

# Depressive status explains a significant amount of the variance in COPD assessment test (CAT) scores

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**Background:** COPD assessment test (CAT) is a short, easy-to-complete health status tool that has been incorporated into the multidimensional assessment of COPD in order to guide therapy; therefore, it is important to understand the factors determining CAT scores.

**Methods:** This is a post hoc analysis of a cross-sectional, observational study conducted in respiratory medicine departments and primary care centers in Spain with the aim of identifying the factors determining CAT scores, focusing particularly on the cognitive status measured by the Mini-Mental State Examination (MMSE) and levels of depression measured by the short Beck Depression Inventory (BDI).

**Results:** A total of 684 COPD patients were analyzed; 84.1% were men, the mean age of patients was 68.7 years, and the mean forced expiratory volume in 1 second (%) was 55.1%. Mean CAT score was 21.8. CAT scores correlated with the MMSE score (Pearson's coefficient  $r=-0.371$ ) and the BDI ( $r=0.620$ ), both  $p<0.001$ . In the multivariate analysis, the usual COPD severity variables (age, dyspnea, lung function, and comorbidity) together with MMSE and BDI scores were significantly associated with CAT scores and explained 45% of the variability. However, a model including only MMSE and BDI scores explained up to 40% and BDI alone explained 38% of the CAT variance.

**Conclusion:** CAT scores are associated with clinical variables of severity of COPD. However, cognitive status and, in particular, the level of depression explain a larger percentage of the variance in the CAT scores than the usual COPD clinical severity variables.

**Keywords:** COPD, CAT, Mini-Mental State Examination, MMSE, Beck Depression Inventory, BDI

## Introduction

COPD assessment test (CAT) is a short, easy-to-complete health status tool that has been developed to help patients and their clinicians assess and quantify the symptoms and impact of COPD and enable better communication between patients and physicians about the consequences of the disease.<sup>1</sup> The CAT has demonstrated its reliability and validity in quantifying disease states in COPD and correlates strongly with other measures of COPD-specific health-related quality of life, such as the St George's Respiratory Questionnaire.<sup>1-3</sup> In addition, the CAT score is a good predictor of the risk of exacerbation,<sup>4</sup> of outcomes during and after exacerbations,<sup>5,6</sup> and even of the risk of death.<sup>7</sup>

The Global initiative for chronic Obstructive Lung Disease (GOLD) has incorporated the CAT score into the multidimensional assessment of COPD and the algorithm of pharmacologic treatment of COPD as a measure of symptom intensity, together with the modified Medical Research Council (mMRC) dyspnea scale.<sup>8</sup> There is some debate about the use of either CAT or mMRC to classify patients into low and high

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symptom levels because several studies have argued that the classification of a given patient may differ according to the scale used.<sup>7,9</sup> In addition, it is important to understand the factors determining CAT scores because some of them, such as comorbidities, may not be influenced by specific COPD medications.<sup>10</sup>

In this study, we have analyzed data from a large population of patients with COPD enrolled in primary care and specialized clinics in order to investigate the determinants of the CAT scores, paying special attention to the impact of cognitive status and depression. The results may help the clinician in the interpretation of CAT results and their impact on the therapeutic management of the disease.

## Methods

### Study population, design, and assessments

This is a secondary analysis of a cross-sectional, observational study conducted in respiratory medicine departments and primary care centers in Spain, aimed at investigating the prevalence and impact of depression in COPD.<sup>11</sup> The study population comprised ambulatory COPD patients who were at least 40 years of age, current or former smokers of at least 10 pack-years, and had stable disease (confirmed by post-bronchodilator forced expiratory volume in 1 second [FEV<sub>1</sub>]/forced vital capacity [FVC] <0.7 and absence of exacerbations in the previous 3 months). All patients who correctly completed the assessments of quality of life, depression, and cognitive function were included in the current analysis. The study was approved by the Institutional Ethics Committee of the Hospital Clínic (Barcelona, Spain) and was conducted according to the principles of the Declaration of Helsinki. All patients signed the written informed consent form before inclusion in the study.

