Factors Affecting Drug Prescription in Patients With Stable COPD: Results From a Multicenter Spanish Study

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OBJECTIVE: To determine what factors are associated with prescription of drugs to patients with stable chronic obstructive pulmonary disease (COPD).

MATERIAL AND METHODS: We studied 568 patients with stable COPD. Assessments included determination of the severity of dyspnea, body mass index, health-related quality of life, and spirometry testing.

RESULTS: The forced expiratory volume in 1 second was significantly associated with prescription of long-acting ß$_2$-adrenergic agonists (odds ratio [OR]=0.98; 95% confidence interval [CI], 0.96-1) and inhaled corticosteroids (OR=0.98; 95% CI, 0.96-1). Quality of life was related to administration of short-acting β_2-adrenergic agonists (OR=1.02; 95% CI, 1-1.03), long-acting β_2-adrenergic agonists (OR=1.02; 95% CI, 1-1.03), ipratropium bromide (OR=1.03; 95% CI, 1-1.04), theophylline drugs (OR=1.02; 95% CI, 1-1.03), and inhaled corticosteroids (OR=1.02; 95% CI, 1-1.03). The severity of dyspnea was significantly associated with prescription of oral corticosteroids (for grade IV dyspnea, OR=15.25; 95% CI, 2.40-97.02). Body mass index was not related to drug administration.

CONCLUSIONS: Drug prescription in patients with stable COPD correlates not only with forced expiratory volume in 1 second but also with other parameters such as health-related quality of life and dyspnea.

Key words: *COPD. FEV_1. Health-related quality of life. Dyspnea. Treatment.*

Factores determinantes de la prescripción farmacológica en los pacientes con EPOC estable. Resultados de un estudio multicéntrico español (IDENTEPOC)

OBJETIVO: Determinar qué factores se relacionan con la prescripción de fármacos en los pacientes con enfermedad pulmonar obstructiva crónica (EPOC) estable.

MATERIAL Y MÉTODOS: Se estudió a 568 pacientes con EPOC estable. La evaluación realizada incluyó la medición del grado de disnea, la determinación del índice de masa corporal, el estudio de la calidad de vida relacionada con la salud y la realización de una espirometría.

RESULTADOS: El volumen espiratorio forzado en el primer segundo se asoció significativamente con la prescripción de β_2-adrenérgicos de acción larga (*odds ratio* [OR] = 0,98; intervalo de confianza [IC] del 95%, 0,96-1) y corticoides inhalados (OR = 0,98; IC del 95%, 0,96-1). La calidad de vida se relacionó con la administración de β_2-adrenérgicos de acción corta (OR = 1,02; IC del 95%, 1-1,03), β_2-adrenérgicos de acción larga (OR = 1,02; IC del 95%, 1-1,03), bromuro de ipratropio (OR = 1,03; IC del 95%, 1-1,04), teofilinas (OR = 1,02; IC del 95%, 1-1,03) y corticoides inhalados (OR = 1,02; IC del 95%, 1-1,03). El grado de disnea mostró una asociación significativa con la prescripción de corticoides orales (para disnea grado IV, OR = 15,25; IC del 95%, 2,40-97,02). No se encontró ninguna relación entre la administración de fármacos y el índice de masa corporal.

CONCLUSIONES: La prescripción farmacológica de los pacientes con EPOC estable viene determinada no sólo por el volumen espiratorio forzado en el primer segundo, sino también por otros parámetros, entre los que se incluyen la calidad de vida relacionada con la salud y la disnea.

Palabras clave: *EPOC. FEV_1. Calidad de vida relacionada con la salud. Disnea. Tratamiento.*

Introduction

Chronic obstructive pulmonary disease (COPD) is a clinical entity characterized by partially reversible airway obstruction. Disease severity is most often defined using

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forced expiratory volume in 1 second (FEV_1). This variable is therefore also used to decide when treatment is necessary in most clinical guidelines, such as those issued by the Spanish Society of Pulmonology and Thoracic Surgery (SEPAR), the British Thoracic Society, the European Respiratory Society, the American Thoracic Society, and the Global Initiative for Chronic Obstructive Lung Disease (GOLD).[1-5]

Some authors have questioned whether FEV_1 is the best variable for assessing individual patients and have suggested the need to include other variables in the systematic evaluation of COPD.[6,7] In fact, this disease is accompanied by a set of local and systemic manifestations that are not always closely related to the severity of airflow limitation. These include dyspnea, deterioration in health-related quality of life, and the appearance of malnutrition.[8] Furthermore, several studies have shown that FEV_1 is not the only variable that influences mortality in such patients and, recently, the importance of other factors such as dyspnea[9] or body mass index (BMI) have been recognized.[10,11] Thus, the pharmacological treatment given to patients with COPD is probably associated not only with FEV_1, but also with other variables related to disease perception or systemic repercussions.

