

# Geographic Variations in Prevalence and Underdiagnosis of COPD\*

## Results of the IBERPOC Multicentre Epidemiological Study

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**Objectives:** To ascertain the prevalence, diagnostic level, and treatment of COPD in Spain through a multicenter study comprising seven different geographic areas.

**Design and participants:** This is an epidemiologic, multicenter, population-based study conducted in seven areas of Spain. A total of 4,035 men and women (age range, 40 to 69 years) who were randomly selected from a target population of 236,412 subjects participated in the study.

**Interventions:** Eligible subjects answered the European Commission for Steel and Coal questionnaire. Spirometry was performed, followed by a bronchodilator test when bronchial obstruction was present.

**Results:** The prevalence of COPD was 9.1% (95% confidence interval [CI], 8.1 to 10.2%), 15% in smokers (95% CI, 12.8 to 17.1%), 12.8% in ex-smokers (95% CI, 10.7 to 14.8%), and 4.1% in nonsmokers (95% CI, 3.3 to 5.1%). The prevalence in men was 14.3% (95% CI, 12.8 to 15.9%) and 3.9% in women (95% CI, 3.1 to 4.8%). Marked differences were observed between sexes in smoking; the percentage of nonsmokers was 23% in men and 76.3% in women ( $p < 0.0001$ ). The prevalence of COPD varied among the areas, ranging from 4.9% (95% CI, 3.2 to 7.0%) in the area of the lowest prevalence to 18% (95% CI, 14.8 to 21.2%) in the area of the highest. There was no previous diagnosis of COPD in 78.2% of cases (284 of 363). Only 49.3% of patients with severe COPD, 11.8% of patients with moderate COPD, and 10% of patients with mild COPD were receiving some kind of treatment for COPD. Multivariate analysis showed that individuals had a higher probability of having received a previous diagnosis of COPD if they lived in urban areas, were of male gender, were > 60 years old, had higher educational levels, had > 15 pack-year smoking history, or had symptoms of chronic bronchitis.

**Conclusions:** COPD is a very frequent disease in Spain, and presents significant geographic variations and a very low level of previous diagnosis and treatment, even in the most advanced cases.

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**Key words:** chronic bronchitis; COPD; epidemiology; prevalence

**Abbreviations:** BDT = bronchodilator test; CI = confidence interval; ERS = European Respiratory Society; OR = odds ratio

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COPD is a frequent cause of morbidity and mortality in developed countries. Despite the campaigns against tobacco smoking, the prevalence of the disease and mortality rates due to COPD continue to increase. The age-adjusted mortality rate increased 47.3% in the United States from 1979 to 1993.<sup>1</sup> Several studies have shown significant differences in COPD prevalence among different countries.<sup>2–12</sup> Although much of this difference can be attributed to smoking habits, environmental factors, and diagnostic or coding practices, it may also reflect biological or genetic differences in the risk of obstructive lung disease.

A further important aspect is the lack of knowledge that many patients have of the disease. Patients at an early stage of the disease are either unaware of their

condition or reluctant to consult their physician for respiratory symptoms.<sup>13</sup> Consequently, most patients with mild disease do not receive active counseling against tobacco smoking or appropriate pharmacologic treatment. Moreover, some treatments administered to patients with COPD are not adequate for the degree of severity of the disease and do not always follow current guidelines.<sup>14,15</sup>

Despite the importance of COPD, data on the epidemiology of the disease in population-based studies that include spirometric determinations are scant and even nonexistent in some countries. Furthermore, there is a lack of information on differences in prevalence among different geographic areas of the same or different countries. The IBERPOC study is a population-based epidemiologic study conducted in seven different geographic areas of Spain to ascertain the prevalence of COPD, the prevalence of the different risk factors, and the frequency of previous diagnosis of the condition. Similarly, we assessed the degree of association of the disease with diverse epidemiologic variables, together with the level of diagnosis and existing treatment.

## MATERIALS AND METHODS

### Design of the Study

This is an epidemiologic, multicenter, population-based study conducted in seven areas of Spain. The areas included in the study were representative of different climates and comprised urban and rural populations (Fig 1). The description of these areas is shown in Table 1.

