

# Prevalence of Chronic Obstructive Pulmonary Disease in an Urban Area. Changes in COPD Ten Years on

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**Purpose:** The prevalence of Chronic obstructive pulmonary disease (COPD) in Spain has been evaluated in the last ten years by EPISCAN in 2007 and EPISCAN II in 2017. This study describes changes in the prevalence of COPD in an urban region of Spain in the last 10 years, its risk factors and underdiagnosis.

**Patients and Methods:** Participants from the Autonomous Community of Madrid (Spain) were selected from both studies up to the age of 80 years. A descriptive analysis of their sociodemographic and clinical characteristics, as well as by gender, was conducted. COPD was defined by a post-bronchodilator ratio <0.70.

**Results:** The prevalence of COPD in the Autonomous Community of Madrid increased non-significantly from 11.0% (95% CI: 8.9–13.5%) to 12.1% (95% CI: 9.6–15.1,  $p=0.612$ ). However, the prevalence by gender showed an increase in women (5.6% to 14.7%,  $p<0.001$ ) and a decrease in men (17.6% to 9.8%,  $p=0.08$ ). Underdiagnosis was reduced from 81.0% to 67.9% ( $p=0.006$ ), although with greater underdiagnosis in women (86.4% in EPISCAN and 100% in EPISCAN II). Smoking was higher in men than in women in EPISCAN (31.2% vs 23.0%,  $p<0.01$ ) but with no differences by gender in EPISCAN II (25.5% men vs 26.0% women,  $p=0.146$ ). Age, smoking, low BMI, and a sedentary lifestyle were consistently associated with COPD.

**Conclusion:** In 10 years in Madrid, there have been no changes in the global prevalence of COPD, but there have been important changes in women, with an increase in its prevalence, smoking habit and underdiagnosis.

**Keywords:** COPD, prevalence, Madrid, spirometry

## Introduction

Chronic obstructive pulmonary disease (COPD) is a major health problem, which has gone from being the fifth leading cause of death in the world in the 1990s to the third leading cause of death today. In 2019, COPD caused 3.2 million deaths globally, and this number could increase to 4.4 million by 2040.<sup>1</sup>

Because of the major impact it has on morbidity, mortality, and related healthcare spending, it is particularly important to determine the prevalence of the disease periodically. So far, a large body of research has been published on this subject, albeit with major differences in the methodologies used, the diagnostic criteria established, and the geographical framework, making it difficult to establish comparisons between the different studies.<sup>2</sup> This major variability is reflected in studies such as PLATINO<sup>3</sup> carried out in different Latin American cities, with rates of prevalence ranging from 7.8% to 19.7%, or the BOLD study,<sup>4</sup> carried out in several continents, which also revealed broad variability in prevalence rates in the different participating countries.

In Spain, the prevalence of the disease has been evaluated through three major population-based epidemiological studies, IBERPOC,<sup>5</sup> EPISCAN<sup>6</sup> and EPISCAN II.<sup>7</sup> The last two have the advantage of having been carried out with the same methodology, protocol, and ten years apart. A direct comparison of the final results of the two studies has revealed

increased prevalence, the broad geographical variability of the results, and the significant underdiagnosis of the disease. In EPISCAN II, Madrid was the only region of Spain in which a higher prevalence of COPD is detected among women than men. Although the prevalence of the disease in women is known to be increasing, this regional peculiarity has not been described in other epidemiological studies in the West.<sup>8</sup> Therefore, we believe that it may be of interest to know not only the prevalence of the disease, but also the trend observed in the disease in one of the most populated urban regions of Spain, in order to evaluate whether the prevention and treatment strategies applied in the healthcare setting are the right ones and whether there are opportunities for improvement.

Therefore, the objective of our study has been to determine changes in the prevalence of COPD in the region of Madrid over the 10-year period between the two EPISCAN surveys, risk factors for COPD, and the percentage of underdiagnosis of this disease.

## Materials and Methods

EPISCAN and EPISCAN II are two observational, population-based, multi-centre, national epidemiological studies, conducted in 2007 and 2017, respectively. The methodology of both studies has been published previously, with the main characteristics summarised in [Table 1](#).<sup>9,10</sup> EPISCAN was conducted in eleven centres in Spain with the participation of two teaching hospitals in the region of Madrid: Hospital Universitario de La Paz and Hospital Universitario de La Princesa. The first EPISCAN study randomly selected participants aged between 40 and 80 years old, using two-stage stratified sampling according to the areas closest to the participating centres. EPISCAN II was carried out ten years later with the inclusion of nineteen hospitals, but just one from the Region of Madrid, the Hospital Universitario la Princesa, but with the same sample size. In the case of EPISCAN II, there was no upper age limit, applying two-stage stratified sampling according to the areas closest to the hospitals.