The objective of this study was to determine what factors are associated with prescription of drugs to patients with stable COPD, paying particular attention to the influence of FEV_1, dyspnea, quality of life, and BMI.

Material and Methods

Design and Study Population

The results presented here form part of the IDENTEPOC project[12,13]—an observational, descriptive, cross-sectional, multicenter study that aimed to assess the prevalence and characteristics of patients diagnosed with COPD in both primary health care and in pulmonology clinics.

Patient recruitment and the sample size estimation took place within the IDENTEPOC study.[12,13] Briefly, the sample size estimation was based on the expected percentage of patients with COPD attended in primary health care clinics (10%) and pulmonology clinics (30%). Patients were randomly selected by general practitioners and pulmonologists throughout Spain. These health care professionals in turn had been randomly selected from the databases of the scientific societies of primary health care and pulmonology. Additional health care professionals were recruited to the study from pharmaceutical industry sources to prevent selection bias. Data were collected between January 1 and June 30, 2000.

The IDENTEPOC study included 898 subjects but, in accordance with the aims of the present study, we excluded patients whose preliminary clinical diagnosis of COPD was not made by spirometry, giving a total of 568 patients analyzed. This sample was large enough to attain the study objectives.

All patients were informed of the characteristics of the study, and all gave informed consent in writing.

Assessment of Patients

Personal data such as anthropometric variables, clinical characteristics, and treatments at the time of assessment were collected for all patients. Clinical data included symptoms, concurrent diseases, consultations for COPD, exacerbations, emergency room visits, admissions to hospital, and admissions to intensive care units.

The severity of dyspnea was classified according to an adapted version of the Medical Research Council scale, which ranges from grade 0 (patients without dyspnea except during vigorous exercise) to grade 4 (patients with dyspnea at rest).[14] Health-related quality of life was assessed using the Spanish version of the St George's Respiratory Questionnaire.[15,16]

Spirometry was always done using internationally standardized methods.[17] We used reference values published by the European Community for Coal and Steel.[18] Patients were stratified according to SEPAR criteria as follows: mild COPD—FEV_1 between 60% and 80% of predicted; moderate COPD—FEV_1 between 40% and 59% of predicted; and severe COPD—FEV_1 less than 40% of predicted. In addition, patients who had a ratio of FEV_1 to forced vital capacity (FVC) below 70% and an FEV_1 above 80% of the reference value—corresponding to mild COPD according to the GOLD guidelines—were included in the analysis.

Statistical Analysis

Data were analyzed with the SPSS statistics package, version 9.0 for Windows. Quantitative data were expressed as means (SD) whereas qualitative data were expressed as percentages. The χ^2 test was used to analyze the relationship between qualitative variables. We used one-factor ANOVA and subsequently the Bonferroni test or the Tamhane T2 test (appropriate for groups with different variances) to study differences between patient groups. Variables that did not have a normal distribution or those with a small sample size were compared with the Kruskal-Wallis test (for comparisons of more than 2 groups) or the Mann-Whitney U test (for comparisons of 2 groups). The Kendall tau-b correlation coefficient measured the relationship between ordinal variables. The multivariate logistic regression analysis was by conditional backward elimination. The variables included in the model were age, sex, concurrent diseases (number of diseases), cough, expectoration, dyspnea, severity of dyspnea, quality of life (overall score obtained on the Spanish version of the St George's Respiratory Questionnaire), BMI, FEV_1, FVC, PaO_2, $PaCO_2$, consultations for COPD, disease exacerbations, emergency room visits for an exacerbation, admission to hospital, and admission to the intensive care unit for an exacerbation in the last year. Finally, a multiple linear regression analysis was used to determine which variables influenced the number of drugs prescribed. The variables chosen were the same as those used in the logistic regression. Statistical significance was set at $P<.05$.