Investigators recorded patients' sociodemographic data and clinical information, including post-bronchodilator spirometric parameters and history of exacerbations. COPD severity was evaluated by the mMRC dyspnea scale<sup>12</sup> and the BODEx (Body mass index, airflow Obstruction, Dyspnea, and Exacerbations) index,<sup>13</sup> whereas comorbidity was rated by the Charlson index.<sup>14</sup> Physical activity was measured by patients' self-reported average minutes walked every weekday, as previously described.<sup>15</sup>

### CAT questionnaire

The CAT is a disease-specific questionnaire to assess the health status in individuals with COPD. The questionnaire consists of eight items: cough, expectoration, dyspnea, chest tightness, going up hills/stairs, confidence leaving home,

activity limitations at home, quality of sleep, and levels of energy, each presented on a five-point scale, providing a total score of 0 (floor) to 40 (ceiling), indicating the impact of the disease.<sup>1,2</sup> When one or two items are missing, their scores can be set to the average of the non-missing scores; when more than two responses are missing in the CAT, a score cannot be calculated.<sup>1,2</sup> We used the validated Spanish version of the CAT.<sup>1</sup>

### Measurement of depressive and cognitive status

Depressive symptoms were evaluated with the short Beck Depression Inventory (BDI). This tool is a 13-item, self-administered questionnaire that evaluates affective, cognitive, motivational, and vegetative symptoms of depression; items are rated from 0 (not at all) to 3 (extreme form of each symptom).<sup>16</sup> We used the established cutoff points for stratifying depression severity: 0–4= no depression, 5–7= mild depression, 8–15= moderate depression, and >15= severe depression.<sup>17</sup>

Cognitive status was assessed by the Mini-Mental State Examination (MMSE),<sup>18,19</sup> which is widely used to screen for cognitive impairment. This instrument explores spatial and temporal orientation, registration, attention and calculation, recall, language, and visual construction in 12 items and 30 questions. The correct answer to a question scores 1 point (total from 0 to 30). A score <27 indicates cognitive impairment.<sup>20</sup>

### Statistical analysis

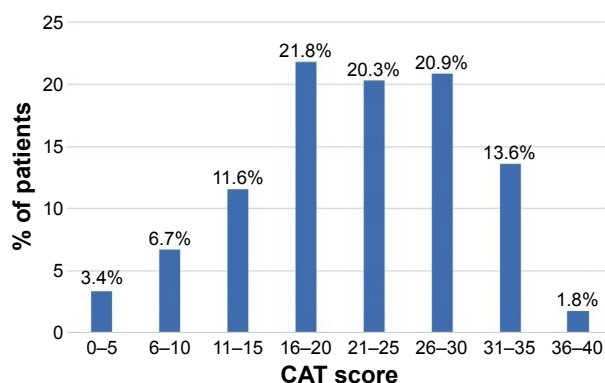
CAT scores of 0–10, 11–20, 21–30, and 31–40 were defined for mild, moderate, severe, and very severe clinical impact, respectively. Continuous variables are expressed as mean and SD. Categorical values are described as absolute and relative frequencies. Fisher's exact test was used for comparisons of qualitative variables, whereas the analysis of variance test was used to determine the relationship between quantitative variables by group. Univariate associations between CAT scores and MMSE and BDI scores were analyzed using Pearson's correlation coefficient. Stepwise forward multiple regression analyses were performed to examine the relative contributions of different variables to the CAT score. In order to establish the contribution of the neuropsychiatric condition, a first model was developed with CAT score as the dependent variable and depression and cognitive status as the only independent variables (Model 1), together and by each variable. Model 2 also included relevant demographic and clinical variables such as age, sex, post-bronchodilator

FEV<sub>1</sub> (%), history of exacerbations (dichotomized as yes/no according to the presence of any exacerbation the previous year), dyspnea, and comorbidity as independent variables. Model 3 was developed with a stepwise automatic selection of variables with a *p*-value <0.15. Finally, the independent contribution of post-bronchodilator FEV<sub>1</sub> (%) and FEV<sub>1</sub>/FVC of CAT variance was also calculated. *p*-values <0.05 were considered significant. Statistical analyses were performed using SAS version 9.1.3 Service Pack 3 software.

