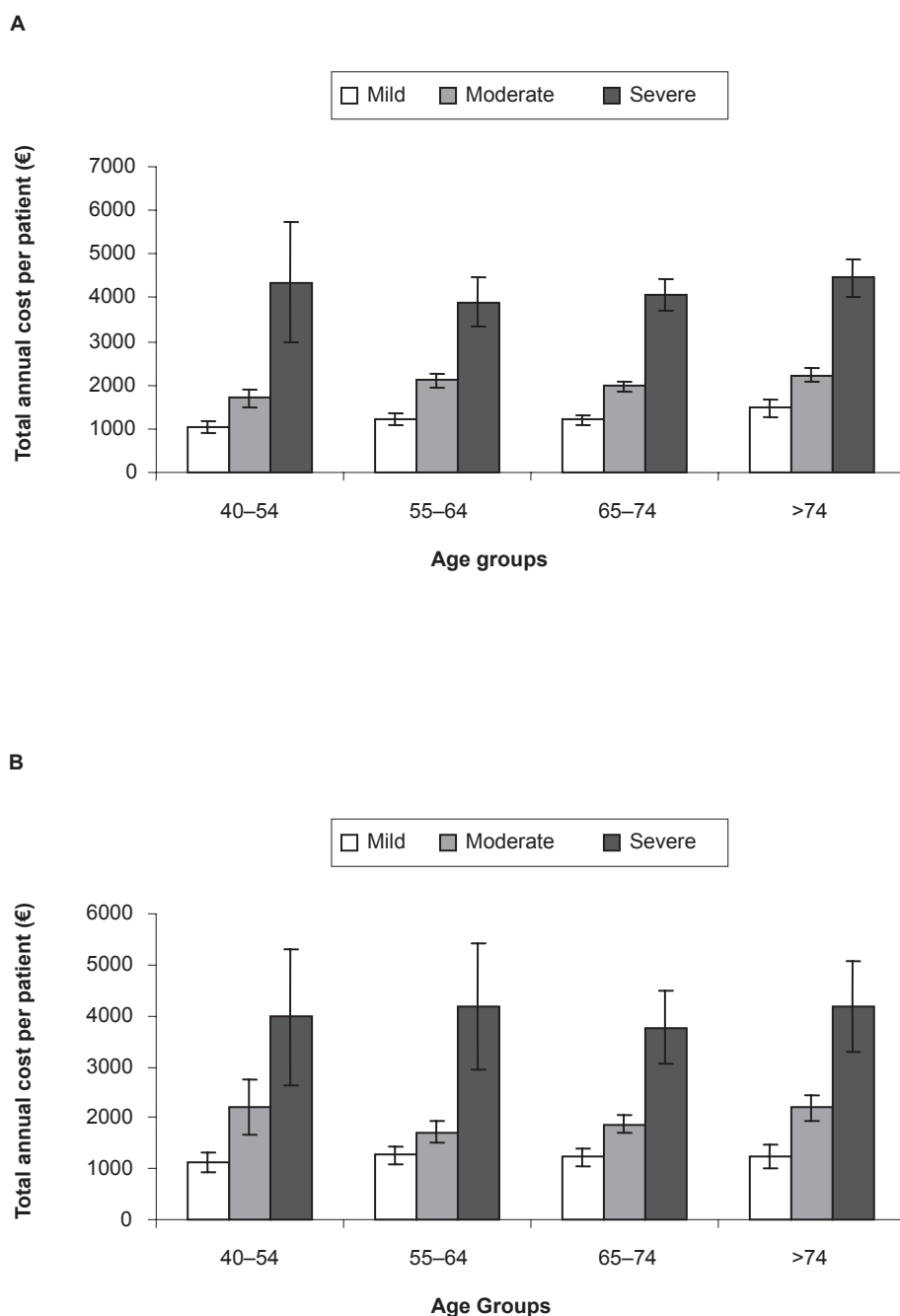
**Notes:** \* $p < 0.05$  between tobacco users, differences between means not significant when not stated. Tobacco use: “Yes” includes current smokers and ex-smokers, “No” includes never smoked.

**Abbreviations:** CI, confidence interval; COPD, chronic obstructive pulmonary disease.

hospitalization component, which represents the largest proportion of the cost. Second most important component in term of cost was drug costs, which in our study represented almost 26% of the total expenses, being this value lower than that obtained in other studies. These differences might be explained by the greater severity of the patients included in our study. Thus, it has been shown an interaction between severity of disease and components of cost; as the severity of the disease increases, not only does the cost increase, but the distribution of costs changes as could be expected to some extent. Hence, hospital stay costs increase with severity of disease, and at the same time drug costs are reduced. In this way, a recent study carried out in our setting showed that drug therapy accounted for 43% of total direct costs in mild COPD, but that this percentage decreased to 37.6% and 28.4% in moderate and severe stages, respectively (Izquierdo Alonso et al 2004).

The reduction of lung function in COPD patients is associated with a higher number of cardiovascular events and deaths from a cardiac cause, although the mechanisms responsible for this association are not well known.

A relationship between COPD and cardiovascular diseases, linked to a systemic inflammatory component, has been observed even in patients with mild or moderate obstruction (Villar Álvarez et al 2008). This study showed that the prevalence of heart disease associated with COPD was high (18.8%), and that it was one of the major determinants of the overall cost of the disease. These results contrast with those obtained in a recent study with a similar prevalence of cardiovascular events, in which no differences were observed in the annual cost per patient according to the presence or absence of these events (Sicras Mainar et al 2007). The authors of this study noted that certain limitations of the study require caution when generalizing the results, such as the design of the study itself, possible variability between the different participating physicians and the coordination of care levels, which complicates measurement of cost-effective interventions. However, and whether or not is confirmed that a relationship exists between COPD and cardiovascular diseases, linked to the systemic inflammatory component present in these patients, not only would it lead to an important advance in knowledge of the disease,



**Figure 2** Analysis of cost by age and disease severity in men (**A**) and women (**B**).

but would allow new treatment strategies to be designed that should act on various inflammatory mediators, with the aim of modifying the risk of developing complications and reducing mortality (Sin et al 2003, 2005; Arroyo-Espliguero et al 2004).

The cost of management of COPD also depends, as was seen in this study, on the severity of airflow obstruction measured by FEV<sub>1</sub>. Along this same line, Hilleman and

colleagues (2000) showed that the severity of COPD was strongly correlated with health care resource utilization and consequently with the total cost of the disease. The average direct cost per patient per year over a 5-year follow-up was US\$1,681 in ATS stage I (American Thoracic Society 1995), \$5,037 in stage II and \$10,812 in stage III. Subsequently, Masa and colleagues (2004) also found an increase in costs as the severity of the disease increased: the cost of



**Table 7** Comparison of different costs by hospitalization

	Hospital admission	N	Mean	Median	95% CI
Cost of hospitalization	No	6015	0.00	0.00	(0.00–0.00)
	Yes	2662	3173.56*	2010.00	(3088.66–3258.46)
Cost of drugs per year	No	6015	465.71	365.00	(455.80–475.61)
	Yes	2662	610.10*	529.25	(593.16–627.03)
Cost of visits to emergency rooms	No	6015	80.69	60.48	(77.16–84.22)
	Yes	2662	291.49*	209.04	(282.24–300.74)
Cost of diagnostic tests	No	6015	98.87	97.32	(96.09–101.64)
	Yes	2662	224.17*	194.64	(216.69–231.66)
Cost of visits to primary care	No	6015	91.86	67.08	(89.84–93.88)
	Yes	2662	158.70*	134.16	(154.17–163.23)
Cost of oxygen therapy per year	No	6015	36.45	0.00	(31.68–41.21)
	Yes	2662	261.56*	221.80	(244.47–278.65)
Cost of visits to pneumologists	No	6015	71.65	70.53	(69.64–73.66)
	Yes	2662	162.46*	141.06	(157.04–167.88)
Cost of disability leave	No	6015	49.84	16.30	(44.41–55.27)
	Yes	2662	105.47*	37.75	(90.65–120.28)
Cost of pneumococcal vaccine	No	6015	4.23	3.89	(4.07–4.40)
	Yes	2662	5.84*	5.67	(5.56–6.11)
Cost of influenza vaccine	No	6015	0.22	0.00	(0.21–0.24)
	Yes	2662	0.16*	0.00	(0.14–0.18)
Total annual cost per COPD patient	No	6015	911.90	816.23	(895.86–927.95)
	Yes	2662	5007.99*	4099.66	(4099.66–5111.82)