Results

A total of 568 patients with COPD, 94.5% of whom were men, were studied. Their mean (SD) age was 67.9 (8.9) years. Smokers or ex-smokers accounted for 91.9% of the population. Table 1 shows the clinical characteristics and lung function variables of these patients. COPD was mild in 18.2% (mean FEV_1: 68.7%

TABLE 1
Characteristics of Patients With Stable Chronic Obstructive Pulmonary Disease (COPD) (n=568)*

Severity of dyspnea†	
0	0
1	144 (25.3)
2	221 (38.9)
3	151 (26.6)
4	16 (2.8)
Unknown	36 (6.4)
Cough†	557 (98.1)
Expectoration†	553 (97.4)
Concurrent disease†	
Hypertension†	138 (24.3)
Ischemic heart disease†	45 (7.9)
Peptic ulcer†	65 (11.4)
Diabetes mellitus†	71 (12.5)
OSAS†	32 (5.6)
Others†	158 (27.8)
Consultations for COPD in last year‡	2 (p25: 1; p75: 4)
Exacerbations in last year‡	1 (p25: 1; p75: 3)
Emergency room visits in last year‡	0 (p25: 0; p75: 1)
Admissions to hospital in last year‡	0 (p25: 0; p75: 1)
Admissions to ICU in last year‡	0 (p25: 0; p75: 0)
Mean BMI, kg/m^2§	27.4 (4.7) [16.0-44.7]
Mean SGRQ§	47.3 (20.7) [1.7-93.6]
FEV_1, %§	44.3 (15.2) [15-104]
FVC, %§	65.8 (18.7) [23-140]
FEV_1/FVC§	0.51 (0.11) [0.27-0.69]
PaO_2, mm Hg§	63.0 (12.2) [7-106]
$PaCO_2$, mm Hg§	42.7 (7.3) [27-96]

*FEV_1 indicates forced expiratory volume in 1 second; FVC, forced vital capacity; BMI, body mass index; p25, 25th percentile; p50, 50th percentile; p75, 75th percentile; OSAS, obstructive sleep apnea syndrome; SGRQ, overall score on Spanish version of the St George's Respiratory Questionnaire; ICU, intensive care unit.
†Data are expressed as number of patients (%).
‡Data are expressed as median followed by percentiles between parentheses.
§Data are expressed as means followed by SD between parentheses and range between square brackets.

[8.6%]); moderate in 38.3% (mean FEV_1: 47.8% [5.7%]), and severe in 43.5% (mean FEV_1: 31.0% [5.9%]). FEV_1, expressed as a percentage of the reference value (FEV_1%), correlated significantly with the severity of dyspnea (r=-0.25) and with overall score on the St George's Respiratory Questionnaire (r=-0.27). A significant correlation was also found between dyspnea and quality of life (r=0.38). None of these variables correlated significantly with BMI. Figure 1 shows the relationship between FEV_1%, dyspnea, and quality of life of the patients studied.

Some sort of regular treatment for COPD was being taken by 96.8% of the patients. The drugs most commonly used were, in descending order, ipratropium bromide (77.8%), inhaled short-acting β_2-adrenergic agonists (65.8%), inhaled corticosteroids (61.0%), long-acting β_2-adrenergic agonists (46.4%), theophyllines (41.3%), and oral corticosteroids (5.6%). Figure 2 shows the percentage of patients using each of these drugs according to the severity of dyspnea, quality of life, FEV_1%, and BMI. Some of these data have been reported in a previous study.[13] Differences in treatments were found for all these variables except BMI.

The results of the multivariate multiple regression analysis are shown in Table 2. The variables predictive