## Results

### Sample characteristics and distribution by CAT score

A total of 1,273 patients were screened, of whom 372 were excluded as they did not meet the inclusion criteria (6 were younger than 40 years, 48 were never smokers or smoked <10 pack-years, 146 did not provide spirometry, 148 did not have airflow obstruction, and 24 had severe cognitive impairment). Of the remaining 901 patients, 684 (76%) provided complete data for all the requested questionnaires and were considered valid for the analysis. Baseline characteristics of the patients with or without completed questionnaires were not significantly different (data not shown). Mean age was 68.7 years (SD =9.3 years), and 570 (84.1%) patients were men. The mean CAT score was 21.8 (SD =8.6), and 57% had a CAT score >20. Distribution of CAT scores by five-point intervals is presented in Figure 1. Patients in primary care had a worse mean CAT score compared with patients in specialized care (23.2 [SD =7] versus 20.5 [SD =8.5], *p*<0.001), despite showing a better mean FEV<sub>1</sub> (%) (54.7% [SD =17.2%] versus 51.3% [SD =16.6%], *p*=0.017). Patients with higher CAT scores were significantly older, had longer COPD duration, poorer lung function and more severe dyspnea, presented more frequent exacerbations



**Figure 1** Distribution of CAT scores among participants.  
**Abbreviation:** CAT, COPD assessment test.

in the preceding year, and more often received domiciliary oxygen therapy. Similarly, cognitive impairment, depressive symptoms, and comorbidity burden were significantly higher in patients with higher CAT scores (Table 1).

### Depressive and cognitive status and correlations with CAT scores

Global mean MMSE and BDI scores were 26.2 (SD =4.2) and 9.0 (SD =6.2), respectively. A total of 516 patients (75.4%) had some degree of depression, and 104 (20.2%) had severe depression. Correlations of the CAT score with MMSE score, BDI score, FEV<sub>1</sub> (%), and FEV<sub>1</sub>/FVC are depicted in Figure 2. The CAT score correlated significantly with the MMSE score (Pearson's *r* coefficient =−0.371, *p*<0.0001) and the BDI score (*r*=0.620, *p*<0.0001). Both FEV<sub>1</sub> (%) and FEV<sub>1</sub>/FVC also correlated significantly with the CAT score, with Pearson's *r* values of −0.151 and −0.100 (both *p*<0.001), respectively. All items of CAT correlated significantly with the BDI scores, with “having energy” showing the strongest correlation (*r*=0.59, *p*<0.0001), followed by “confidence leaving the house” (*r*=0.57, *p*<0.0001) and “chest tightness” showing the weakest correlation (*r*=0.37, *p*<0.001).

### Factors associated with CAT scores – multivariate analysis

In the multivariate analysis, Model 1 showed that both cognitive status and depression were associated with the CAT score, with a good fit of the model (*p*<0.001) and explained 40% of the full variance of CAT score (Table 2). Model 2, which also included the most relevant demographic and clinical variables, explained 43% of the CAT variance, although several variables emerged as not significantly related with CAT score. Model 3 with a stepwise automatic selection of variables – MMSE score, BDI score, post-bronchodilator FVC (%), post-bronchodilator FEV<sub>1</sub>/FVC, degree of dyspnea, and Charlson Index – explained nearly 45% of the CAT full variance (Table 2). When the variables were tested independently, MMSE score alone explained almost 14% of the CAT variance and BDI score alone explained 38% of it. In contrast, FEV<sub>1</sub> (%) alone explained 2% of the CAT score variance, whereas FEV<sub>1</sub>/FVC explained 1% of it (Table 3).