Forced spirometry with bronchodilator test was performed using a pneumotachograph according to standardized procedures and reference values indicated in [Table 1](#). Different guidelines used in both studies were comparable. Each spirometry was reviewed, and only spirograms that met acceptability and reproducibility criteria were included.

As shown in [Table 1](#), the definitions of COPD were the same.<sup>11</sup> Similarly, both studies classified participants according to the lower limit of normal (LLN)<sup>12</sup> to minimise potential false-negatives in the younger population and false-positives in the older population.<sup>13</sup> Identical questions were asked about previous medical diagnoses compatible with COPD, pharmacological treatments used, and clinical questionnaires were applied to determine underdiagnosis of the disease.

Both studies were approved by their respective ethics committees, and all participants signed informed consent. In order to carry out this sub-study, participants from the Region of Madrid were analysed from the primary databases. The two data sets were then merged by matching the identical variables and discarding those that did not match or had a different definition. The recommendations of the STROBE declaration for observational studies have been followed in the preparation of the study.<sup>14</sup> The study has also been approved by the scientific committees of EPISCAN and EPISCAN II, and has been carried out under the researcher's own initiative and without any funding. Flowchart of the study is shown in [Figure 1 Supplementary Material](#).

## Statistical Analysis

An initial descriptive comparative analysis was made between the main sociodemographic characteristics and clinical variables of both studies, as well as by gender. Because EPISCAN II included patients with a different age range than EPISCAN, only those participants within the same age range (40–80 years) were included in the comparative analysis, so that both populations were as similar as possible. The mean and standard deviation (SD) of the quantitative variables were calculated, using the Shapiro–Wilk and Kolmogorov–Smirnov tests to confirm the normality of the continuous variables. Homoscedasticity was verified using Levene's test.<sup>15</sup> When the distributions were normal and homoscedastic, a parametric test (*t*-test) was performed, and when one of these two assumptions was not met, a non-parametric test (Mann–Whitney–Wilcoxon test) was performed. In the case of qualitative variables, proportions were compared using the  $\chi^2$  test or Fisher's exact test, whenever necessary. Prevalences were calculated as percentages with a 95% CI.

Risk factors for COPD were analysed using a crude and multivariate logistic regression model. In addition, a mediation analysis was conducted for each study (EPISCAN and EPISCAN II) with the dependent variable COPD prevalence and the independent variable gender, using smoking status (smokers and ex-smokers) as a mediator. In all comparisons,  $p < 0.05$  was considered statistically significant. All analyses were performed using R (R Development Core Team, 2015) statistical software.

**Table I** Comparison of Study Designs Used in 2007 and 2017

Methodology	EPISCAN (2007)	EPISCAN II(2017)
<b>Participating areas</b>	Barcelona, Burgos, Cordoba, Huesca, Madrid (Hospital de La Princesa y Hospital La Paz), Oviedo, Sevilla, Valencia, Vic y Vigo	Asturias, Barcelona, Burgos, Caceres, Guadalajara, Huesca, Logroño, Madrid (Hospital de La Princesa), Murcia, Navarra, Palma de Mallorca, Salamanca, Santander, Sevilla, Tenerife, Valencia, Vigo, Vitoria, Zaragoza
<b>Age</b>	40-80 years	> 40 years
<b>Fieldwork</b>	May 2006 to July 2007	April 2017- February 2019
<b>Sampling</b>	Random sample of general population via commercially available database	Random sample of general population via commercially available database
<b>Spirometer</b>	Master Scope CT; VIASYS Healthcare, Germany	Carefusion Jaeger Spiro Vyntus, Germany
<b>Spirometry guidelines</b>	ATS/ERS 2005 <sup>35</sup>	SEPAR 2013 <sup>36</sup>
<b>Reference values</b>	Quanjer et al <sup>37</sup>	Quanjer et al <sup>38</sup>
<b>COPD definition</b>	post-bronchodilator FEV <sub>1</sub> /FVC < 0.7	post-bronchodilator FEV <sub>1</sub> /FVC < 0.7 (11) o FEV <sub>1</sub> /FVC < LLN
<b>Bronchodilator test</b>	After two inhalations of salbutamol an increase in FEV <sub>1</sub> and/or FVC > 12% of control and > 200 mL <sup>39</sup>	After four inhalations of salbutamol an increase in FEV <sub>1</sub> and/or FVC > 12% of control and > 200 mL <sup>40</sup>
<b>COPD staging</b>	Post-bronchodilator FEV <sub>1</sub> - Mild ≥ 80% - Moderate: 50–80% - Severe: 30–50% - Very severe: < 30%	Post-bronchodilator FEV <sub>1</sub> - Mild ≥ 80% - Moderate: 50–80% - Severe: 30–50% - Very severe: < 30%

**Abbreviations:** COPD, chronic obstructive pulmonary disease; EPI-SCAN, Epidemiologic Study of COPD in Spain; ATS, American Thoracic Society; ERS, European Respiratory Society; GOLD, Global Initiative for Chronic Obstructive Lung Disease; FEV<sub>1</sub>, forced expiratory volume in 1 s; FVC, forced vital capacity; % pred, % predicted; LLN, lower limit of normal.