### Selection of Participants

The total target population consisted of 236,412 subjects included in the administrative census and residing in the seven



FIGURE 1. Geographic distribution of the areas of the study.

study areas. From these, a randomized, age- and sex-stratified sample of 5,014 individuals (2,592 women and 2,512 men aged 40 to 69 years) was considered for inclusion; this represents 729 individuals per area. The sample size was calculated under the assumption of an expected COPD prevalence of 6%, a maximum absolute error of 2%, and a 30% nonresponse rate. Noneligible subjects included those living outside the study area for > 6 months per year, institutionalized persons, and those with ages outside the range at the time of recruitment.

### Field Work

Field work was performed from October 1996 to April 1997. A trained pneumologist was responsible for contacting participants, and conducted the interviews and pulmonary function tests in each area.

Eligible individuals were randomly selected from the database, which included the 236,412 subjects of the censuses, by software designed specially for the study. A minimum of two unanswered contacts, either by mail or telephone, was required for an individual to be considered a nonresponder. In such cases, the subject was replaced randomly by another of the stratum from the database. Deceased individuals were also replaced. In contrast, subjects with physical or mental handicaps were not replaced. Refusal to participate was considered when an eligible and contacted subject refused to participate on at least two occasions. In this case, the subject was not replaced and was invited to reply to a brief questionnaire by telephone with data on tobacco consumption and the existence of respiratory disease and/or respiratory symptoms.

The European Commission for Steel and Coal questionnaire validated in Spanish was used,<sup>16</sup> and information was also collected on smoking habits and socioeconomic level. Along with the questionnaires, the subjects were requested to undergo spirometry, as described below.

### Spirometry

Spirometry was performed according to the American Thoracic Society guidelines,<sup>17</sup> with the same type of portable spirometer (DATOSPIR-200; Sibel S.A; Barcelona, Spain) used in all seven areas. The predicted values of Roca et al<sup>18</sup> were used. Subjects whose FEV<sub>1</sub>/FVC value was < 88% predicted in men or < 89% in women underwent a bronchodilator test (BDT) with two inhalations of salbutamol, using an inhalation chamber. The BDT result was considered positive if the difference between FEV<sub>1</sub> or FVC before and after the test was > 200 mL and its relative increase was > 12%.

### Diagnostic Criteria of COPD

For the diagnosis of COPD, subjects were required to have no previous diagnosis of asthma (reply on the European Commission for Steel and Coal questionnaire) and present the functional obstruction criteria of the European Respiratory Society (ERS) on spirometry<sup>19</sup> (*ie*, a FEV<sub>1</sub>/FVC ratio in percentage predicted < 88% in men or < 89% in women). In order to avoid the inclusion of patients with reversible airway obstruction due to asthma, diagnosis of COPD was reserved for subjects with negative BDT findings or, in the case of a positive BDT result, values after the challenge still had to fulfil the criteria for bronchial obstruction. In the few patients in whom BDT had not been performed, an absolute FEV<sub>1</sub>/FVC value < 81% and FEV<sub>1</sub> < 70% predicted were required for the diagnosis of COPD, so that possible reversible obstructions that could pass unnoticed were reasonably avoided. ERS criteria were also followed for staging COPD severity.<sup>19</sup>

**Table 1—Geographic Characteristics, Census, Target Population, and Method of Contact**

Geographic Areas	Habitat	Size of Target Population, No.	Climate	Contact
Oviedo	Urban	68,032	Atlantic	Mail
Burgos	Urban	55,275	Continental	Telephone
Caceres	Urban	4,989	Continental	Telephone
Madrid	Urban	31,999	Continental	Telephone
Seville	Rural	25,125	Continental	Mail
Manlleu (Barcelona)	Rural	6,253	Mediterranean	Telephone
Biscay	Rural	96,668	Atlantic	Telephone

A subject was considered to be a smoker if he or she consumed at least one cigarette, pipe, or cigar a day, and an ex-smoker if he or she had completely stopped consumption of any type of tobacco for at least the previous 6 months.

Diagnosis of chronic bronchitis was considered when the symptoms of chronic cough with sputum production were present for at least 3 months per year in 2 consecutive years.