## Discussion

The CAT questionnaire is a very useful tool for quantifying the impact of COPD in patients with this disease.<sup>1,9</sup> It was designed as a simple questionnaire that can be used in everyday clinical practice to understand the health status of

**Table 1** Demographic and clinical characteristics of the study population

Variable	CAT score category				All (N=684)
	0–10 (n=69)	11–20 (n=228)	21–30 (n=282)	31–40 (n=105)	
Age (years)	65.8±10.5	68.7±9.4	69.5±9.1*	68.8±8.9	68.7±9.3
Sex (men)	57 (82.6)	197 (87.6)	227 (81.4)	89 (85.8)	570 (84.1)
Active smoker	16 (23.2)	44 (19.5)	60 (21.6)	25 (24.3)	145 (21.4)
COPD duration (years)	7.6±6.2	10.1±7.6	12.1±6.6	15.8±9.4***	11.5±7.7
FVC (mL)	3,291±824	2,959±883	2,812±927	2,858±994***	2,917±922
FVC (%)	78.5±16.9	69.8±16.1	69.2±17.4	68.4±18.1***	70.2±17.2
FEV <sub>1</sub> (mL)	1,876±616	1,725±739	1,630±719	1,619±759***	1,685±725
FEV <sub>1</sub> (%)	58.0±15.3	53.5±15.8	51.4±16.6	48.6±17.5***	52.3±16.3
FEV <sub>1</sub> /FVC	56.5±11.8	55.8±11.2	53.5±12.3	53.0±13.8**	5.5±12.2
Cough (yes)	34 (49.3)	171 (76.7)	255 (91.7)	102 (97.1)***	562 (83.3)
Expectoration (yes)	30 (43.5)	137 (62.0)	222 (89.4)	93 (89.4)***	482 (72.3)
Dyspnea (yes)	56 (81.2)	220 (96.5)	279 (99.6)	105 (100)***	660 (96.8)
Exacerbations in the previous year (yes)	47 (68.1)	192 (84.2)	268 (95.0)	91 (86.7)***	598 (87.4)
Oxygen therapy at home (yes)	3 (4.6)	29 (13.4)	87 (32.0)	39 (40.2)***	158 (24.3)
BODEx	1.4±1.4	2.2±1.5	3.4±1.8	4.2±1.6***	3.0±1.9
MMSE	28.8±1.8	27.0±3.5	25.7±4.0	23.9±5.7***	26.2±4.2
BDI score	3.5±3.3	6.0±3.9	10.8±5.5	14.4±7.4***	9.0±6.2
Depression (yes)	18 (26.1)	142 (62.3)	255 (90.4)	101 (96.2)***	516 (75.4)
Severe depression (yes)	1 (1.4)	9 (3.9)	54 (19.1)	40 (38.1)***	104 (15.2)
Charlson index	0.8±1.1	1.0±1.0	1.6±1.4	2.4±2.0***	1.4±1.4
Minutes walked per day	78.4±39.3	69.9±49.8	56.9±41.5	40.8±29.8***	61.2±44.2

**Notes:** Data are presented as mean ± SD or n (%). \*Differences in age were significant for the comparison between CAT 0–10 and CAT 21–30,  $p < 0.05$ , \*\* $p < 0.01$ , \*\*\* $p < 0.001$  (Fisher's test or ANOVA).