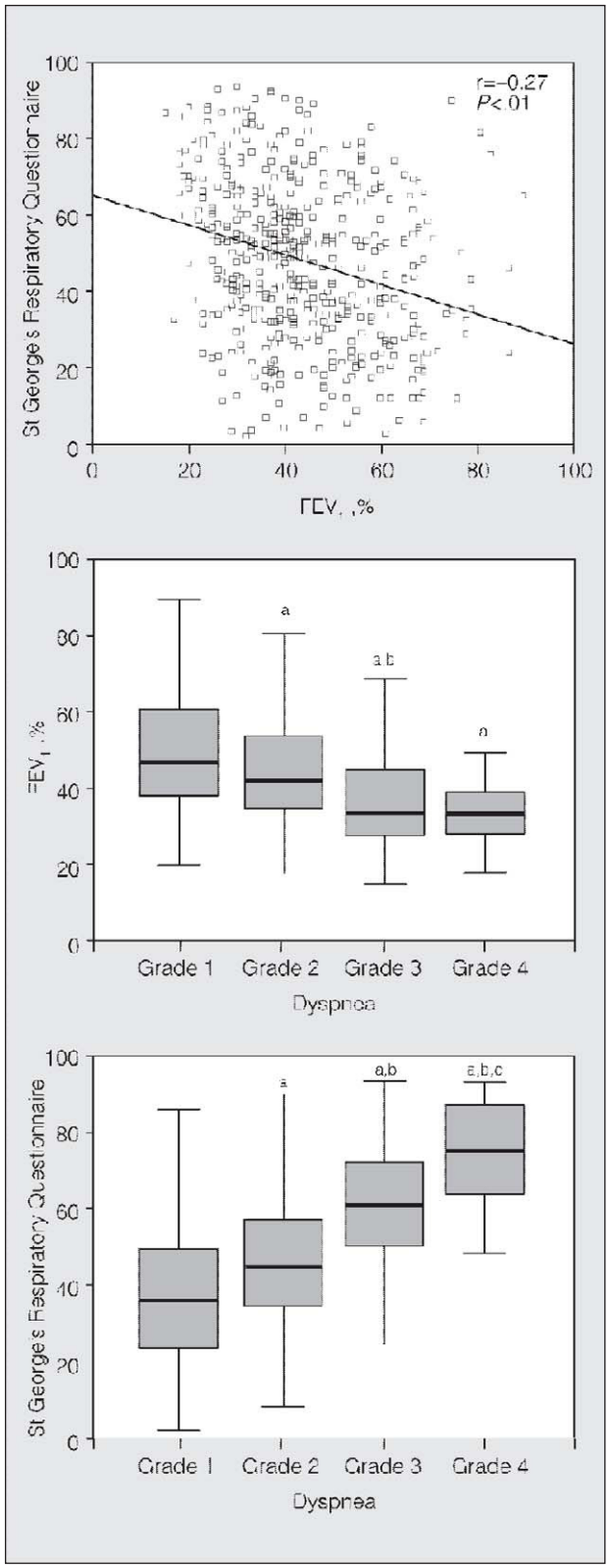

Figure. 1. Relationship between severity of dyspnea, overall score on the St George's Respiratory Questionnaire, and forced expiratory volume in 1 second expressed as a percentage of the reference value (FEV_1 %).
[a]Significantly different (*P*<.05) from grade 1 dyspnea.
[b]Significantly different (*P*<.05) from grade 2 dyspnea.
[c]Significantly different (*P*<.05) from grade 3 dyspnea.