#### Quality Control

The following methods were followed for quality control: (1) The field work was performed by seven trained pneumologists with the same equipment in all areas. (2) All seven investigators underwent a training session prior to the study, which included a concordance test in the performance of spirometry. Results of this test have been published previously<sup>20</sup>; briefly, an excellent agreement was found between determinations of FVC, FEV<sub>1</sub>, and FEV<sub>1</sub>/FVC obtained by all investigators in a wide range of FEV<sub>1</sub> values. The intraindividual coefficient of correlation was 4% and intraclass coefficients of correlation for the investigators were 0.99 for measures of FVC and FEV<sub>1</sub> and 0.958 for FEV<sub>1</sub>/FVC.<sup>20</sup> (3) An independent observer (MM) reviewed 537 spirometries that corresponded to 11.9% of those performed. A variation in FVC and FEV<sub>1</sub> > 5% was found in 22 cases, representing 4.1% of the spirometries reviewed. (4) All questionnaires submitted to the Central Office (Pharma Consult Services S.A.; Barcelona, Spain) were reviewed by two monitors to filter inconsistencies and missing data. (5) A review was made of medical records of individuals who refused to participate but answered the short telephone questionnaire. Medical records were available for 306 individuals (35% of refusals). No significant differences were observed between the self-reported diagnosis of asthma, chronic bronchitis, emphysema or COPD, smoking habits and respiratory symptoms, and the information registered in medical records.

#### Statistical Analysis

The 95% confidence intervals (CIs) for the point estimators of the prevalence of COPD in the total population, as well as in the different strata, were calculated. Comparisons between categorical variables were performed using the point estimators and the 95% CI of the corresponding odds ratios (ORs). A logistic regression model was constructed with COPD diagnosis as the dependent variable, and smoking, social level, age, sex, and place of residence (rural/urban) as independent variables. Statistical analysis was performed with the SPSS software for Windows 7.5.2S (SPSS; Chicago, IL).

## RESULTS

### *Participation and Distribution of the Study Population*

The detailed description of participation rates in the study, both global and in different areas, has been published recently.<sup>21</sup> In brief, to achieve the aim of 5,014 interviews, a total of 5,827 attempts at contact were made, of which 860 subjects (14.8%) did not respond and were replaced; 918 subjects (18%) refused to participate, although 882 of these subjects (94.6%) agreed to answer the short questionnaire by telephone. In all, 4,035 complete interviews were achieved, which represent 69.2% of the 5,827 contact attempts and 81.4% of the individuals contacted. Complete interviews and short questionnaires taken together yielded an overall total of 4,967 useful contacts, which represented 97.3% of the total expected sample (4,967 of 5,014). A total of 3,978 spirometries were performed. Spirometry could not be performed in 52 subjects: lack of collaboration in 28 subjects, tracheotomy in 6 subjects, neurologic disease or mental retardation in 8 subjects, and unknown causes in 10 subjects.

From analysis of the short telephone questionnaires, we observed that persons who declined to participate in the study were somewhat younger (age [SD], 53 [9] years vs 53.4 [8.6] years;  $p < 0.0001$ ) and more often were men (56.9% vs 49%;  $p < 0.0001$ ). The number of smokers and ex-smokers (49.5% vs 49.9%;  $p =$  not significant) was similar in both groups. The group of refusals presented a lower frequency of previous bronchial asthma diagnosis (1.7% vs 4.9%;  $p < 0.0001$ ). However, previous diagnosis of chronic bronchitis, emphysema, or COPD was similar in both groups (2.82% vs 4.7%;  $p =$  not significant).

### *Prevalence of COPD*

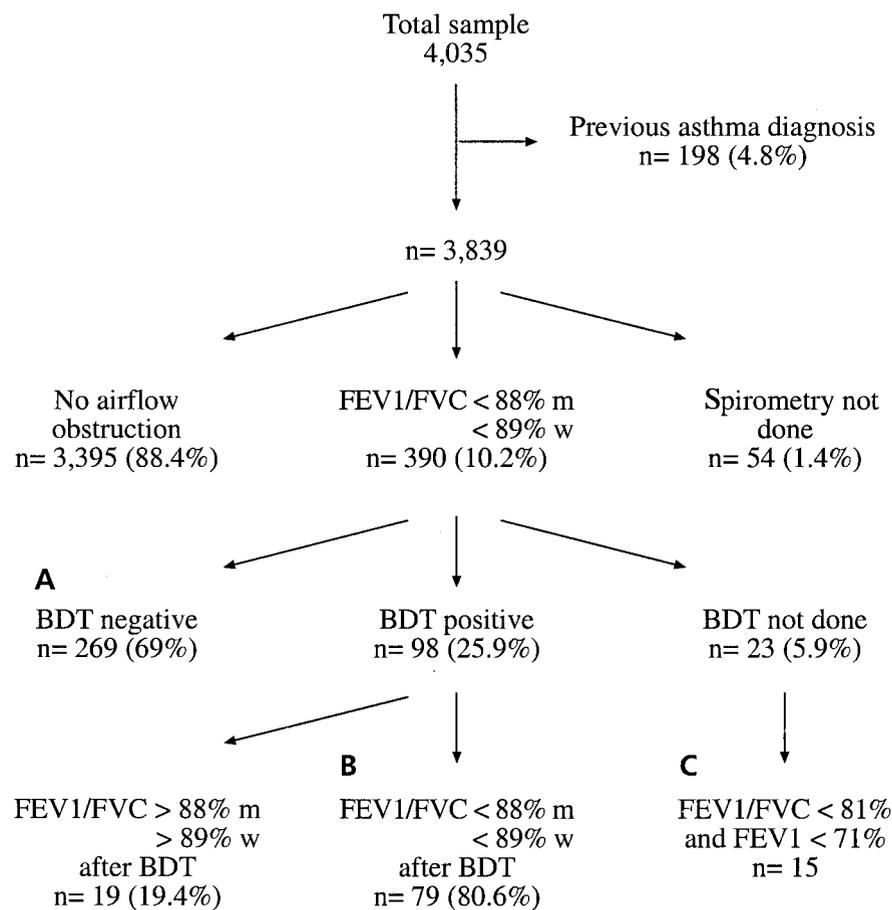
The overall prevalence of COPD and its relationship with tobacco consumption are shown in Figure

2. In all, 363 individuals had a diagnosis of COPD. Thus, the prevalence was 9.11% (363 of 3,981; 95% CI, 8.1 to 10.2%). Functionally, the majority of COPD diagnoses were based on the presence of chronic irreversible airflow limitation (74.1% of cases). A BDT result was positive in 21.7% of COPD patients. In only 15 cases (4.1% of all cases) was the diagnosis of COPD made without a BDT having been performed. The prevalence of COPD was 15% (95% CI, 12.8 to 17.1%) in smokers, 12.8% (95% CI, 10.7 to 14.8%) in ex-smokers, and 4.1% (95% CI, 3.3 to 5.1%) in nonsmokers. Women presented a prevalence of 3.9% (95% CI, 3.1 to 4.8%) and men were 14.3% (95% CI, 12.8 to 15.9%). The prevalence of COPD rose significantly in the male group as age and tobacco consumption increased. The prevalence

of COPD regarding smoking habits is presented in Table 2; odds ratios (ORs) were calculated based on the prevalence in nonsmokers. In smokers of > 30 pack-years and subjects > 60 years old, COPD prevalence was 40.3% (95% CI, 34.4 to 46.2%). Very marked differences existed regarding tobacco consumption between sexes: 76.3% of women did not smoke vs 23% of men ( $p < 0.0001$ ). Differences were also significant when ex-smokers (8.8% vs 40.8%;  $p < 0.001$ ) and active smokers (14.9% vs 36.2%;  $p < 0.001$ ) were compared.

#### COPD Prevalence According to Areas Studied

Significant differences were found in prevalence rates when the areas of the study were compared; ORs were calculated based on the prevalence in



Cases of COPD: A + B + C = 363 cases  
BDT: Bronchodilator test.

FIGURE 2. Prevalence of COPD.

**Table 2—Prevalence of COPD Stratified by Sex, Tobacco Consumption, and Age Group\***

Sex/Age Group, yr	Nonsmokers	Pack-Years of Smokers and Ex-smokers			Global (Smokers and Ex-smokers)
		1 to 14	15 to 30	> 30	
<b>Men</b>					
40 to 49	3/159 (1.9)	8/189 (4.2)	13/217 (6)	26/147 (17.7)	49/568 (8.6)
	1	2.3 (0.6–8.8)	3.3 (0.9–11.8)	11.1 (3.3–37.8)	4.9 (1.5–15.9)
50 to 59	8/152 (5.3)	10/112 (8.9)	15/156 (9.6)	47/230 (20.4)	73/504 (14.5)
	1	1.7 (0.6–4.6)	1.9 (0.8–4.6)	4.6 (2.1–10.1)	3.0 (1.4–6.5)
60 to 69	13/140 (9.3)	10/90 (11.1)	18/86 (20.9)	106/263 (40.3)	137/448 (30.6)
	1	1.2 (0.5–2.9)	2.6 (1.2–5.6)	6.6 (3.5–12.3)	4.3 (2.3–7.9)
<b>Women</b>					
40 to 49	16/477 (3.4)	3/208 (1.4)	8/79 (10.1)	3/32 (9.4)	14/329 (4.3)
	1	0.4 (0.1–1.4)	3.2 (1.3–7.8)	2.3 (0.8–10.8)	1.3 (0.6–2.6)
50 to 59	15/539 (2.8)	3/64 (4.7)	0/23 (0)	0/15 (0)	3/109 (2.8)
	1	1.7 (0.4–6.1)	—	—	0.9 (0.3–3.4)
60 to 69	29/556 (5.2)	2/26 (7.7)	0/13 (0)	1/7 (14.3)	3/49 (6.1)
	1	1.5 (0.3–6.7)	—	3.0 (0.3–26.0)	1.2 (0.3–4.0)

\*Data are presented as No./Total subjects (%) or as OR (95% CI).

Caceres, which was the lowest of the seven areas (Table 3). With respect to the mean prevalence of the study, Oviedo, Caceres, and Seville presented significantly lower values, while Manlleu presented the highest COPD rates ( $p < 0.001$ ). Differences also existed among the zones of the study regarding COPD severity and the percentage of cases found in women and nonsmokers. Twenty-two percent of overall COPD cases were severe. Caceres presented the highest percentage of severe cases (46%) while Manlleu presented the lowest; the differences were significant compared with the overall ( $p = 0.006$  and  $p = 0.044$ , respectively).

Women presented 22% of COPD cases (80 of 363), with respect to this percentage, Caceres was the only area presenting significant differences compared with the global, with only 3.7% of women ( $p = 0.014$ ).

Among all COPD cases, 23.4% cases (84 of 363) were observed in nonsmokers. The differences were significant: Manlleu and Burgos had the highest percentage of nonsmokers (39% and 36.9%, respectively;  $p < 0.0001$  and  $p = 0.006$  compared with the global) and Caceres, Biscay, and Madrid had the lowest (3.7, 6.2, and 8%, respectively;  $p = 0.009$ ,  $p = 0.002$ , and  $p = 0.006$  compared with the global).

**Table 3—COPD Prevalence Rate in the Areas Studied\***

Prevalence	Oviedo	Burgos	Caceres	Madrid	Manlleu	Seville	Biscay	Total
COPD prevalence, %	6.1†	10.3	4.9	9.8	18‡	6.3§	8.2	9.1
95% CI	4.4–8.3	7.6–12.7	3.2–7.0	7.4–12.7	14.8–21.2	4.5–8.6	6.1–10.7	8.1–9.9
OR (95% CI)	1.2 (0.7–2.1)	2.2 (1.4–3.5)	1	2.1 (1.3–3.4)	4.7 (2.7–6.6)	1.3 (0.8–2.2)	1.7 (1.1–2.8)	
Prevalence in smokers	10.2†	16.2	12.5	20.8†	25.3‡	9.0†	18.5	15.0 (12.8–17.1)
Prevalence in ex-smokers	9.7	11.8	4.7‡	15.9	28.0‡	8.5§	11.9	12.8 (10.7–14.8)
Prevalence in nonsmokers	2.3	7.1†	0.4‡	1.6†	11.9‡	2.8	1.0†	4.1 (3.3–5.1)
Percentage of nonsmokers among COPD cases	18.4	36.9†	3.7†	8†	39.1‡	18.4	6.25†	23.4
Percentage of women among COPD cases	23.7	29	3.7§	14	28.9	21.1	16.7	22
Mild COPD	31.6	48	23	18	52.5†	37	33	38.3
Moderate COPD	42	32	31	52	33	47	48	39.7
Severe COPD	26.3	20	46†	30	14.5§	16	19	22
Prevalence of previous asthma diagnosis	6.5	3.5	2.7	3.9	6.7	6.8	3.8	4.9 (4.2–5.5)