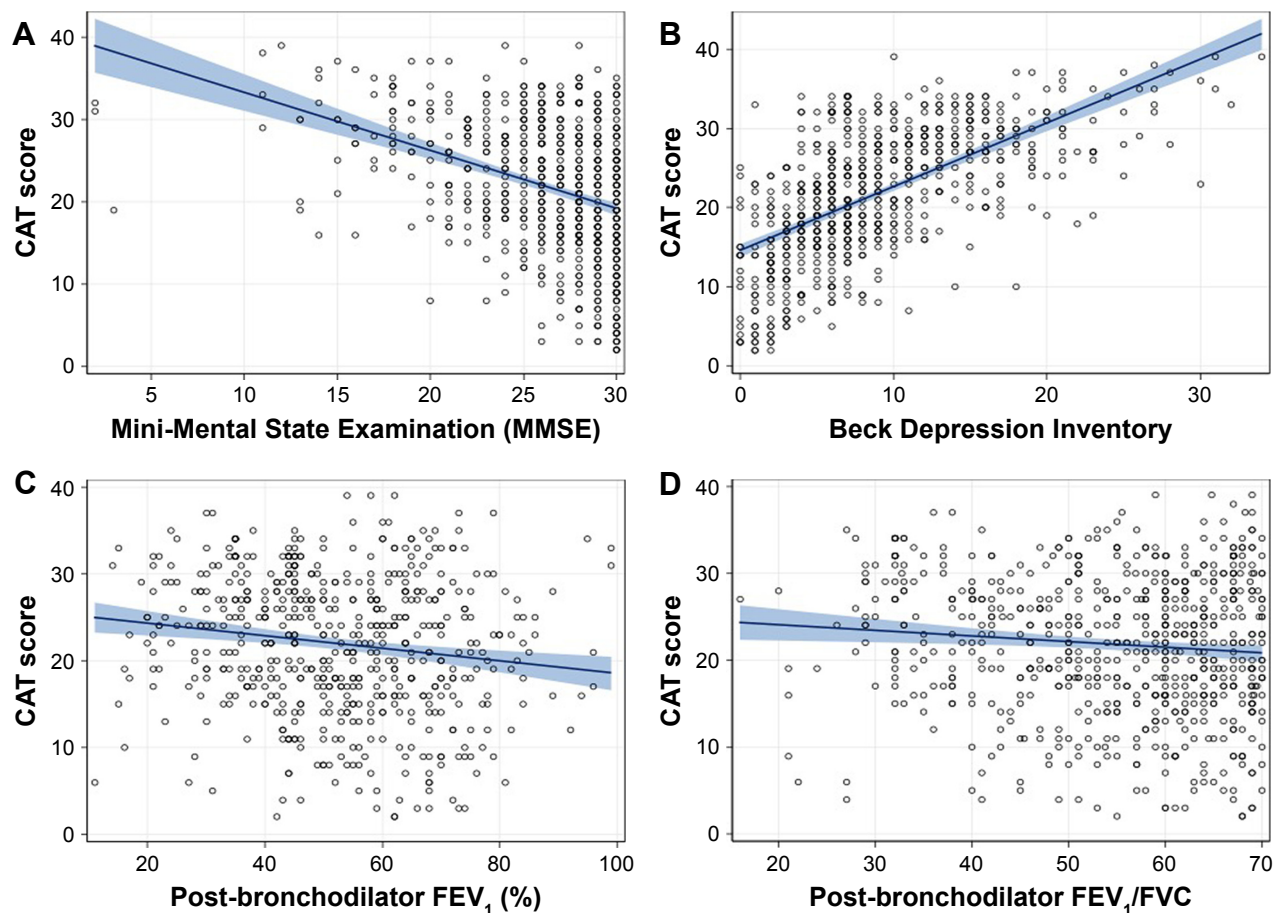
**Abbreviations:** ANOVA, analysis of variance; BDI, Beck Depression Inventory; BODEx, body mass index, airflow obstruction, dyspnea, and exacerbations; CAT, COPD assessment test; FEV<sub>1</sub>, forced expiratory volume in 1 second; FVC, forced vital capacity; MMSE, Mini-Mental State Examination.

patients and facilitate communication between patients and physicians.<sup>1</sup> Due to its excellent psychometric characteristics and its predictive value for different outcomes in COPD, the GOLD has incorporated the CAT score into the algorithm of pharmacologic treatment of COPD as a measure of symptom intensity, together with the mMRC dyspnea scale.<sup>8</sup> However, the CAT is more than a scale of intensity of symptoms; CAT scores correlate very well with the scores of the St George's Respiratory Questionnaire, the most widely used disease-specific, health-related quality of life questionnaire in COPD,<sup>1,21</sup> suggesting that this tool provides information that goes beyond the level of symptoms.

The multivariate model developed with all the study variables demonstrated the association of CAT scores with the usual characteristics of COPD severity (age, lung function impairment, degree of dyspnea, and comorbidity) and with the MMSE and BDI scores. This model explained up to 45% of CAT variability. However, a model including only MMSE and BDI scores explained 40% and the BDI alone explained 38% of CAT variability.

The relationship between CAT scores and depression has been demonstrated in previous studies. Lee et al,<sup>22</sup> in a study of 803 patients with COPD, using the patient health questionnaire-9 to assess depressive symptoms found a

significant correlation between both questionnaires ( $r=0.631$ ,  $p < 0.001$ ) and that the patient health questionnaire-9 score explained 45% of the variance of CAT. Morishita-Katsu et al,<sup>21</sup> in a study on 109 patients with COPD, found a correlation coefficient of 0.464 between CAT and the depression score of the Hospital Anxiety and Depression Scale (HADS), even higher than  $-0.393$  found between CAT and the 6-minute walk distance. In a stepwise multiple regression analysis, only depression in HADS and baseline dyspnea index were significantly associated with CAT scores and together explained 36% of the variance.<sup>21</sup> Similarly, Dodd et al<sup>23</sup> found a correlation coefficient between HADS depression score and CAT of 0.36 among 261 COPD patients included in a rehabilitation program. Finally, another study in Japan with 336 COPD patients found a significant association between CAT and depressive symptoms on HADS (HADS depression score  $\geq 11$ ); other comorbidities significantly associated with CAT scores were gastroesophageal reflux disease, arrhythmia, and anxiety.<sup>10</sup> It is interesting to compare the correlation observed between CAT scores and scores of the depression questionnaires (0.620 in our study and between 0.36 and 0.63 in other publications, depending on the population and the questionnaires used) with those observed between CAT and COPD-specific physiologic measures,



**Figure 2** Correlation between CAT score and MMSE scores (A), BDI scores (B), post-bronchodilator FEV<sub>1</sub> (% predicted) (C), and post-bronchodilator FEV<sub>1</sub>/FVC (D). **Abbreviations:** BDI, Beck Depression Inventory; CAT, COPD assessment test; FEV<sub>1</sub>, forced expiratory volume in 1 second; FVC, forced vital capacity; MMSE, Mini-Mental State Examination.

**Table 2** Multivariate regression analysis for CAT score variance

Variable	Model 1	Model 2	Model 3
BDI score	0.73 (0.04)***	0.65 (0.04)***	0.68 (0.05)***
MMSE score	-0.23 (0.06)***	-0.14 (0.06)	-0.13 (0.07)*
Age		0.006 (0.02)	-0.07 (0.03)**
Sex		-0.31 (0.66)	
Post-bronchodilator FVC (%)		NA	-0.06 (0.02)***
Post-bronchodilator FEV <sub>1</sub> (%)		-0.03 (0.02)	
Post-bronchodilator FEV <sub>1</sub> /FVC		NA	-0.9 (0.02)***
Dyspnea		-6.90 (1.35)***	-6.60 (1.44)***
Previous exacerbations		-1.20 (0.72)	
Charlson index		0.66 (0.18)**	0.60 (0.20)**
R <sup>2</sup>	0.40	0.43	0.45
p-value	<0.001	<0.001	<0.001

**Notes:** