

# Prevalence of COPD in Spain: impact of undiagnosed COPD on quality of life and daily life activities

M Miravittles,<sup>1</sup> J B Soriano,<sup>2</sup> F García-Río,<sup>3</sup> L Muñoz,<sup>4</sup> E Duran-Tauleria,<sup>5</sup> G Sanchez,<sup>6</sup> V Sobradillo,<sup>7</sup> J Ancochea<sup>8</sup>

► Additional information about the population of the study is published online only at <http://thorax.bmj.com/content/vol64/issue10>

<sup>1</sup> Fundació Clínic, Institut d'Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS), Barcelona, Spain; <sup>2</sup> Fundació Caubet-CIMERA, Bunyola, Illes Balears, Spain; <sup>3</sup> Pneumology Department, Hospital La Paz, Madrid, Spain; <sup>4</sup> Pneumology Department, Hospital Reina Sofía, Córdoba, Spain; <sup>5</sup> IMIM/CREAL, Barcelona, Spain; <sup>6</sup> Medical Department, GlaxoSmithkline, Madrid, Spain; <sup>7</sup> Pneumology Department, Hospital de Cruces, Bilbao, Spain; <sup>8</sup> Pneumology Department, Hospital La Princesa, Madrid, Spain (CIBER de Enfermedades Respiratorias (CIBERES))

Correspondence to: Dr M Miravittles, Servei de Pneumologia, Hospital Clínic, Villarroel 170, 08036 Barcelona, Spain; [marcm@separ.es](mailto:marcm@separ.es)

Received 23 February 2009  
Accepted 10 June 2009  
Published Online First  
23 June 2009

## ABSTRACT

**Aims:** This study aimed to determine the prevalence of chronic obstructive pulmonary disease (COPD) in Spain and identify the level of undiagnosed disease and its impact on health-related quality of life (HRQL) and activities of daily living (ADL).

**Methods:** A population-based sample of 4274 adults aged 40–80 years was surveyed. They were invited to answer a questionnaire and undergo prebronchodilator and postbronchodilator spirometry. COPD was defined as a postbronchodilator FEV<sub>1</sub>/FVC (forced expiratory volume in 1 s/forced vital capacity) ratio of <0.70.

**Results:** For 3802 participants with good-quality post-bronchodilator spirometry, the overall prevalence of COPD was 10.2% (95% CI 9.2% to 11.1%) and was higher in men (15.1%) than in women (5.6%). The prevalence of COPD stage II or higher was 4.4% (95%CI; 3.8%–5.1%). The prevalence of COPD increased with age and with cigarette smoking and was higher in those with a low educational level. A previous diagnosis of COPD was reported by only 27% of those with COPD. Diagnosed patients had more severe disease, higher cumulative tobacco consumption and more severely impaired HRQL compared with undiagnosed subjects. However, even patients with undiagnosed COPD stage I+ already showed impairment in HRQL and in some aspects of ADL compared with participants without COPD.

**Conclusions:** The prevalence of COPD in individuals between 40 and 80 years of age in Spain is 10.2% and increases with age, tobacco consumption and lower educational levels. The rate of diagnosed COPD is very high and undiagnosed individuals with COPD already have a significant impairment in HRQL and ADL.

The prevalence of chronic obstructive pulmonary disease (COPD) varies from country to country, mainly due to the effects of cumulative exposure to smoking and the increased life span of the population. There are increasingly more data on the prevalence and distribution of COPD from around the world, but until very recently most have been derived from expert opinion and not from well-conducted epidemiological studies using postbronchodilator spirometry<sup>1</sup>; moreover, studies differed in terms of age bands as well as in the use of different criteria of COPD.<sup>2–3</sup> Therefore, direct comparisons between prevalences obtained in different countries are not always possible. The Global Initiative for Chronic Obstructive Lung Disease (GOLD) has resulted in an agreement on spirometric thresholds for diagnosis and severity and has become the gold standard, at least for epidemiological purposes.<sup>2</sup>

An epidemiological survey conducted from 1997 to 1998 in adults between 40 and 70 years of age in Spain reported a prevalence of COPD of 9.1%<sup>3</sup> according to the old European Respiratory Society (ERS) criteria for COPD.<sup>4</sup> Interestingly, only 22% had a previous diagnosis of the disease.<sup>5</sup> Early diagnosis is important to encourage smoking cessation, appropriate pharmacological treatment and physical exercise. The demonstration of impairment in activities of daily living (ADL) and health-related quality of life (HRQL), even in early undiagnosed disease, should alert clinicians of the importance of case detection in subjects at risk.

The main aim of the present study was to determine the GOLD-defined prevalence of COPD in Spain. Additionally, we aimed to identify the burden of undiagnosed COPD in the general population in terms of impairment in HRQL and ADL.

## METHOD

### Design of the study

The protocol of the EPI-SCAN study has been published elsewhere.<sup>6</sup> Briefly, it was a multicentre, cross-sectional, population-based, observational study conducted in 11 sites in 10 cities in Spain (Barcelona, Burgos, Córdoba, Huesca, Madrid (two areas), Requena, Sevilla, Oviedo, Vic and Vigo) representing different geographic, climatic and socio-economic regions. A priori sample size calculation estimated that assuming an expected prevalence of 12% derived from a previous study, and considering the different COPD criteria used in both surveys,<sup>4</sup> with a precision of  $\pm 1$  and with 20% of losses, a total sample of 5071 individuals would be required to fulfil the primary study goal, assuming a 5% alpha error and with 80% power. The participating sites agreed to recruit a population sample of at least 369 adults aged 40–80 years who were not institutionalised, and who were living in a well-defined administrative area covered by a reference hospital.