**Note:** \* $p < 0.05$  between hospital admitted patients, differences between means not significant when not stated.

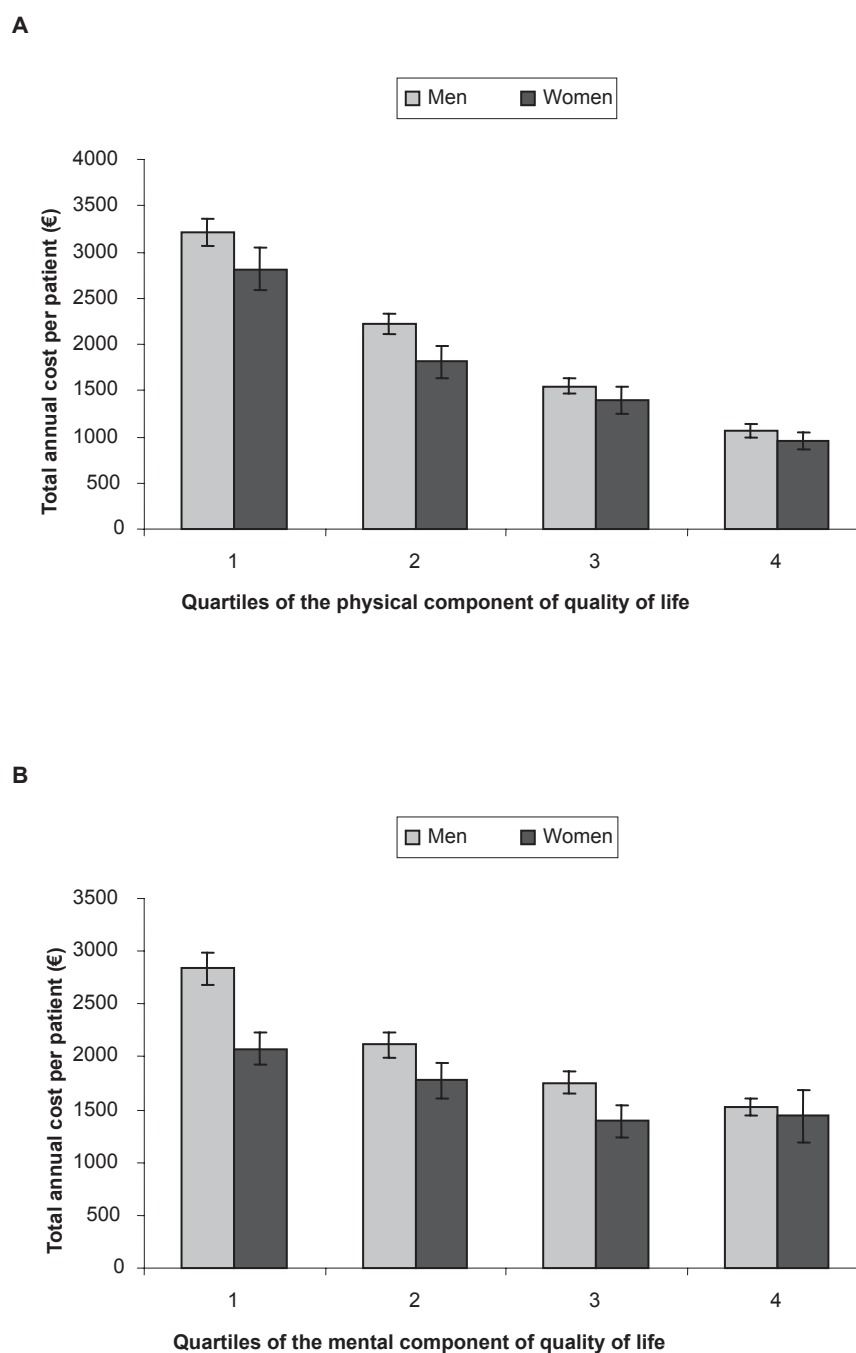
**Abbreviations:** CI, confidence interval; COPD, chronic obstructive pulmonary disease.

severe COPD was 7 times that of mild COPD and 3 times that of moderate COPD. Despite the above, a more recent study showed that although airflow obstruction is a valid predictor of health care resource utilization, its influence is small, and that the presence of comorbid conditions and symptoms of dyspnea are better predictors of costs (Mapel et al 2005).

Various authors have suggested the existence of other factors that may influence the cost of COPD (Miravittles et al 2001; Soler et al 2001). One of these is health-related quality of life, which could explain why some COPD patients have a high utilization of health care resources and generate a high demand for these resources, as pointed out by Soler and colleagues (2001). Our study showed that the physical component of quality of life is one of the factors independently influencing the overall cost of COPD. Previous studies that assessed the health status of patients with this disease in Spain found a worse quality of life in those who had more dyspnea, a greater degree of obstruction, were treated with more drugs, suffered more exacerbations, and required more visits to emergency rooms and hospital admissions

(Miravittles et al 2002, 2004; Sanjuás et al 2002; De Miguel et al 2004; Carrasco Garrido et al 2006).

Health care resource utilization is another of the major components of the cost of COPD, as shown in previous works (Mapel et al 2005). In this study, it was observed that among the factors determining the cost of COPD were the number of visits to the primary care physicians, the pneumologists and emergency rooms, as well as the number of hospital admissions and their duration. Therefore, strategies for management of COPD should emphasize measures to control chronic symptoms and reduce exacerbations and hospitalizations, because the largest part of the cost of this disease is related to hospitalization. Furthermore, a previous study analyzing the costs of hospitalization found that the cost of the stay accounted for 70% of the total cost of care of the hospitalized COPD patient, whereas the cost of medical care, examinations or the drugs used was less than a third of the total (Serra 2002). In this context, optimization of resources does not lie in controlling the number of complementary examinations, but in reducing the number of days of hospital stay (Escarrabil 2003).



**Figure 3** Cost by quartiles of the physical component (A) and the mental component (B) of quality of life by sex.

The indirect costs of COPD are more difficult to assess. There are few articles in Spain that have assessed this component and the results obtained varied widely, which has made their interpretation difficult (Krief 1996; Izquierdo 2003). It has been shown that patients with COPD have greater impairment of their ability to work and therefore are more likely to be disabled from work than those without this disease (Sin et al 2002). However, the estimated prevalence

of work disability due to COPD remains controversial. Thus, Arancón (2002) indicated that asthma and COPD accounted for 3% of permanent work disabilities in Spain in the period 1999–2000, a figure that rose to 5.3% in the group of patients between 50 and 64 years of age. However, this figure is very far from that estimated by the Spanish Society of Pneumology and Chest Surgery (SEPAR), which indicated that 35% of permanent work disabilities are due to COPD

**Table 8** Linear regression model to evaluate ability of variables to predict total costs

Variable	B	Standard error	T	Significance	95% CI	
Heart disease	227.9	72.4	-3.1	0.002	85.8	369.9
Physical component (SF-12)	-8.9	3.0	-2.9	0.003	-14.8	-3.0
FEV <sub>1</sub>	-10.6	2.2	-4.8	0.000	-14.9	-6.3
No of visits to primary care	22.8	5.2	4.3	0.000	12.6	33.0
No of visits to pneumology	216.5	21.5	10.0	0.000	174.3	258.8
No of visits to emergency rooms	180.5	14.4	12.4	0.000	152.1	209.0
No of hospital admissions	1143.1	33.8	33.7	0.000	1076.6	1209.6
Duration of stay in days	50.0	3.4	14.4	0.000	43.2	56.8
Duration of disability leave	16.9	0.9	17.3	0.000	15.0	18.9

**Abbreviations:** CI, confidence interval; COPD, chronic obstructive pulmonary disease; FEV<sub>1</sub>, forced expiratory volume in one second; SF-12, short form 12-item quality of life questionnaire.

(Álvarez-Sala et al 2001; Pauwels et al 2001). Regardless of the actual prevalence, this study found that the duration of disability leaves was a factor that contributed independently to increasing the cost of this disease.

There are some limitations in our study. We excluded subjects with serious neurological and psychiatric diseases, and patients with recent exacerbations of COPD. As these disorders are expected to be associated with higher utilization of health care resources, we can not exclude an underestimation of the real cost of COPD. In spite of these limitations, the data presented along with the predicted increase in the health care cost of COPD in the future, both in terms of its direct and indirect costs (Pauwels et al 2001), underscore the need for developing strategies aimed to optimize the use of resources devoted to the management of COPD, with special attention to early diagnosis.

## Disclosure

The authors report no conflicts of interest in this work.

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