\*Data are presented as %, or % (95% CI) unless otherwise indicated.

† $p < 0.01$  with respect to total numbers.

‡ $p < 0.001$  with respect to total numbers.

§ $p < 0.05$  with respect to total numbers.

**Table 4—Distribution by Age, Gender, and Smoking Habits in the Seven Areas of the Study\***

Variables	Oviedo	Burgos	Caceres	Madrid	Manlleu	Seville	Biscay	Total
Subjects, No.	618	630	553	509	539	601	585	4035
Age (SD), yr	54.7 (8.3)	53.9 (8.6)	54 (8.8)	53.9 (8.7)	53 (7.9)	50.5 (7.9)	53.7 (8.2)	53.4 (8.6)
Men	49.3	48.2	48.1	47.7	49.5	52	47.5	48.9
Nonsmokers	49.7	53.3	48.1	50.7	59.4†	41.1‡	49.7	50.2
Ex-smokers	24.9	24.1	23	24.8	24.5	25.5	24.4	24.5
Smokers	25.4	22.5	28.9†	24.6	16.1‡	33.4†	25.5	25.4
Male	24.6	28†	15.4‡	21.8	27	18.5‡	24.8	23
nonsmokers								
Female	74.1	77	78.4	77.1	91.2†	65.6‡	72.3	76.3
nonsmokers								

\*Data are presented as % unless otherwise indicated.

†Values significantly higher than the mean.

‡Values significantly lower than the mean.

On analyzing the possible explanations for these differences, we found differences concerning tobacco consumption ( $p < 0.001$ ) among most areas. Manlleu presented the highest figure of nonsmokers and Seville the lowest, while other zones presented similar values. No differences were observed in percentages of ex-smokers (Table 4).

#### Previous Diagnosis of COPD and Related Factors

Of the cases of COPD found, 78.2% cases (284 of 363) had not been diagnosed previously; 19.3% of the cases detected (70 of 363) were being treated. Treatment had been indicated in 49.3% of severe cases (39 of 79), 11.8% of moderate cases (17 of 144), and 10% of mild cases (14 of 140).

The results of logistic regression analysis that show the variables related to the previous diagnosis of COPD are presented in Table 5. Tobacco consumption  $> 15$  pack-years, age  $> 60$  years, living in the city, male gender, having a higher educational level ( $> 12$  years vs  $< 12$  years of schooling), and existence of chronic bronchitis and other thoracic diseases had a significant association with the previous

diagnosis of COPD, chronic bronchitis, or emphysema. Social class, history of sinusitis, hay fever, lung infection, and industrial occupation did not enter the final logistic model.

#### DISCUSSION

Our results reveal a great variation in the prevalence of COPD among the different areas studied, with a global prevalence of 9.1%, oscillating between 4.9% and 18%, an evident predominance in men, and a low level of previous diagnosis and treatment.

In this study, we attempted to avoid possible biases derived from our population sample and the methodology. First, the sample was chosen using a random sample from official censuses of the populations studied, stratified by age groups and sex. Although sampling fractions of the seven areas were different, this should not influence results, since an age- and sex-stratified random sampling proportional allocation was used. In fact, both areas with higher sampling fraction displayed the lowest and the highest prevalences, thus ruling out any systematic bias. Second, the participation rate achieved in the study was very high (69.2% of contact attempts and 81.4% of contacts established), which guarantees the reliability of the results. The third aspect is the possible bias related to nonparticipation. The high number of replies to the short telephone questionnaire (94.6%) permitted us to prove that the prevalences of previously diagnosed COPD, emphysema, or other chronic lung diseases did not differ significantly between participants and refusers. This fact was also confirmed with revision of the clinical histories of some of the refusers.

Diagnostic criteria of COPD usually pose problems in population studies because COPD and chronic airflow limitation, which includes bronchial asthma, may not be differentiated<sup>2,4,5</sup> and criteria of

**Table 5—Factors Associated With COPD Diagnosis**

Factors	OR	95% CI	p Value
Age, $\geq 60$ yr vs $< 60$ yr	2.15	1.67–2.77	$< 0.0001$
Gender, men vs women	1.77	1.24–2.5	0.0014
Habitat, urban vs rural	2.24	1.17–4.28	0.0142
Study level, $> 12$ vs $< 12$ yr of schooling	1.77	1.28–2.44	0.0005
Other thoracic diseases	2.95	2.16–4.03	$< 0.0001$
Chronic bronchitis	1.58	1.07–2.34	0.0209
Tobacco consumed, pack-years			$< 0.0001$
Do not smoke	1		
Up to 15	1.2	0.76–1.88	0.4288
From 15 to 30	2.2	1.43–3.38	0.0003
$> 30$	5.43	3.73–7.91	$< 0.0001$

airflow obstruction may vary.<sup>2-12</sup> In the present study, the criteria used to define COPD excluded patients with a previous diagnosis of bronchial asthma. Furthermore, the functional values used in our study were those indicated by the ERS to define COPD,<sup>19</sup> and special attention was paid to the exclusion of subjects with reversible airway obstruction. When it was not possible to perform a BDT, the functional values used to define COPD decreased arbitrarily, so that possible reversible obstructions that might go unnoticed were avoided. The arbitrary values adopted in the study were based on the Intermittent Positive Pressure Breathing Trial,<sup>22</sup> which showed the mean value of bronchodilation in COPD to be 5% above the predicted FEV<sub>1</sub>; thus, with the cutoff values chosen in our study (FEV<sub>1</sub>/FVC < 81% of predicted and FEV<sub>1</sub> < 70% of predicted), it would be very difficult for a subject to be misclassified as COPD in absence of results of a BDT. Our results confirm this hypothesis, since the mean variation over predicted FEV<sub>1</sub> after a BDT in our COPD patients was only 2.6%.

Comparison of the prevalences observed in this work with those of other studies is difficult to establish, owing to the use of different criteria for the diagnosis. Variable prevalences have been described in Europe: a British study found results similar to ours, with a prevalence of COPD in the general population of 9.9%<sup>9</sup> in those aged 60 to 75 years and 52% of the cases identified had not been previously diagnosed. Lange et al<sup>3</sup> in Copenhagen reported a chronic airflow obstruction prevalence of 9.5% in men and 8.6% in women 40 to 59 years old, which doubles the figures found by Bakke et al<sup>2</sup> in Norway in this age group using the same predicted values (4.5% in men and 4.8% in women). Differences in prevalence have been observed in studies in other parts of the world.<sup>4-11</sup> There are few studies in Spain, and they include small population samples. Marco et al<sup>5</sup> studied a sample of 600 men aged 40 to 60 years recruited from the general population and found a prevalence of 6.8%. Brotons et al<sup>4</sup> included a similar number of men and women aged 35 to 65 years and established a prevalence of 6.4%, which was higher in men (10.5%) than in women (1.8%).

The unexpected difference found in the prevalence of COPD among the areas studied is difficult to explain. Although much of this difference could be attributed to smoking habits, environmental factors, and diagnostic or coding practices, it may also reflect biological or genetic differences in the risk of obstructive lung disease. Differences in smoking habits do seem not to explain most of this variation, since these differences were small in magnitude and, moreover, the area with the highest prevalence was

the area with the highest percentage of those who had never smoked. Differences in prevalence of chronic airway obstruction have been observed in different ethnicities: a study in Canada showed that ethnic origin made significant contributions to the estimated risk of airflow obstruction independent of the effects of age and smoking, with Britons having 3.2 times the risk of East Europeans and 1.9 times the risk of North Americans for airway obstruction.<sup>23</sup> In the study by Samet et al,<sup>24</sup> the prevalence of chronic bronchitis and emphysema studied by questionnaire was lower in Hispanics than in Anglo-Saxons, both in men and women. Although Spain is a relatively small country, some areas have not had significant migratory movements and their populations are not mixed. In this respect, marked geographic differences have also been observed in the prevalence of  $\alpha_1$ -antitrypsin deficiency, which is more frequent in the north of Spain than in the center and south.<sup>25</sup> The possible influence of genetic factors that predispose to airway obstruction is reinforced by the results of the epidemiologic study on bronchial asthma, the results of which showed that the diagnosis of asthma was as much as three times more frequent in some regions of Spain than in other regions.<sup>26</sup> No clear geographic gradient (north-south or east-west) in prevalence could be identified, nor an influence of climate on prevalence.

It is interesting to observe that both areas with the highest prevalences showed an excess of mild cases and of cases detected in women and also had the highest prevalence of cases among patients who had never smoked. This points to other environmental or professional exposures not related to tobacco smoking, together with possible genetic factors, as the cause of the irreversible airway obstruction. The design of the study did not permit investigation of these unexpected differences, although further research has been started to try to find an explanation for these findings.

The probability of having a previous diagnosis of COPD was significantly associated with several factors such as tobacco consumption, age, urban living, and level of studies, suggesting that the intensity of symptoms associated with cumulative smoking, together with greater awareness of the disease and easier access to medical care for those living in urban areas, facilitates the diagnosis of COPD. A study in Spain showed unemployed people to be at 2.06 increased risk of simple chronic bronchitis, due in part to the higher prevalence of smoking, poorer housing, and previous occupational exposures among the unemployed; however, unemployed people consistently reported less frequent contact with specialized practitioners,<sup>27</sup> thus explaining in part the lower rate of previous diagnosis among lower socioeco-

nomic levels. Results of the Copenhagen City Heart Study indicate that socioeconomic factors operating from early in life affect the adult risk of developing COPD, independently of smoking.<sup>28</sup>

In our study, COPD was much more frequent in men. This fact has been observed frequently in studies in Spain<sup>4</sup> and France,<sup>12</sup> although these differences have not been observed in works in Denmark,<sup>3</sup> Norway<sup>2</sup> or Sweden.<sup>6</sup> Even in the latter study, prevalence of chronic bronchitis was higher in women of all age groups,<sup>6</sup> related to a higher prevalence of smoking among women in some Scandinavian countries. The key role of tobacco consumption in the pathogenesis of COPD needs no further comment; however, from our results the increased risk of COPD appears with cumulative consumption of > 15 pack-years in men > 60 years old, or > 30 pack-years in men of all ages, while consumption of < 15 pack-years showed nonsignificant ORs compared with nonsmokers. Comparisons in women are hampered by the small number of smokers or ex-smokers among them.

Only 21.8% of COPD cases found in our study had been diagnosed previously, and only 19.3% of the patients were treated. Furthermore, less than half of our identified severe patients with FEV<sub>1</sub> < 50% were receiving any kind of treatment for their respiratory disease. This situation is frequent in other epidemiologic studies in Spain; Marco et al<sup>5</sup> found that only 25% of their patients with COPD had had a previous spirometry. In a survey on primary care in Spain, Miravittles et al<sup>15</sup> found that only 47% of patients treated and followed up because of chronic respiratory symptoms had spirometry performed. In the study of Renwick and Connolly,<sup>11</sup> 63.1% of subjects with COPD received no treatment, even though 70% of those not treated reported respiratory symptoms. Banerjee et al<sup>29</sup> found a prevalence of reversible airway obstruction in > 40% of the sample, although only 3% of the patients were treated.

In conclusion, the prevalence of COPD in Spain is high, with marked differences among regions and a low level of previous diagnosis and treatment. These data should stimulate the search for patients with COPD in early stages of the disease and the adoption of more aggressive preventive measures.

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