The study was approved by the Ethics Committee of the Hospital Clínic de Barcelona, as a reference IRB and consequently by the local Ethics Committees of the participating centers. All subjects provided written informed consent to participate in the study.

### Study population

Participants were selected using a commercially available database that contained information on the telephone numbers of 3 728 305 residents in the areas selected, which represents >90% of the

households in those areas. Using random-digit telephone dialing, adults aged 40–80 years were identified, and those who agreed to join the study were contacted by phone by the local investigator to schedule a clinical visit. The subjects who could not be contacted after at least three attempts or those with mental disabilities were randomly replaced with new contacts. Responses to a minimal data questionnaire were obtained from all the subjects contacted.

### COPD definitions

We used the definition of COPD proposed by GOLD: a postbronchodilator FEV<sub>1</sub>/FVC (forced expiratory volume in 1 s/forced vital capacity) ratio below 0.70. The severity of COPD was also determined by the GOLD criteria.<sup>2</sup> The definition of GOLD stage 0 was according to that prevailing at the time that the study was designed: presence of chronic cough and sputum production with normal spirometry. Previous diagnosis of COPD was considered when the interviewee gave a positive answer to a previous diagnosis of COPD, emphysema or chronic bronchitis.

### Measurements and instruments

Each subject answered a detailed written questionnaire compiled from a series of validated questionnaires. Data obtained included: demographic information; educational level; respiratory history and symptoms; smoking and family history; occupation; medication; and use of health services. Additionally, they completed the modified Medical Research Council (mMRC) questionnaire for dyspnoea<sup>7</sup> and the Spanish version of the European Commission for Steel and Coal (ECSC) questionnaire of respiratory symptoms.<sup>8</sup>

Lung function data were obtained at each site using the same equipment, Master Scope CT version 5.2 (VIASYS Healthcare, Hoechberg, Germany). Lung function was measured before and 15–30 min after inhalation of 200 mg of salbutamol according to American Thoracic Society (ATS) recommendations.<sup>9</sup> Calibration was checked daily with a 3 litre syringe. Participants performed up to eight forced expiratory manoeuvres to obtain three acceptable manoeuvres (FEV<sub>1</sub> and FVC variation  $\leq 200$  ml). According to the results of spirometry and the ECSC questionnaire, patients were classified into three different study groups: COPD (stages I–IV), GOLD stage 0 and control subjects. All subjects with COPD, as well as an equal number of GOLD stage 0 and control subjects recruited consecutively were invited to fill out a series of standardised questionnaires.

The London Chest Activity of Daily Living (LCADL) scale<sup>10</sup> translated into Spanish and validated,<sup>11</sup> is a specific questionnaire that consists of 15 items and four activity groups: self-care (4 items), domestic (6 items), physical (2 items) and leisure time (3 items). A global score as well as a score for each group of activities is obtained. The EQ-5D questionnaire, translated into Spanish and validated,<sup>12</sup> is a generic HRQL questionnaire that contains a descriptive system with five dimensions (mobility, self-care, daily activities, pain and anxiety or depression), and a visual analogue scale (VAS) that has a thermometer the ends of which are labelled with “the worst health state” and “the best health state”, with scores from 0 to 100, respectively. The St George’s Respiratory Questionnaire (SGRQ) is a specific HRQL questionnaire, translated into Spanish and validated,<sup>13</sup> that contains 50 items distributed in three dimensions: symptoms, activities and impact. The scores range from 0 to 100, with the lowest scores indicating a better HRQL.

### Field work and quality control

The field work was done from May 2006 to July 2007 by one fully certified staff chest physician and one research nurse at each site. The results of the first 1745 spirometries representing all sites were centrally reviewed for quality. We verified that 89.1% of manoeuvres had an adequate initiation; 85.6% had a duration of at least 6 s and 90.6% reached a satisfactory tele-expiratory plateau. Considered globally, 80.3% of spirometric tracings fulfilled all acceptability criteria and 95.3% and 96.4% fulfilled the reproducibility criteria for FEV<sub>1</sub> and FVC, respectively, according to the ATS 2004 consensus.<sup>9</sup>

### Statistical analysis

We estimated the overall COPD prevalence, the prevalence by age, gender, smoking status and severity of COPD, and the prevalence of risk factors and their association with other variables such as ADL and HRQL. The significance of comparisons was evaluated using the  $\chi^2$  test or Fischer exact test for categorical variables, and the Student t test or the Mann–Whitney parametric test for continuous variables. Following univariate analysis, two logistic regression models were constructed as an exploratory analysis to identify independent risk factors for COPD and factors significantly associated with the previous diagnosis of COPD compared with patients with undiagnosed COPD. The variables included in the first model were: age, gender, pack-years of smoking, educational level and centre. Variables included in the second model were the same plus severity of COPD by GOLD stages and SGRQ total score. Bilateral two-tailed hypotheses were formulated and 95% CIs were calculated, and a p value  $< 0.05$  was considered as statistically significant. The Bonferroni correction for multiple comparisons at an alpha level of 0.01 was applied. Statistical software (SPSS version 15.0 for Windows; SPSS, Chicago, Illinois, USA) was used.

### RESULTS

Of a total of 4274 subjects randomly contacted by telephone at the 11 sites, 3885 agreed to participate in the study and a final group of 3802 (88.9%) were available for analysis (complete minimum data set on gender, age and lung function). The 389 (9.1%) who refused to take part in the survey were slightly older and there were more women and never and former smokers (see Supplementary material).

Table 1 shows the demographic and lung function characteristics of the study population.

### COPD prevalence

Table 1 and fig 1 show the overall prevalence according to gender and age group. The overall COPD prevalence defined by the GOLD criteria was 10.2% (95% CI 9.2% to 11.1%), higher in men (15.1%) than in women (5.6%), and was significantly higher in subjects aged  $\geq 70$  years (22.9%) (table 2). The sample analysed allowed a precision of 96% for an estimate of 10.2% prevalence. COPD prevalence by the GOLD classification of severity was distributed as follows: mild, 56.4%; moderate, 38.3%; severe, 4.6%; very severe, 0.5%. The prevalence of GOLD stage II or higher was 4.4% (95% CI 3.8% to 5.1%), being 7.1% in men and 2.0% in women. The prevalence of GOLD stage 0 was 6.7% (95% CI 5.9% to 7.5%), 8.1% in men and 5.5% in women. A total of 408 (10.7%) individuals presented a restrictive spirometry pattern (FVC  $< 80\%$  and FEV<sub>1</sub>/FVC  $> 0.7$ ), and they had a higher body mass index (BMI) and lower

**Table 1** Demographic characteristics, smoking and lung function

Variable	Total (n = 3802)
Gender, men, n (%)	1797 (47.3)
Age, mean (SD)	56.6 (10.7)
BMI, mean (SD)	27.4 (4.5)
Smoking history, n (%)	
Smoker	989 (26.0)
Ex-smoker	174 (30.9)
Never smoker	1635 (43.1)
Pack-years (smokers and ex-smokers)	26.0 (21.5)
Education, n (%)	
Less than primary school	358 (9.4)
Primary school	1393 (36.7)
Secondary school	1105 (29.1)
University degree	912 (24.0)
Missing	30 (0.8)
Spirometry (postbronchodilator)	
FVC (litres)	3.74 (1.0)
FVC (% predicted)	96.8 (16.3)
FEV <sub>1</sub> (litres)	2.94 (0.9)
FEV <sub>1</sub> (% predicted)	102.1 (19.4)
FEV <sub>1</sub> /FVC	0.79 (0.08)
Previous diagnosis of COPD, chronic bronchitis or emphysema, n (%)	203 (5.3)
Previous diagnosis of asthma, n (%)	261 (6.9)
City size:	
Small (<100 000 inhabitants)	1078 (28.3%)
Medium (100 000–500 000)	1268 (33.3%)
Large (>500 000)	1456 (38.3%)

BMI, body mass index; COPD, chronic obstructive pulmonary disease. FEV<sub>1</sub>, forced expiratory volume in 1 s; FVC, forced vital capacity.

educational level compared with the subjects with normal spirometry (see Supplementary material)

### Prevalence of risk factors

The overall prevalence of smoking was 26%, and 30.9% of subjects were ex-smokers. A total of 57% of women were never smokers compared with only 27.2% of men ( $p < 0.05$ ). The prevalence of COPD was significantly higher in heavy smokers

than in non-smokers and in smokers of  $\leq 30$  pack-years (table 3). The prevalence of COPD in never smokers was 6.1% (100 out of 1635 subjects), representing 25.9% of the subjects with COPD (100 of 386 subjects). Only 35% of the cases of COPD in never smokers had COPD GOLD stages II–IV (prevalence of GOLD II–IV in never smokers of 2.1%).

Table 4 shows the multiple logistic regression analysis of factors associated with COPD. The variables significantly associated with having COPD were older age, male gender, higher tobacco consumption and poor educational level.

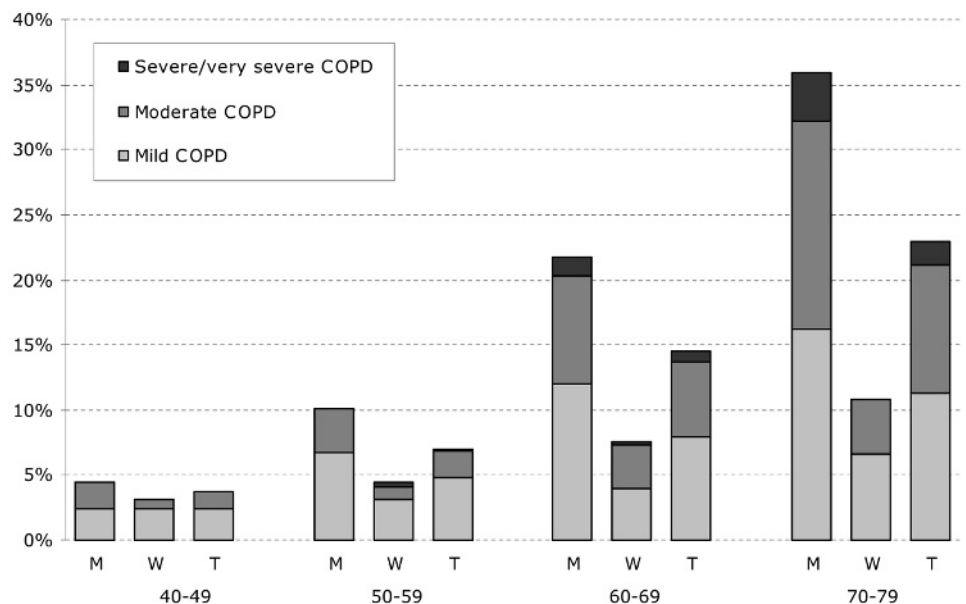
### Factors associated with previous diagnosis of COPD

A total of 26.9% of identified COPD cases had a previous diagnosis of COPD, ranging from 16% of those with mild disease to 35.1% of those with moderate and 85% of those with severe and very severe disease. Multiple logistic regression analysis of factors associated with previous diagnosis of COPD demonstrated that being older than 70, and having a smoking history of  $>30$  pack-years, more severe disease and an impaired HRQL were associated with a higher probability of being diagnosed with COPD (table 4).