## Results

The main demographic characteristics and clinical variables of the participants in the 2007 and 2017 studies are compared in Table 2. The subgroup of EPISCAN II participants aged 40 to 80 is shown in a separate column, with all of the study comparisons made with this subgroup. Compared with the participants in the first EPISCAN survey, EPISCAN II participants were found to have a higher mean age ( $56.9 \pm 10.7$  vs  $58.7 \pm 9.4$  years), a higher percentage of male participants, taller, lower body mass index, and a higher level of education ( $p < 0.05$ ). No statistically significant differences were found in terms of occupation or smoking habits, although the mean number of pack-years was significantly higher among EPISCAN II participants ( $31.5 \pm 22.7$  pack-years vs  $27.1 \pm 22.4$  pack-years,  $p = 0.001$ ). With regard to lung function, small significant differences were observed in the post-bronchodilator forced expiratory volume measurements.

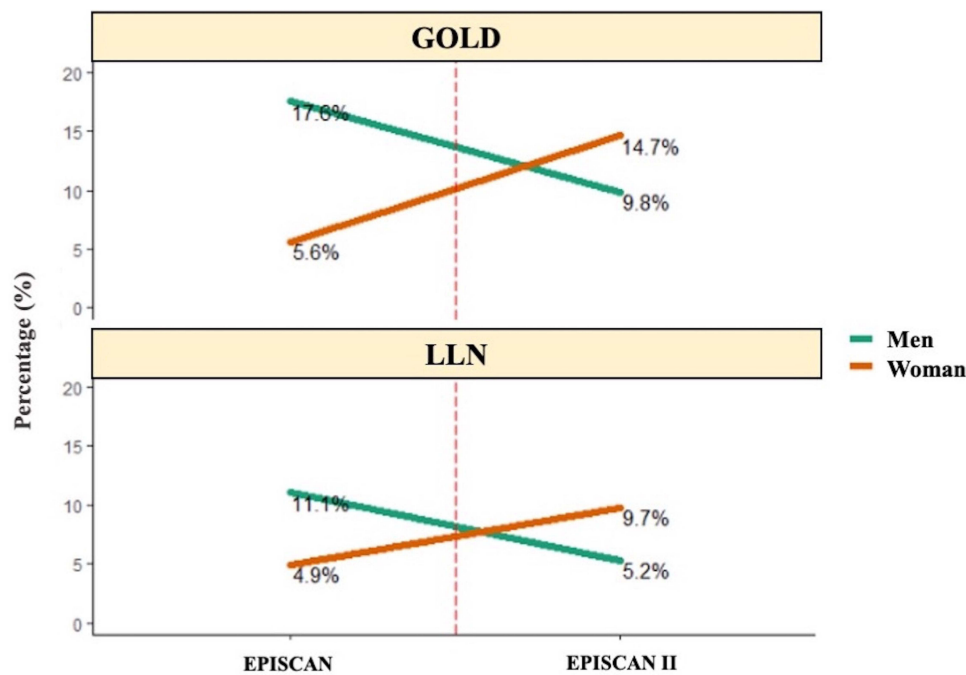
The overall prevalence of COPD in the region of Madrid according to GOLD showed no statistically significant differences, although a numerical increase of 1.1 percentage points was observed: 11% (CI 95%: 8.9–13.5%) in EPISCAN, compared to 12.1% (95% CI: 9.6–15.1%) in EPISCAN II, not statistically significant ( $p = 0.612$ ). The percentages when estimating prevalence by LLN were very similar: 7.7% (CI 95%: 5.9–9.8) in EPISCAN compared to 7.4% in EPISCAN II (95% CI: 5.4–9.8),  $p = 0.906$ .

However, when analysing prevalence changes by gender, marked differences were found with an increase in prevalence among women from 5.6% to 14.7% ( $p < 0.001$ ) and a decrease among men from 17.6% to 9.8% ( $p = 0.008$ ). Similarly, according to LLN, prevalence among women increased from 4.9% to 9.7% ( $p < 0.025$ ) and among men it decreased from 11.1% to 5.2% ( $p < 0.014$ ) (Figure 1). The characteristics of the participants in both studies analysed from a gender perspective is shown in Table 1 Supplementary Material.