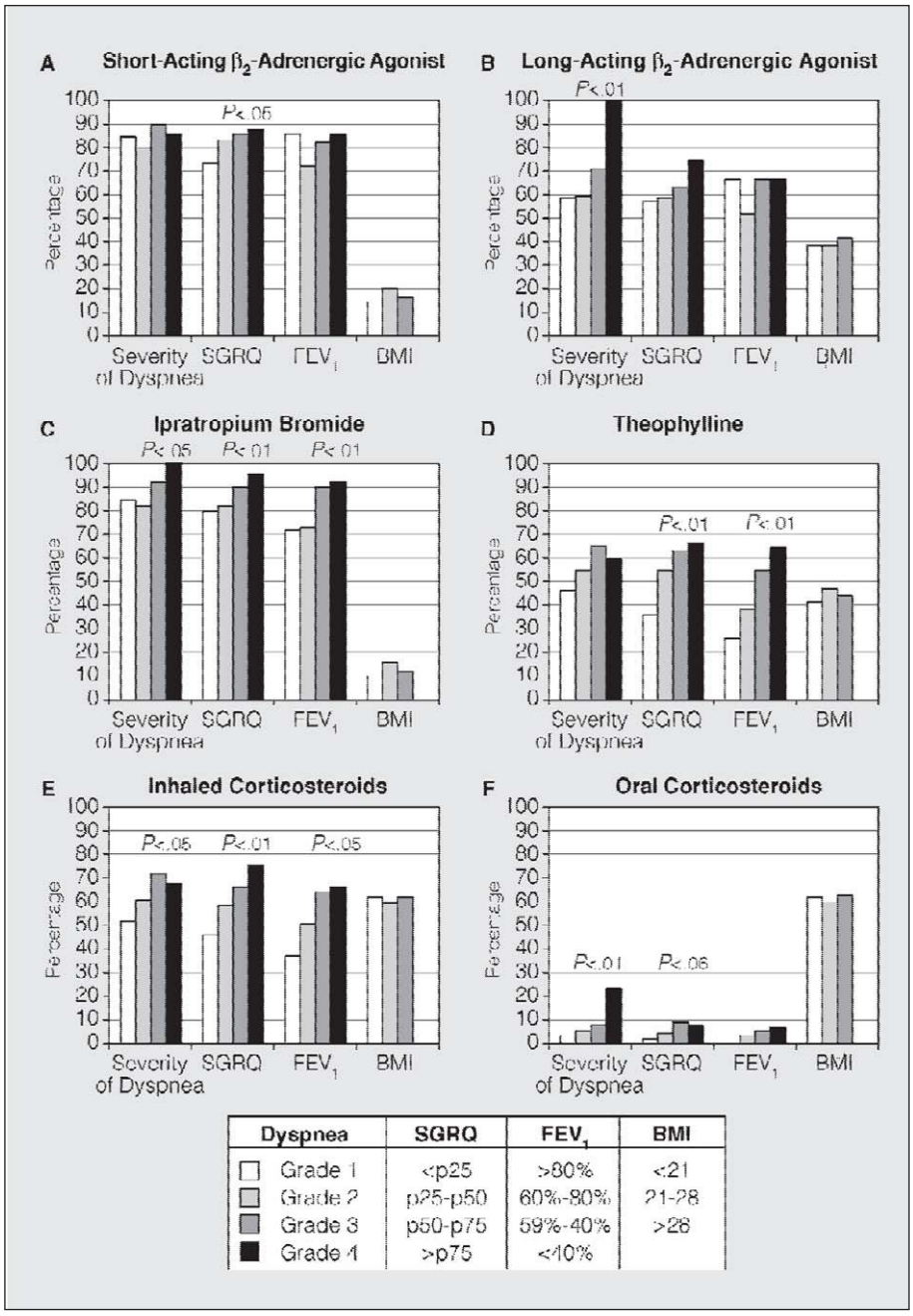

Figure 2. Percentage of patients with stable chronic obstructive pulmonary disease prescribed a given drug. FEV_1 indicates forced expiratory volume in 1 second; SGRQ, overall score on Spanish version of the St George's Respiratory Questionnaire; BMI, body mass index; p25, 25th percentile; p50, 50th percentile; p75, 75th percentile.

of drug prescription in patients with COPD were as follows: *a)* health-related quality of life, for prescription of short- and long-acting β_2-adrenergic agonists, ipratropium bromide, theophyllines, and inhaled corticosteroids; *b)* FEV_1%, for prescription of long-acting β_2-adrenergic agonists and inhaled corticosteroids; *c)* concurrent disease, for short- and long-acting β_2-adrenergic agonists; *d)* dyspnea, for oral corticosteroids; *e)* age, for long-acting β_2-adrenergic agonists; *f)* sex, for theophyllines; *g)* PaO_2, for theophyllines; *h)* $PaCO_2$, for long-acting β_2-adrenergic agonists; *i)* FVC expressed as a percentage of predicted, for ipratropium bromide; *j)* consultations for COPD in the last year, for inhaled corticosteroids; *k)* emergency room visits for a COPD exacerbation in the last year, for inhaled corticosteroids; and *l)* admission to hospital for a COPD exacerbation in the last year, for short-acting β_2-adrenergic agonists. Table 3 shows the percentage of patients receiving drugs belonging to each of the pharmacological groups by the number of consultations, exacerbations, and admissions to hospital.

The patients were receiving a mean of 3.2 (1.1) different drugs and 73.1% were receiving a combination of at least 3 different drugs. The most

TABLE 2
Variables Predictive of Drug Prescription in Patients With Stable Chronic Obstructive Pulmonary Disease*

Drug	OR (95% CI)	*P*
Short-acting β_2-adrenergic agonists		
Overall score on the St George's Respiratory Questionnaire	1.02 (1.00-1.03)	.0025
Admissions to hospital for COPD in the last year	2.92 (1.53-5.57)	.0001
Concurrent disease	1.82 (1.05-3.17)	.0032
Long-acting β_2-adrenergic agonists		
FEV_1, %	0.98 (0.96-1.00)	.0035
Overall score on the St George's Respiratory Questionnaire	1.02 (1.00-1.03)	.0013
Age	0.97 (0.94-1.00)	.0063
Concurrent disease	0.57 (0.33-0.97)	.0038
$PaCO_2$	0.95 (0.91-0.99)	.0009
Ipratropium bromide		
FVC, %	0.98 (0.96-0.99)	.0006
Overall score on the St George's Respiratory Questionnaire	1.03 (1.00-1.04)	.0003
Theophyllines		
PaO_2, %	0.95 (0.93-0.97)	<.0001
Overall score on the St George's Respiratory Questionnaire	1.02 (1.00-1.03)	.0003
Sex, male	5.78 (1.24-26.92)	.0026
Inhaled corticosteroids		
FEV_1, %	0.98 (0.96-1.00)	.0032
Overall score on the St George's Respiratory Questionnaire	1.02 (1.00-1.03)	.0006
Emergency room visits in last year	0.5 (0.29-0.89)	.0017
Consultations for COPD in last year	3.00 (1.51-5.95)	.0002
Oral corticosteroids†		
Grade 2 dyspnea	1.81 (0.36-8.98)	.0468
Grade 3 dyspnea	2.63 (0.53-13.14)	.0237
Grade 4 dyspnea	15.25 (2.40-97.02)	.0004

*COPD indicates chronic obstructive pulmonary disease; FEV_1, forced expiratory volume in 1 second; FVC, forced vital capacity; OR, odds ratio; CI, confidence interval. The variables included in the model were age, sex, concurrent disease, cough, expectoration, dyspnea, severity of dyspnea, quality of life (overall score on the Spanish version of the St George's Respiratory Questionnaire), consultations for COPD in the last year, COPD exacerbations in the last year, emergency room visits for COPD exacerbations in the last year, admissions to hospital for COPD exacerbations in the last year, body mass index, PaO_2, $PaCO_2$, FEV_1, and FVC.
†Grade 1 dyspnea taken as reference.

common combination, prescribed for 10% of the patients, was short-acting β_2-adrenergic agonists, ipratropium bromide, theophyllines, and inhaled corticosteroids. The distribution of the main variables assessed in this study according to the total number of drugs prescribed is shown in Table 4. Administration of a greater number of drugs was significantly associated with more severe airway obstruction, a lower score on the quality of life questionnaire, and more severe dyspnea, but not with BMI. The number of drugs was significantly correlated with FEV_1% (r=–0.22), severity of dyspnea (r=0.23), and quality of life (r=0.25). No correlation was found between this variable and BMI. The multiple regression analysis showed that the variables predictive of the number of drugs were FEV_1%, overall score on the St George's Respiratory Questionnaire, and admissions to hospital for COPD exacerbations in the last year. According to this model (Table 5):

No. drugs =(–0.017×FEV_1%)+(0.013×overall score on St George's Respiratory Questionnaire)+(0.24×admissions to hospital for COPD in the last year)+3.2

No other baseline anthropometric, clinical, or lung function variable improved the predictive capacity of this model (Table 5). Dyspnea appeared as a predictive variable if health-related quality of life was excluded.

Discussion

Our results indicate that treatment of patients with COPD is determined not only by the severity of airway obstruction but also by other factors such as dyspnea and, above all, health-related quality of life. The prognostic usefulness of a multidimensional scale that incorporates an assessment of symptoms, exercise testing, and BMI, in addition to spirometry, has recently been shown.[19] However, in our study, we found no association between drug prescription and BMI. Other variables predictive of drug prescription in these

TABLE 3
Drug Prescription, by Number of Consultations, Exacerbations, and Admissions to Hospital in the Last Year*

	Short-Acting β_2 Adrenergic Agonist	Long-Acting β_2 Adrenergic-Agonist	Ipratropium Bromide	Theophyllines	Inhaled Corticosteroids	Oral Corticosteroids
Consultations						
0	54 (80.6)	36 (52.2)	59 (85.5)	31 (58.5)	34 (42.0)	4 (4.9)
1	41 (70.7)	30 (49.2)	57 (90.5)	31 (60.8)	32 (46.4)	4 (5.8)
2	85 (73.9)	69 (58.5)	101 (86.3)	55 (56.7)	76 (58.9)	9 (7.0)
3	72 (82.8)	54 (62.1)	68 (78.2)	34 (43.6)	61 (62.9)	3 (3.1)
≥4	143 (93.5)	117 (77.5)	139 (89.7)	79 (59.4)	129 (77.2)	12 (7.2)
Emergency Room Visits						
0	195 (80.6)	155 (61.5)	205 (83.0)	97 (46.4)	165 (58.7)	10 (3.6)
1	96 (82.1)	75 (65.2)	100 (85.5)	61 (60.4)	72 (56.7)	11 (8.7)
≥2	90 (90.9)	64 (66)	97 (93.3)	58 (64.4)	77 (72.0)	10 (9.3)
Hospitalizations						
0	232 (79.7)	185 (61.1)	242 (82)	129 (50.4)	192 (57.1)	17 (5.1)
1	117 (91.4)	85 (65.9)	125 (91.9)	67 (57.8)	100 (70.4)	12 (8.5)
≥2	38 (95.0)	29 (69.0)	43 (97.7)	24 (66.7)	31 (68.9)	1 (2.2)

*Data are expressed as number of patients (%).

TABLE 4
Distribution of Main Variables That Determine Drug Prescription by the Number of Drugs Used*

Variable	No. of Drugs		
	<3 (n=143)	3 (n=186)	>3 (n=239)
Age†	68.1 (10.7) [42-97]	67.3 (8.6) [35-83]	68.4 (8.1) [43; 90]
Severity of dyspnea†	1.8 (0.07) [1-4]	2.0 (0.06) [1-4]§	2.3 (0.05) [1-4]§,‖
SGRQ†	39.3 (18.3) [1.7-92.5]	43.9 (20.7) [2.1-92.1]	55.3 (19.2) [5.0-93.6]§,‖
FEV_1,%†	50.2 (16) [17-104)	45.1 (14.6) [20-87]§	39.7 (13.0) [15-90]§,‖
Consultations for COPD‡	106 (80.3)	156 (89.1)	198 (87.6)
Emergency room visits‡	44 (35.5)	65 (40.1)	123 (56.2)§,‖
Hospitalizations‡	32 (25.4)	50 (30.7)	105 (46.9)§,‖
BMI†	27.2 (4.5) [18.4-43.4]	27.6 (5.1) [18.1-44.7]	27.3 (4.8) [16.0-40.1]

*COPD indicates chronic obstructive pulmonary disease; FEV_1%, forced expiratory volume in 1 second expressed as a percentage of the theoretical value; BMI, body mass index; SGRQ, overall score on the St George's Respiratory Questionnaire.
†Data are expressed as means followed by SD between parentheses and range between square brackets.
‡Data are expressed as number of patients (%).
§Significant differences (P<.05) with group receiving <3 drugs
‖Significant differences (P<.05) with group receiving 3 drugs.

patients were age, sex, concurrent diseases, consultations related to COPD, emergency room visits, admissions to hospital, PaO_2, $PaCO_2$, and FVC. These findings reflect those for an unselected population attended by general practitioners and pulmonologists in Spain and are therefore not influenced by assignment of treatments mandated when patients enter a trial.

TABLE 5
Multiple Regression Analysis for Number of Drugs (r^2=0.17)*

Variable	B	SE of B	β	t	*P*
Constant	3.2	0.24		13.4	<.001
FEV_1%	–0.017	0.004	–0.221	–4.5	<.001
Overall Score on St George's Questionnaire	0.013	0.003	0.245	4.8	<.001
Hospitalizations for COPD	0.240	0.120	0.101	2.0	.046

*COPD indicates chronic obstructive pulmonary disease; SE, standard error; FEV_1, forced expiratory volume in 1 second expressed as percentage of reference value.

FEV_1 is a powerful tool for assessing the extent to which lung function of patients with COPD is affected. This variable is also used to assess the efficacy of bronchodilators, even though only a small percentage of COPD patients show improvement in FEV_1 in the bronchodilator test.[1] In our study, we found no association between administration of ipratropium bromide and the severity of airway obstruction, despite it being the most widely prescribed drug. On the other hand, we did find an association between severity of airway obstruction and the prescription of long-acting β_2-adrenergic agonists and inhaled corticosteroids. This finding might be explained in a variety of ways. Most of the patients were receiving anticholinergic agents. This would explain the lack of association between use of such drugs and FEV_1. However, we did find an association between the use of these agents and FVC, reflecting their greater prescription in more advanced phases of the disease in which this variable may decrease because of air trapping. In contrast, although treatment often used to start with anticholinergic agents in patients with confirmed diagnoses of COPD and persistent symptoms, increasing numbers of authors are now recommending long-acting β_2-adrenergic agonists as the initial treatment of choice in stable COPD because these agents have proven more effective than ipratropium bromide.[20] Finally, it has been shown that inhaled corticosteroids are beneficial in patients in advanced stages of the disease.[21] Recent guidelines recommend their use in patients with severe COPD and frequent exacerbations that require antibiotics or oral corticosteroids and in patients who respond favorably in a treatment trial or in those with bronchial hyperreactivity.[1,5]

Dyspnea is the main symptom of COPD,[22] but contrary to what might be expected, it is only weakly associated with the severity of airway obstruction. This can be explained by the many complex physiological and psychological factors that influence when dyspnea appears.[22,23] Bronchodilators seem to improve dyspnea by decreasing dynamic hyperinflation, regardless of changes in FEV_1, which may be small.[24] Previous studies have shown that there is a direct relationship between prescription of respiratory medication and severity of dyspnea, both in primary health care[25] and in specialist care.[26] In our study, dyspnea was only predictive of administration of oral corticosteroids. The role of these drugs in the management of stable COPD is controversial. It has been found that 30% of the patients with COPD benefit from treatment with corticosteroids and that this benefit may have more to do with improvement of asthmatic components in the patients than with the course of COPD itself.[27]

Health-related quality of life includes physical, psychological, and social aspects that are unique for each individual.[28] In our study, this variable correlated weakly with lung function tests and more strongly with dyspnea, in agreement with other studies.[14,28] Several clinical trials have shown that quality of life improves for patients with COPD after administration of bronchodilators.[29,30] Furthermore, a negative association has been observed between the state of health of patients with stable COPD and the number of drugs prescribed for treatment.[31] In the present study, we

found that worse quality of life is predictive of administration of most of the drugs used in the management of these patients, namely, anticholinergic agents, short- and long-acting β_2-adrenergic agonists, theophyllines, and inhaled corticosteroids.

Malnutrition was associated with a decrease in various lung function variables and with worse dyspnea and quality of life in patients with COPD.[32,33] We found no significant correlation between BMI and severity of airway obstruction, dyspnea, or quality of life of the patients, in contrast to other studies. This may be because BMI did not influence prescription of drugs in our patients. In other recent studies carried out in Spain, no relationship between BMI and the number of drugs prescribed for respiratory diseases was found.[31]

Another variable predictive of drug prescription in patients with COPD was sex. We found that the probability of receiving treatment with theophyllines was higher in men. This finding can be explained by the later diagnosis of COPD in women and the current increased controversy surrounding the use of these drugs. With regard to age, we have found in this study that this variable is associated with administration of long-acting β_2-adrenergic agonists. Elderly patients are more likely to have concurrent diseases and be receiving multiple treatments. Therefore, in such patients, these drugs might be prescribed less often because the profile of adverse effects is worse than that of other bronchodilators, in particular, anticholinergic agents.[35] This would also justify the less frequent use of these drugs in patients with concurrent disease, for whom short-acting β_2-adrenergic agonists are preferred. Short-acting β_2-adrenergic agonists are thus usually used as needed when symptoms deteriorate for whatever reason. Other variables predictive of drug prescription in this study were PaO_2 and $PaCO_2$—a finding which has not often been reported and which might be explained by the greater disease severity associated with measurement of such variables.

Finally, the consultations made in connection with the disease, emergency room visits, and admissions to hospital are also factors that have a significant influence on the treatment that patients with COPD receive. Roche et al,[26] in a study of a group of 631 patients with COPD attending a pulmonology clinic, reported that the visit led to a change in at least one drug in 66% of the patients. In addition to the reason for the consultation, other factors associated with changes in treatment and with the final prescriptions in this study were the severity of dyspnea and FEV_1.

Emergency room visits and admissions to hospital for COPD exacerbations also significantly influenced the drugs prescribed to these patients. In a recent study, it was observed that the bronchodilator treatments most often added to patients with exacerbations of chronic bronchitis and COPD were β_2-adrenergic agonists—prescribed in 18.5% of the patients.[36] We also observed a relationship between admission to hospital in the last year for COPD and prescription of short-acting β_2-adrenergic agonists.

The mean number of drugs prescribed in our study was slightly higher than that reported by other authors.[26] Our results indicate once more that there is a relationship between the number of drugs prescribed and the severity of dyspnea, quality of life, and FEV_1% of the patients, but not between the number of drugs and BMI. Moreover, we found that quality of life and FEV_1% of the patients figured among the variables predictive of the number of drugs prescribed. However, quality of life may be hard to measure in normal clinical practice. We therefore excluded this variable from the model and found that dyspnea then became a predictive variable. The advantage in using dyspnea is that only a few minutes are needed to ask the patient what daily activities may cause dyspnea, and this information can be readily obtained at the same time as the medical history.

In conclusion, drug prescription to patients with stable COPD is determined not only by the severity of airway obstruction, but also by other factors not included in treatment guidelines such as dyspnea and, above all, health-related quality of life. This observation is of great interest, as it suggests that current clinical guidelines do not take into account all the factors that characterize the disease and so, in practice, physicians apply broader criteria to determine which treatment to prescribe.

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