### Impact of COPD on ADL and HRQL

A group of 343 (88.8%) patients with COPD, 172 (67.2%) subjects with GOLD stage 0 COPD and a control group of 380 consecutive non-COPD subjects agreed to answer the LCADL, EQ-5D and SGRQ questionnaires. Patients with COPD had impaired ADL and HRQL measured with both the generic and specific instruments. When we considered the patients with undiagnosed COPD, they also showed a statistically significant impairment in HRQL measured with the SGRQ and a statistically significantly worse VAS score in the EQ-5D (73.8 (16) vs 77.2 (16) in controls;  $p < 0.05$ ) with a preserved utility score. They also showed a statistically significant impairment in some dimensions of ADL: self-care, domestic and physical. In contrast, individuals with GOLD stage 0 had similar scores in the LCADL compared with non-COPD participants, but they also showed statistically significant impairment in the VAS EQ-5D and the SGRQ (table 5).

**Figure 1** Chronic obstructive pulmonary disease (COPD) prevalence (postbronchodilator FEV<sub>1</sub>/FVC (forced expiratory volume in 1 s/forced vital capacity)  $< 0.70$ ) and GOLD (Global Initiative for Chronic Obstructive Lung Disease) severity stages by gender and age group. M, men; W, women; T, total.



**Table 2** COPD prevalence and COPD GOLD II+ prevalence and 95% CI according to gender and age group

	40–49 years	50–59 years	60–69 years	70–80 years	Total
<b>COPD GOLD I–IV</b>					
Men	4.4% (2.8% to 6.1%)	10.2% (7.6% to 12.8%)	21.7% (17.7% to 25.6%)	35.9% (30.5% to 41.4%)	15.1% (13.5% to 16.8%)
Women	3.2% (1.8% to 4.5%)	4.4% (2.8% to 6.1%)	7.5% (5.0% to 10.0%)	10.7% (7.3% to 14.1%)	5.6% (4.6% to 6.7%)
All	3.8% (2.7% to 4.8%)	7.0% (5.6% to 8.6%)	14.5% (12.1% to 16.8%)	22.8% (19.5% to 26.2%)	10.2% (9.2% to 11.1%)
<b>COPD GOLD II–IV</b>					
Men	2.1% (0.9% to 3.2%)	3.3% (1.8% to 4.9%)	9.8% (6.9% to 12.7%)	19.7% (15.1% to 24.2%)	7.1% (5.9% to 8.3%)
Women	0.8% (0.1% to 1.4%)	1.3% (0.4% to 2.2%)	3.5% (1.8% to 5.3%)	4.1% (1.9% to 6.3%)	2.0% (1.4% to 2.7%)
All	1.4% (0.7% to 2.0%)	2.2% (1.4% to 3.1%)	6.6% (4.9% to 8.3%)	11.6% (9.1% to 14.2%)	4.4% (3.8% to 5.1%)

The prevalence of respiratory symptoms in the total population, COPD and GOLD 0 COPD is presented in the Supplementary material. COPD, chronic obstructive pulmonary disease; GOLD, Global Initiative for Chronic Obstructive Lung Disease.

**DISCUSSION**

The results of this large epidemiological study have demonstrated an overall prevalence of GOLD-defined COPD in the Spanish population between 40 and 80 years of age of 10.2%. The prevalence is almost three times higher in men than in women and increases with age, cumulative tobacco consumption and low education level. Interestingly, only 27% of the cases detected reported a previous diagnosis of the disease, while the probability of being diagnosed increased with age, intensity of smoking, the severity of the disease and the impairment in HRQL. Even patients with undiagnosed COPD had a significant impairment in HRQL and in some ADL.

Our results are similar to the 9.1% prevalence of COPD obtained around 10 years ago in another epidemiological study using the old ERS criteria for COPD in Spain in subjects between 40 and 69 years of age.<sup>3</sup> Although the smoking prevalence among women has increased in Spain in the last decades,<sup>14</sup> it appears that the prevalence of COPD in women has not yet fully reflected this increase,<sup>15</sup> being 3.9% in 1998<sup>3</sup> and 5.6% in the current survey. The current findings are similar to those reported in a recent systematic review of epidemiological studies which concluded that the prevalence of physiologically defined COPD in adults aged ≥40 years worldwide ranges around 9–10%.<sup>1</sup> However, the BOLD initiative has reported significant differences between countries, ranging from 11.4% in China to 26.1% in Austria.<sup>16</sup> These differences may be related, at least in part, to differences in genetic background, smoking habits and exposure to other environmental risk factors, and are accompanied by differences in diagnostic rates and in manage-

ment of the disease around the world.<sup>17</sup> The COPD prevalence observed in our study fits in the low range, but is higher than the 7.8% observed in Mexico,<sup>18</sup> 8.9% in Colombia<sup>19</sup> and 8.2% reported in another large study in China.<sup>20</sup>

There are controversies over the use of the GOLD definition for COPD, particularly in the elderly population as the FEV<sub>1</sub>/FVC ratio falls with age<sup>21</sup>; therefore, using this definition may result in overdiagnosis of COPD.<sup>22</sup> However, we used this definition to be able to compare our results with the majority of recently published studies on COPD prevalence.<sup>16–20</sup> Another way of circumventing this problem is to consider the prevalence of GOLD stage II or higher COPD that requires a postbronchodilator FEV<sub>1</sub> <80% predicted. Considering this criterion, the prevalence dropped to 4.4%, within the range observed in some sites in the PLATINO study (2.6% in Mexico and 5.7% in Caracas and Sao Paulo)<sup>18</sup> but clearly below the mean prevalence of 10.1% observed in BOLD.<sup>16</sup> These differences justify the need to conduct studies to investigate the local prevalence of COPD in different countries or geographic areas.

The main risk factors for COPD identified in our study were older age, increased tobacco consumption and low educational level. However, there were 6.1% of never smokers who fulfilled the thresholds of airflow obstruction compatible with a definition of COPD, who represented 26% of the COPD cases detected. This is similar to the prevalence of 5.2% in never smokers in Colombia who also represented 30% of their COPD cases<sup>19</sup> and in line with the calculated 23% of the burden of COPD attributed to never smokers.<sup>23</sup> It is of note that most non-smokers among subjects identified as having COPD are elderly subjects

**Table 3** Chronic obstructive pulmonary disease (COPD) prevalence according to smoking history

Gender	Age group	Non-smokers	Pack-years (smokers and ex-smokers)			Total (smokers and ex)
			1–14	15–30	>30	
Men	40–49	3/153 (2.0)	6/152 (4.0)	10/197 (5.1)	7/83 (8.4)	23/432 (5.3)
	OR (95% CI)	1	2.1 (0.5 to 8.6)	2.7 (0.7 to 10.0)	4.6 (1.2 to 18.3)	2.8 (0.8 to 9.5)
	50–59	5/134 (3.7)	4/100 (4.0)	16/135 (11.9)	26/139 (18.7)	46/374 (12.3)
	OR (95% CI)	1	1.1 (0.3 to 4.2)	3.5 (1.2 to 9.8)	5.9 (2.2 to 15.9)	3.6 (1.4 to 9.3)
	60–69	10/114 (8.8)	7/59 (11.9)	18/87 (20.7)	54/147 (36.7)	79/293 (27.0)
	OR (95% CI)	1	1.4 (0.3 to 2.1)	2.7 (1.2 to 6.2)	6.0 (2.9 to 12.5)	3.8 (1.9 to 7.6)
	70–80	19/88 (21.6)	7/38 (18.4)	22/53 (41.5)	58/116 (50.0)	87/207 (42.0)
	OR (95% CI)	1	0.8 (0.3 to 2.1)	2.6 (1.2 to 5.5)	3.6 (1.9 to 6.7)	2.6 (1.5 to 4.6)
Women	40–49	4/223 (1.8)	1/178 (0.6)	12/214 (5.6)	4/44 (9.1)	17/436 (3.9)
	OR (95% CI)	1	0.3 (0 to 2.7)	3.3 (1.0 to 10.0)	5.5 (1.3 to 22.9)	2.2 (0.7 to 6.6)
	50–59	11/318 (3.5)	2/118 (1.7)	7/115 (6.1)	7/55 (12.7)	16/288 (5.6)
	OR (95% CI)	1	0.5 (0.1 to 2.3)	1.8 (0.7 to 4.8)	4.1 (1.5 to 11.1)	1.6 (0.7 to 3.5)
	60–69	24/322 (7.5)	2/33 (6.1)	1/40 (2.5)	5/27 (18.5)	8/100 (8.0)
	OR (95% CI)	1	0.8 (0.2 to 3.5)	0.3 (0 to 2.3)	2.9 (1.0 to 8.1)	1.1 (0.5 to 2.5)
	70–80	24/283 (8.5)	2/15 (13.3)	3/8 (37.5)	5/10 (50.0)	10/33 (30.3)
	OR (95% CI)	1	1.7 (0.4 to 8.0)	6.5 (1.5 to 29.0)	10.8 (2.9 to 40.0)	4.7 (2.0 to 11.0)

**Table 4** Chronic obstructive pulmonary disease (COPD) risk factors and factors associated with previous diagnosis of COPD: multiple logistic regression analysis

Variable	COPD risk factors	Factors associated with previous diagnosis of COPD
	OR (95% CI)	OR (95% CI)
Age:		
50–59 years	1.7 (1.1 to 2.5)	4.2 (0.9 to 17.7)
60–69 years	4.0 (2.7 to 5.8)	3.9 (0.9 to 16.0)
70–80 years	7.6 (5.1 to 11.2)	6.4 (1.6 to 25.2)
Gender, men	1.9 (1.4 to 2.5)	1.9 (0.8 to 4.5)
Smoking:		
1–14 pack-years	1.0 (0.68 to 1.6)	0.4 (0.06 to 2.2)
15–30 pack-years	2.6 (1.86 to 3.7)	1.5 (0.5 to 4.7)
More than 30 pack-years	5.1 (3.69 to 7.1)	3.1 (1.2 to 7.9)
Education:		
Less than primary school	1.6 (1.1 to 2.5)	0.7 (0.2 to 2.1)
Primary school	1.3 (0.9 to 1.8)	0.6 (0.3 to 1.6)
Secondary school	1.1 (0.8 to 1.5)	0.5 (0.2 to 1.4)
Severity of COPD:		
GOLD II	NA (NA)	1.9 (1.0 to 3.6)
GOLD III–IV		16.7 (3.9 to 70.8)
SGRQ:		
5–17 units (second tertile)	NA (NA)	4.7 (1.3 to 17.5)
More than 17 units (third tertile)		11.4 (3.1 to 41.2)

Reference categories: age, between 40 and 49 years; gender, female; never smoker; education, University degree.

Severity of COPD: GOLD I; SGRQ <5 units (first tertile).

GOLD, Global Initiative for Chronic Obstructive Lung Disease; SGRQ, Saint George's Respiratory Questionnaire.

with mild COPD.<sup>5 20 22 23</sup> In fact, the population-attributable risk due to smoking in COPD is almost 80% in those aged 60–62 years but decreases in the elderly.<sup>24</sup> The probable explanation for the decreased importance of smoking in COPD in the ageing is the use of the fixed ratio for the definition of airflow obstruction.

The presence of chronic symptoms (cough and sputum production) in a smoker without airflow obstruction was labelled as GOLD stage 0 COPD in the previous GOLD guidelines. In our study, 6.7% of individuals fulfilled this criterion. Interestingly, a novel finding of our study was that GOLD stage 0 participants presented a significant impairment in HRQL without impairment in ADL, compared with a control population without COPD. The relevance of GOLD stage 0 has been questioned since it does not always represent the first step in the development of COPD<sup>25</sup> and, in

fact, it has not been included in the last edition of the GOLD guidelines.<sup>2</sup>

Only 27% of the identified cases reported a previous diagnosis consistent with COPD. This percentage is slightly higher than the 21.8% observed in 1998 in Spain<sup>5</sup> and is in accordance with other studies around the globe—that is, 20% in the UK,<sup>26</sup> 19% in Greece,<sup>27</sup> 11.3% in Latin America<sup>28</sup> or even 9.4% in Japan.<sup>29</sup> Although undiagnosed patients had a milder airflow obstruction, remarkably they had a significant impairment in HRQL and reduced levels of ADL. Both HRQL and level of physical activity are not only markers of “well-being” but also important predictors of survival in patients with COPD.<sup>30 31</sup> These results suggest that, at least in some cases, undiagnosed patients represent earlier disease compared with diagnosed individuals and highlight the importance of early recognition of the disease

**Table 5** Results of the LCADL, EQ-5D and SGRQ questionnaires in patients with chronic obstructive pulmonary disease (COPD) according to previous diagnosis, stage 0 COPD and control subjects

Mean (95% CI)	Control (n = 378)	Stage 0 (n = 172)	Diagnosed COPD (n = 100)	Undiagnosed COPD (n = 235)	All COPD (n = 335)
<b>LCADL</b>					
Total	15.7 (15.3 to 16.0)	15.8 (15.2 to 16.5)	19.1 (17.4 to 20.8)***	15.6 (15.0 to 16.2)	16.6 (16.0 to 17.3)*
Self-care	4.2 (4.1 to 4.2)	4.2 (4.1 to 4.3)	5.3 (4.9 to 5.7)***	4.4 (4.3 to 4.6)*	4.7 (4.5 to 4.8)***
Domestic	5.9 (5.7 to 6.1)	5.8 (5.4 to 6.2)	6.2 (5.1 to 7.3)*	5.2 (4.8 to 5.6)*	5.5 (5.1 to 5.9)
Physical	2.5 (2.4 to 2.6)	2.7 (2.6 to 2.9)	3.9 (3.6 to 4.2)***	2.8 (2.7 to 2.9)*	3.1 (3.0 to 3.3)***
Leisure	3.1 (3.0 to 3.1)	3.1 (3.0 to 3.2)	3.7 (3.4 to 3.9)***	3.1 (3.1 to 3.2)	3.3 (3.2 to 3.4)***
<b>EQ-5D</b>					
VAS score	77.2 (75.6 to 78.8)	72.0 (69.5 to 74.5)***	64.0 (55.8 to 72.1)***	73.9 (71.8 to 75.9)*	70.9 (69.1 to 72.7)***
Utility score	0.90 (0.85 to 0.95)	0.88 (0.81 to 0.95)	0.77 (0.66 to 0.88)***	0.90 (0.84 to 0.96)	0.86 (0.81 to 0.91)*
<b>SGRQ</b>					
Total	8.8 (7.6 to 10.0)	17.0 (15.0 to 19.0)***	34.3 (24.8 to 43.8)***	15.6 (13.8 to 17.4)***	21.2 (19.2 to 23.2)***
Symptoms	11.1 (9.7 to 12.5)	31.7 (29.2 to 34.2)**	41.8 (31.5 to 52.1)***	20.3 (17.9 to 22.7)**	26.7 (24.3 to 29.1)***
Activity	12.6 (10.7 to 14.5)	20.1 (17.2 to 23.0)**	46.6 (34.4 to 58.8)***	22.6 (19.8 to 25.4)***	29.7 (27.0 to 32.4)***
Impact	5.6 (4.6 to 6.6)	9.9 (8.1 to 11.7)***	24.6 (15.0 to 34.2)***	9.6 (8.0 to 11.2)***	14.1 (12.3 to 15.9)***

\*p<0.05; \*\*p<0.01; \*\*\*p<0.001 in the comparisons vs control, except the group of those diagnosed with COPD that was compared with those with undiagnosed COPD. EQ-5D, EuroQol 5 Dimensions questionnaire; LCADL, London Chest Activities of Daily Living; SGRQ, Saint George's Respiratory Questionnaire; VAS, visual analogue scale.

and the need for extensive use of spirometry in order to decrease the burden of undiagnosed airflow obstruction in the community.<sup>32</sup> Interestingly, in a previous survey, only 42.6% of adults who consulted a doctor in Spain for chronic respiratory symptoms underwent spirometry,<sup>33</sup> and programmes of office spirometry have been hampered by the lack of expertise, time and motivation of primary care physicians.<sup>34 35</sup>

In summary, the current study has found a prevalence of GOLD-defined COPD of 10.2% in Spain, with a large proportion of undiagnosed disease. Despite having milder obstruction, patients with undiagnosed COPD have a significant impairment in HRQL and physical activities. Early detection of COPD is still an unresolved issue.

**Acknowledgements:** We thank the staff and participants in the EPI-SCAN study, and particularly Mónica Sarmiento (IMS Health Economics and Outcomes Research, Barcelona, Spain) for the monitoring and data management of the study.

**Funding:** The EPI-SCAN study has been funded by an unrestricted grant from GlaxoSmithKline Spain.

**Competing interests:** GS is a full-time employee of GlaxoSmithKline, drug manufacturer and sponsor of the study. However, the subject of the study is epidemiological with no drugs involved. The rest of authors do not have any conflict of interest with relation to the contents of the manuscript.

**Ethics approval:** The study was approved by the Ethics Committee of the Hospital Clinic de Barcelona, as a reference IRB and consequently by the local Ethics Committees of the participating centres.

**Provenance and peer review:** Not commissioned; externally peer reviewed.

## REFERENCES

- Chapman KR, Mannino DM, Soriano JB, *et al*. Epidemiology and costs of chronic obstructive pulmonary disease. *Eur Respir J* 2006;**27**:188–207.
- Rabe KF, Hurd S, Anzueto A, *et al*. Global Initiative for Chronic Obstructive Lung Disease. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease: GOLD executive summary. *Am J Respir Crit Care Med* 2007;**176**:532–55.
- Sobradillo V, Miravittles M, Gabriel R, *et al*. Geographical variations in prevalence and underdiagnosis of COPD. Results of the IBERPOC multicentre epidemiological study. *Chest* 2000;**118**:981–9.
- Siafakas NM, Vermeire P, Pride NB, *et al*. on behalf of the task force. ERS consensus statement. Optimal assessment and management of chronic obstructive pulmonary disease (COPD). A consensus statement of the European Respiratory Society (ERS). *Eur Respir J* 1995;**8**:1398–420.
- Miravittles M, Ferrer M, Pont A, *et al*. Characteristics of a population of COPD patients identified from a population-based study. Focus on previous diagnosis and never smokers. *Respir Med* 2005;**99**:985–95.
- Ancochea J, Badiola C, Duran E, *et al*. The EPI-SCAN survey to assess the prevalence of chronic obstructive pulmonary disease in Spanish 40-to-80-years-olds: protocol summary. *Arch Bronconeumol* 2009;**45**:41–7.
- Bestall JC, Paul EA, Garrod R, *et al*. Usefulness of the Medical Research Council (MRC) dyspnoea scale as a measure of disability in patients with chronic obstructive pulmonary disease. *Thorax* 1999;**54**:581–6.
- Minette A. Questionnaire of the European Community for Coal and Steel (ECSC) on respiratory symptoms. 1987—updating of the 1962 and 1967 questionnaires for studying chronic bronchitis and emphysema. *Eur Respir J* 1989;**2**:165–77.
- American Thoracic Society. Standardization of spirometry, 1994 update. *Am J Respir Crit Care Med* 1995;**154**:1107–36.
- Garrod R, Bestall JCM, Paul EA, *et al*. Development and validation of a standardized measure of activity of daily living in patients with severe COPD: the London Chest Activity of Daily Living scale (LCADL). *Respir Med* 2000;**94**:589–96.
- Vilaró J, Gimeno E, Sánchez Fdez N, *et al*. Actividades de la vida diaria en pacientes con enfermedad pulmonar obstructiva crónica: validación de la traducción española y análisis comparativo de 2 cuestionarios. *Med Clin (Barc)* 2007;**129**:326–32.
- Badia X, Roset M, Montserrat S, *et al*. La versión española del EUROQoL: descripción y aplicaciones. *Med Clin* 1999;**112**(supl 1):79–85.
- Ferrer M, Alonso J, Prieto L, *et al*. Validity and reliability of the St. George's Respiratory Questionnaire after adaptation to a different language and culture: the Spanish example. *Eur Respir J* 1996;**9**:1160–6.
- Encuesta Nacional de Salud 2006. Madrid: Instituto Nacional de Estadística. Ministerio de Sanidad y Consumo. In: <http://www.msc.es/estadEstudios/estadisticas/encuestaNacional/encuestaNac2006/EstilosVidaPorcen> (accessed 8 Jul 2009).
- Soriano JB, Miravittles M. Datos epidemiológicos de EPOC en España. *Arch Bronconeumol* 2007;**43**(Suppl 1):2–9.
- Buist AS, McBurnie MA, Vollmer WM, *et al*. on behalf of the BOLD Collaborative Research Group. International variation in the prevalence of COPD (the BOLD study): a population-based prevalence study. *Lancet* 2007;**370**:741–50.
- Miravittles M, Murio C, Tirado-Conde G, *et al*. Geographic differences in clinical characteristics and management of COPD: the EPOCA study. *Int J Chron Obstruct Pulmon Dis* 2009;**4**:45–53.
- Menezes AM, Perez-Padilla R, Jardim JR, *et al*. PLATINO Team. Chronic obstructive pulmonary disease in five Latin American cities (the PLATINO study): a prevalence study. *Lancet* 2005;**366**:1875–81.
- Caballero A, Torres-Duque CA, Jaramillo C, *et al*. Prevalence of COPD in five Colombian cities situated at low, medium, and high altitude (PREPOCOL study). *Chest* 2008;**133**:343–9.
- Zhong N, Wang C, Yao W, *et al*. Prevalence of chronic obstructive pulmonary disease in China. A large, population-based survey. *Am J Respir Crit Care Med* 2007;**176**:753–60.
- Mannino DM, Buist AS, Vollmer WM. Chronic obstructive pulmonary disease in the older adult: what defines abnormal lung function? *Thorax* 2007;**62**:237–41.
- Hardie JA, Buist AS, Vollmer WM, *et al*. Risk of over-diagnosis of COPD in asymptomatic never-smokers. *Eur Respir J* 2002;**20**:1117–22.
- Celli BR, Halbert RJ, Nordyke RJ, *et al*. Airway obstruction in never smokers: results from the Third National Health and Nutrition Examination Survey. *Am J Med* 2005;**118**:1364–72.
- Lindberg A, Bjerg-Bäcklund A, Rönmark E, *et al*. Prevalence and underdiagnosis of COPD by disease severity and the attributable fraction of smoking. Report from the Obstructive Lung Disease in Northern Sweden Studies. *Respir Med* 2006;**100**:264–72.
- Vestbo J, Lange P. Can GOLD stage 0 provide information of prognostic value in chronic obstructive pulmonary disease? *Am J Respir Crit Care Med* 2002;**166**:329–32.
- Shahab L, Jarvis MJ, Britton J, *et al*. Prevalence, diagnosis and relation to tobacco dependence of chronic obstructive pulmonary disease in a nationally representative population sample. *Thorax* 2006;**61**:1043–7.
- Tzanakis N, Anagnostopoulou U, Filaditaki V, *et al*. Prevalence of COPD in Greece. *Chest* 2004;**125**:892–900.
- López-Varela MV, Muñio A, Pérez-Padilla R, *et al*. Treatment of chronic obstructive pulmonary disease in 5 Latin American cities: the PLATINO study. *Arch Bronconeumol* 2008;**44**:58–64.
- Fukuchi Y, Nishimura M, Ichinose M, *et al*. COPD in Japan: the Nippon COPD epidemiology study. *Respirology* 2004;**9**:458–65.
- Domingo-Salvany A, Lamarca R, Ferrer M, *et al*. Health-related quality of life and mortality in male patients with chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 2002;**166**:680–5.
- Gracia-Aymerich J, Lange P, Benet M, *et al*. Regular physical activity modifies smoking-related lung function decline and reduces risk of chronic obstructive pulmonary disease. A population-based cohort study. *Am J Respir Crit Care Med* 2007;**175**:458–63.
- Coultas DB, Mapel D, Gagnon R, *et al*. The health impact of undiagnosed airflow obstruction in a national sample of United States adults. *Am J Respir Crit Care Med* 2001;**164**:372–7.
- Miravittles M, de la Roza C, Morera J, *et al*. Chronic respiratory symptoms, spirometry and knowledge of COPD among general population. *Respir Med* 2006;**100**:1973–980.
- Miravittles M, de la Roza C, Naberan K, *et al*. Use of spirometry and patterns of prescribing in COPD in primary care. *Respir Med* 2007;**101**:1753–60.
- Lusuardi M, De Benedetto F, Paggiaro P, *et al*. A randomized controlled trial on office spirometry in asthma and COPD in standard general practice. *Chest* 2006;**129**:844–852.

## APPENDIX. MEMBERS OF THE SCIENTIFIC COMMITTEE OF THE STUDY AND PARTICIPATING CENTRES

### Scientific committee

Julio Ancochea, Hospital La Princesa (Madrid)  
 Guadalupe Sanchez, GlaxoSmithKline (Madrid)  
 Enric Duran, Institut Municipal d'Investigació Mèdica (IMIM) (Barcelona)  
 Francisco García Río, Hospital La Paz (Madrid)  
 Marc Miravittles, Hospital Clínic (Barcelona)  
 Luis Muñoz, Hospital Reina Sofía (Córdoba)  
 Víctor Sobradillo, Hospital de Cruces (Bilbao)  
 Joan B Soriano, Fundació Caubet-CIMERA Illes Balears (Mallorca)

### Participating sites and coordinators

Julio Ancochea, Hospital La Princesa (Madrid)  
 Luis Borderias, Hospital San Jorge (Huesca)  
 Francisco García Río, Hospital La Paz (Madrid)  
 Jaime Martínez, Hospital Central de Asturias (Oviedo)  
 Teodoro Montemayor, Hospital Virgen de la Macarena (Sevilla)  
 Luis Muñoz, Hospital Reina Sofía (Córdoba)  
 Luis Piñeiro, Hospital Xeral Cies (Vigo)  
 Joan Serra, Hospital General de Vic (Vic, Barcelona)  
 Juan José Soler-Cataluña, Hospital General de Requena (Requena, Valencia)  
 Antoni Torres, Hospital Clínic (Barcelona)  
 José Luis Viejo, Hospital General Yagüe (Burgos)