**Table 2** Demographic and clinical characteristics of participants in 2007 and 2017 in the Community of Madrid

	EPISCAN	EPISCAN II	EPISCAN II (40-80 yrs)	P -value	Test
<b>Subjects (n)</b>	715 (56.8%)	600 (45.6%)	544 (43.2%)		
<b>Age (yrs), mean±SD</b>	56.9 ± 10.7	60.8±11.5	58.7 ± 9.48	P < 0.001	Mann-Whitney-Wilcoxon
<b>Age range, n (%)</b>				P < 0.001	Chi-squared
40–50 yrs	225 (31.5%)	103(17.3%)	103 (18.9%)		
50–60 yrs	212 (29.7%)	202 (33.7%)	202 (37.1%)		
60–70 yrs	162 (22.7%)	147 (24.5%)	147 (27.0%)		
70-80 yrs	116 (16.2%)	92 (15.3%)	92 (16.9%)		
80-90 yrs	0	56 (9.3%)	0		
<b>Males, n (%)</b>	324 (45.3%)	304 (50.7 %)	286 (52.6%)	P = 0.013	Chi-squared
<b>Smoking history, pack-yrs mean±SD</b>	27.1± 22.4	32.2±23.6	31.5 ± 22.7	P =0.001	Mann-Whitney-Wilcoxon
<b>Smoking status, n (%)</b>				P =0.583	Chi-squared
Smoker	191 (26.7%)	149 (24.8%)	140 (25.7%)		
Former smoker	235 (32.9%)	214 (35.7%)	194 (35.7%)		
Never smoker	289 (40.4%)	237 (39.5%)	210 (38.6%)		
<b>Weight, kg mean±SD</b>	73.8 ± 14.4	74.7±16.3	75.4 ± 16.4	P =0.104	Mann-Whitney-Wilcoxon
<b>Height, cm mean±SD</b>	163 ± 9.3	167±9.7	168 ± 9.4	P < 0.001	Mann-Whitney-Wilcoxon
<b>BMI, kg/m<sup>-2</sup> mean (±SD)</b>	27.7 ± 4.7	26.7±4.8	26.7 ± 4.8	P < 0.001	Mann-Whitney-Wilcoxon
<b>University education, n (%)</b>	221 (30.9%)	454 (75.7%)	419 (77.0%)	P < 0.001	Chi-squared
<b>Lives alone, n (%)</b>	23 (11.9%)	165 (27.5%)	140 (25.7%)	P < 0.001	Chi-squared
<b>Work environment with exposure to fumes, dust or other substances %</b>	213 (29.8%)	15 (27.3%)	15 (30.0%)	P = 1.00	Chi-squared
<b>Previous diagnoses, n(%)</b>					
COPD	10 (1.4%)	25 (4.2%)	66 (12.1%)	P < 0.001	Chi-squared
Chronic bronchitis	22 (3.1%)	25 (4.2%)	20 (3.7 %)	P = 0.668	Chi-squared
Emphysema	5 (0.7%)	6 (1%)	4 (0.7%)	P = 1.000	Chi-squared
Asthma	60 (8.4%)	57 (9.5%)	52 (9.6%)	P = 0.535	Chi-squared
<b>Symptoms, n(%)</b>					
Cough	71 (9.9%)	90 (15.4%)	80 (14.8%)	P = 0.012	Chi-squared
Expectoration	63 (8.8%)	92 (15.6%)	80 (15.0%)	P =0.001	Chi-squared
Wheezing	282 (39.6%)	189 (31.6%)	167 (30.8%)	P = 0.002	Chi-squared
Dyspnoea	73 (10.2%)	98 (16.4%)	72 (13.3%)	P = 0.111	Chi-squared
<b>FVC % post-BD, ml mean±SD</b>	100 ± 15.8	101.6±18.2	102.0 ± 17.5	P = 0.008	Mann-Whitney-Wilcoxon
<b>FEV<sub>1</sub> % post-BD, ml mean±SD</b>	105.06 ± 19.4	102.6±15.8	103.0 ± 15.3	P =0.004	Mann-Whitney-Wilcoxon
<b>Prevalence COPD GOLD, n(%)</b>	79 (11.0%)	84 (14%)	66(12.1%)	P = 0.612	Chi-squared
<b>Prevalence LLN, n(%)</b>	55 (7.7%)	46 (7.7%)	40 (7.4%)	P = 0.906	Chi-squared

**Abbreviations:** BMI, body mass index; FVC, forced vital capacity; FEV<sub>1</sub>, forced expiratory volume in 1 s; COPD, chronic obstructive pulmonary disease; GOLD, Global Initiative for Chronic Obstructive Lung Disease; LLN, lower limit of normal.



**Figure 1** Changes in COPD prevalence from 2007 to 2017, by sex in Madrid.

**Abbreviations:** GOLD, Global Initiative for Chronic Obstructive Lung Disease; LLN, lower limit of normal.

Evaluating these changes by age group (Figure 2), EPISCAN shows an increase in the prevalence of COPD among men, both by GOLD ( $p < 0.001$ ) and by LLN ( $p < 0.002$ ). In EPISCAN II, there was also an increase in prevalence with age according to the GOLD criteria ( $p < 0.013$ ) and according to LLN ( $p = 0.06$ ), except in the age group of 50 to 59 years old, when there was a small decrease in prevalence. With regard to women, EPISCAN also showed an upward trend, although not as significant according to the GOLD criteria ( $p = 0.406$ ), being particularly worrying among younger age groups. According to LLN, the highest percentage of prevalence was observed in the first age group, with a subsequent decrease ( $p = 0.958$ ). In EPISCAN II, the trend with age is not so clear, with a small decrease in the group aged 60 to 69 years and a subsequent upward swing in the older age brackets according to GOLD ( $p = 0.181$ ) and according to LLN ( $p = 0.264$ ).

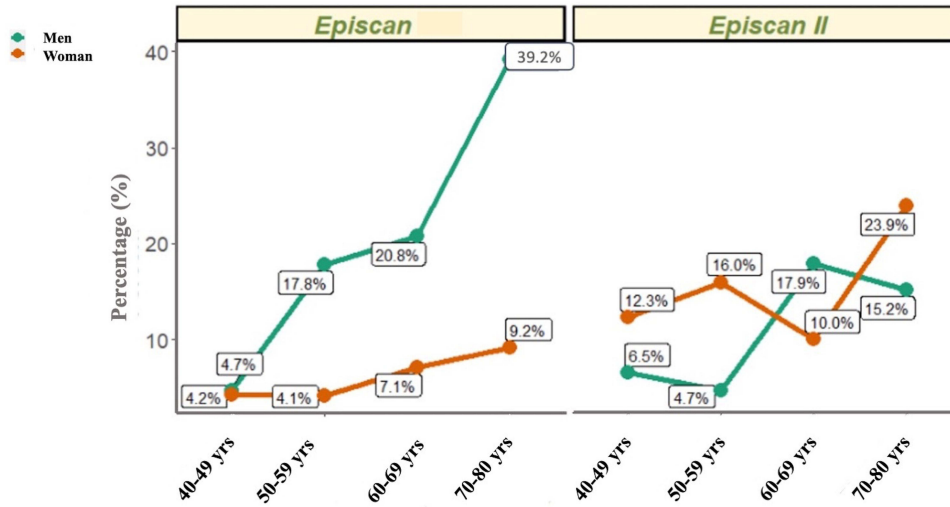
In terms of comparison of smoking habits, there were no statistically significant differences between the two studies, although there were differences found according to the analysis by gender (Figure 3). In EPISCAN, a lower percentage of smokers was found among women compared to men (23.0% vs 31.2%,  $p < 0.01$ ), but in EPISCAN II, this proportion was equal for both genders (26.0% vs 25.5%,  $p = 0.146$ ). Also, in EPISCAN, the percentage of non-smokers was significantly higher among women than men (51.9% vs 26.5%,  $p < 0.001$ ), decreasing significantly and balancing out in EPISCAN II (36.7% vs 40.7%,  $p = 0.518$ ).

In addition, a mediation analysis showed that gender (female) on COPD diagnosis was fully mediated by smoking habit (smoker or former smoker). However, in EPISCAN II, compared to EPISCAN, regression coefficient between gender and smoking habit decreased and was not significant, fact that might suggest a gender changed in smoking habit (Figure 2 Supplementary Material).

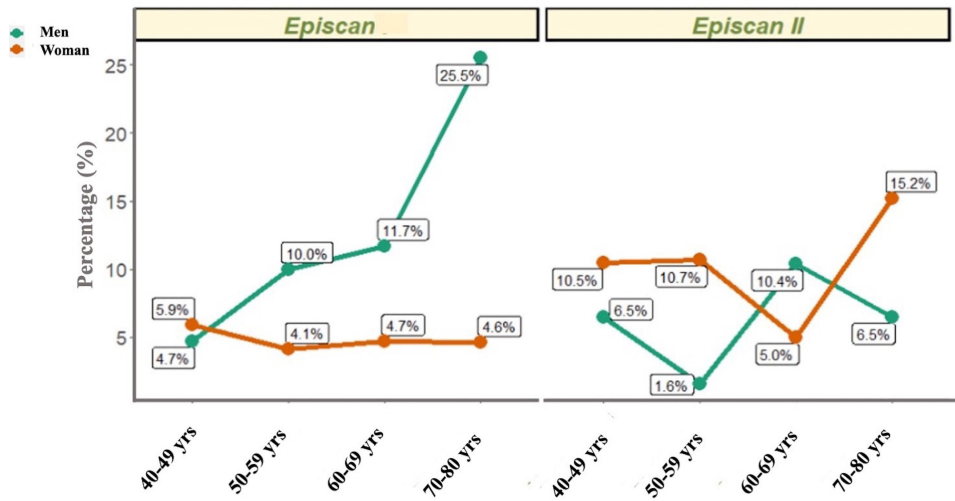
The global underdiagnosis of COPD based on the criteria proposed by GOLD decreased from 81% in EPISCAN to 67.9% in EPISCAN II ( $p = 0.006$ ). Underdiagnosis according to LLN also showed a decrease although not as striking as it is according to GOLD criteria (74.5% EPISCAN vs 69.6% EPISCAN II). When analysing these data by gender, clear differences were again found. Among women, an increase in underdiagnosis was observed, reaching 100% in EPISCAN II ( $p = 0.046$ ), and among men a non-significant percentage decrease was found (78.9% vs 67.9%,  $p = 0.085$ ).

For all the EPISCAN data as a whole, we analysed the variables associated with the presence of COPD (Table 3). In the bivariate analysis, age over 60, male gender, smoking, lack of education, BMI  $< 21$ , and a sedentary lifestyle were

**GOLD**

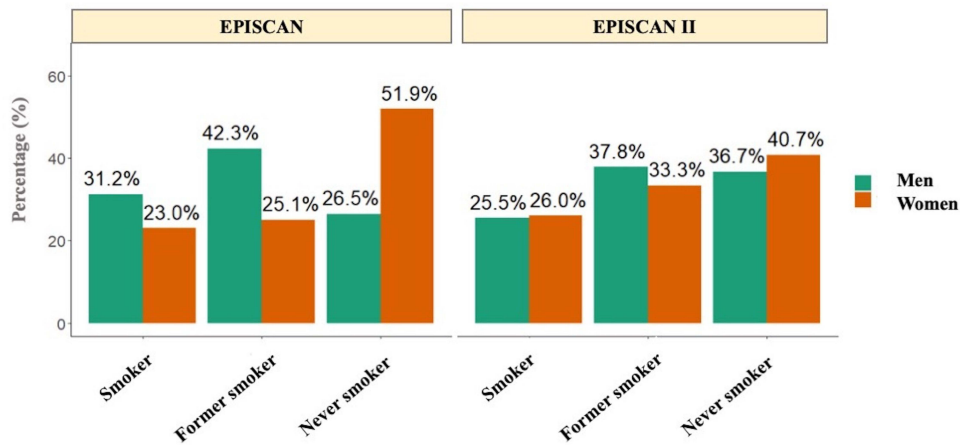


**LLN**



**Figure 2** Changes in COPD prevalence from 2007 to 2017, by sex and age in Madrid.

**Abbreviations:** GOLD, Global Initiative for Chronic Obstructive Lung Disease; LLN, lower limit of normal.



**Figure 3** Smoking habits by sex in EPISCAN and EPISCAN II subjects.

**Table 3** Factors associated with COPD

Factor	Categories	Crude		Multivariate	
		OR [IC 95%]	P-value	OR [IC 95%]	P-value
<b>Age</b>	40–49 yr (ref)	-	-	-	-
	50–59 yr	1.6 [0.9–2.8]	0.099	2.9 [1.3–6.4]	0.009
	60–69 yr	2.4 [1.4–4.2]	0.001	5.7 [2.5–13.5]	<0.001
	70–79 yr	4.1 [2.4–7.2]	<0.001	15.3 [6.3–37.1]	<0.001
<b>Sex</b>	Male	1.6 [1.1–2.3]	0.009	2.6 [1.5–4.5]	0.001
	Female (ref)	-	-	-	-
<b>Smoking status</b>	Current	3.7 [2.3–5.8]	<0.001	8.9 [4.2–19.1]	<0.001
	Former	2.4 [1.5–3.8]	<0.001	3.4 [1.7–6.9]	<0.001
	Never (ref)	-	-	-	-
<b>Education</b>	No education	2.1 [1.0–4.5]	0.049	2.3 [0.9–5.5]	0.065
	Primary education (ref)	-	-	-	-
	Secondary education	0.7 [0.4–1.2]	0.177	0.7 [0.4–1.4]	0.344
	University education	0.7 [0.5–1.2]	0.177	0.8 [0.4–1.5]	0.426
<b>Occupational and biomass exposure history</b>	No (ref)	-	-	-	-
	Yes	0.8 [0.5–1.3]	0.344	1.5 [0.8–2.7]	0.199
<b>BMI (kg/m<sup>2</sup> mean)</b>	<21	2.0 [1.2–3.6]	0.013	6.7 [2.5–18.0]	<0.001
	≥21 (ref)	-	-	-	-
<b>YPAS</b>	1 y 2 (ref)	-	-	-	-
	3–4	4.6 [2.6–8.4]	<0.001	4.9 [2.0–12.0]	<0.001

**Abbreviations:** ref, reference; BMI, body mass index; YPAS, Yale physical activity survey.

associated with an increased risk of COPD. In the multivariate analysis, the direction and magnitude of the associations were maintained except for the level of education.

Finally, we performed the same analysis splitting by study ([Table 2 Supplementary Material](#)) and gender ([Table 3 Supplementary Material](#)) variables to show how the risk factors differ between EPISCAN and EPISCAN II and between women and men. In the bivariate analysis for study, gender and occupational and biomass exposure history showed a different direction and magnitude between EPISCAN and EPISCAN II, which only gender differed, also for multivariate analysis. While, in the bivariate and multivariate analyses for gender analysis, university education and occupational and biomass exposure history, showed a different direction and magnitude between genders.

## Discussion

The results of this study have shown that the overall prevalence of COPD in the population aged 40 to 80 in the region of Madrid did not undergo any major changes between 2007 and 2017, and there has been a non-statistically significant increase from 11% to 12.1%. However, these similar figures at the global level, mask important differences that emerge when analysed from a gender perspective: among women, a significant increase in prevalence and underdiagnosis has been observed, while among men the trend has been the opposite, with a decrease in prevalence and no differences in underdiagnosis. Age, smoking, and low weight of participants have been the most associated risk factors for the disease.

Disease prevalence has been defined on the basis of spirometric criteria as in other epidemiological studies.<sup>9,10,16</sup> It is well known that prevalence may vary according to the spirometric criteria used, with higher percentages obtained according to GOLD among older and younger participants. The definition of COPD in our study was established according to the GOLD criteria in order to draw comparisons with most epidemiological studies published to date. However, prevalence according to LLN has also been evaluated, with younger participants (40–50 years) presenting a higher prevalence of this disease defined by this criterion than by the fixed post-bronchodilator ratio established by GOLD.<sup>17,18</sup>

In the region of Madrid prevalence of COPD only increase 1.1 percentage points between 2007 and 2017. It could be because the geographical setting, population, design and methodology of EPISCAN and EPISCAN II was very similar, unlike other epidemiological studies carried out in this regard. Prevalence has been higher than the national average published in EPISCAN II<sup>7</sup> and unlike in previous studies in which there appeared to be a downward trend.<sup>16</sup> There are possible factors that have been previously described in the literature that could explain this higher prevalence.<sup>19–21</sup> The first of these is smoking, with the prevalence of smokers in Madrid being higher than the national average observed in EPISCAN II.<sup>7</sup> Another factor to be taken into account is environmental pollution and the urban area where the study was carried out. The Hospital Universitario de la Princesa is located in the city centre, in an urban environment under the direct influence of road traffic and, therefore, with greater exposure to environmental pollution than other regions included in EPISCAN II.

The influence of these factors has also been analysed as a possible explanation of the slight increase in prevalence in the region itself between the two studies, with smoking habits being very similar in 2007 and 2017. With regard to environmental pollution, the levels analysed by the different automatic measurement stations as part of Madrid City Council's air quality monitoring network were similar between the two studies. The levels of suspended particles (PM10 and PM2.5, particles smaller than 10 and 2.5 microns, respectively) fell slightly between 2007 and 2017, but in contrast, despite legislative changes in this area in recent years, in 2017 there was a notable increase in levels of nitrogen dioxide pollution (NO<sub>2</sub>) influenced by prevailing weather conditions and possibly by a surge in traffic. Although the two EPISCAN participating centres have a different geographical location, the measurements published by the stations closest to the two hospitals did not show any major differences.<sup>22,23</sup>

In relation to the analysis by gender, there has been an important change in the tendency of the disease that had been detected in previous years. In EPISCAN II study, Madrid was the only region where prevalence among women exceeded the level among men. The systematic review published by Ntritsos et al<sup>8</sup> found an overall prevalence among women of 6.2% with clear geographical variations, reaching up to 8.4% in urban populations. This factor, together with a greater smoking habit, ageing and higher socioeconomic status among women in Madrid in 2017, could explain this higher prevalence detected in the region. Additionally, mediation analysis using smoking habit as mediator, dependent variable COPD prevalence and the independent variable gender showed that COPD diagnosis was fully mediated by smoking habit (smoker or former smoker) and a gender change in smoking habit between EPISCAN and EPISCAN II which could be related to the increased prevalence of COPD in the female gender.

Changes have also been observed in relation to smoking by gender. Among men, the number of smokers has declined in line with the downward trend detected since the late 80s. In contrast, the percentage of smokers has increased in women and is higher than men, even among participants in the lowest age bracket, which is more worrying. This phenomenon is consistent with previous reports on changes in tobacco use in Spain and other developed countries where, due to the fact that women are taking up smoking at a younger age, the difference in habit between the two genders has narrowed.<sup>24</sup> It is known that tobacco use among women is influenced by socioeconomic status, with higher prevalence figures in countries with higher per capita income. In Europe, in 2018, the prevalence of women smokers was 19%, the highest in the world, with the overall prevalence being 9%<sup>25</sup> and a higher percentage detected in our study in 2017. This phenomenon may be due to the fact that in Madrid a decrease in the prevalence of smoking in women was detected up to 2014. From that year onwards, consumption increased again, and it is in the population subgroup aged 45–60 that this sustained increase has been evident, due to the fact that the cohorts of young smokers from the 1980s and 1990s have now reached this age bracket.<sup>26</sup> The greater susceptibility of women to tobacco smoke is well known, with a higher impact on the deterioration of lung function in women, even with lower cumulative consumption and at younger ages.<sup>27,28</sup> This phenomenon could explain why in our study, despite the lower PYI (pack-year index) in women, the prevalence of the disease has been higher than among men.



The underdiagnosis of COPD is similar in both studies: 73% in EPISCAN and 74.7% in EPISCAN II, which could reflect a stagnation in the diagnosis of the disease and the inadequacy of strategies to modify it. This problem is even more pronounced among women. Our study found that although women reported a higher percentage of symptoms (cough, expectoration, and dyspnoea) than men, none of the participants included in the 2017 study with obstructive spirometry had a previous diagnosis of COPD. For this reason, the rate of underdiagnosis among women reached 100%. This difference in underdiagnosis by gender has been demonstrated in previous studies, especially in European cohorts,<sup>29</sup> with several causes associated with this high level of underdiagnosis. The perception of the disease as a pathology associated with men, the high level of public ignorance surrounding the disease, and the anxiety and depression that sometimes lead to a different perception of dyspnoea among women are several of the factors described.<sup>30,31</sup>

Older age, smoking, a sedentary lifestyle, and especially BMI < 21 are the variables that present a more consistent association with COPD. This relationship has already been described in previous studies, and the important role of malnutrition in these patients is known with underweight individuals with lower lung function compared to those with higher BMI ranges.<sup>32,33</sup> A possible explanation for this inverse correlation between BMI and lung function decline is the increasing resting energy consumption, non-respiratory skeletal muscle atrophy due to decreased peripheral oxygen availability and systemic inflammation.

One of the limitations of our study is the establishment of a COPD diagnosis by means of spirometric criteria. The clinical diagnosis of the disease is based on risk exposure, clinical criteria, and bronchial obstruction<sup>34</sup> since the potential causes of non-reversible spirometric obstruction are different. However, to date all epidemiological studies are based on spirometric criteria, which have been used in EPISCAN, EPISCAN II and GOLD, in order to compare their results. Another limitation is the small sample size, having focused the study on a single region and an urban setting. As strengths, it should be noted that, by comparing studies conducted in the same geographical region using practically the same methodology, it has been possible to eliminate the major variability that exists in most of the studies carried out so far.

In conclusion, the prevalence of COPD in the Region of Madrid has not varied significantly in the ten-year period between the EPISCAN and EPISCAN II surveys, although there has been a change in the trend of the disease, with a higher prevalence, underdiagnosis and increased smoking among women in recent years. That is why greater efforts should be made to improve diagnosis, promote awareness of the disease, and implement greater measures to prevent and control smoking, especially among women.

## Ethics Approval

The study was approved by the Ethics Committee of the Hospital La Princesa (Madrid). Register number: 2899. The study was conducted in accordance with the ethical principles of the Declaration of Helsinki.

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## Author Contributions

All authors made substantial contributions to conception and design, acquisition of data, or analysis and interpretation of data; took part in drafting the article or revising it critically for important intellectual content; agreed to submit to the current journal; gave final approval of the version to be published; and agree to be accountable for all aspects of the work.

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## Disclosure

EGC has received speaker fees from GlaxoSmithKline, Chiesi and Pfizer. TAP has received speaker fees from AstraZeneca, GlaxoSmithKline, Chiesi, Novartis and Pfizer. JA has received company training fees from AstraZeneca, Boehringer Ingelheim, Chiesi, GlaxoSmithKline and Novartis and speaker fees from AstraZeneca, GlaxoSmithKline, Boehringer Ingelheim, Roche and Faes Farma. All other authors declare no conflicts of interest in this work.

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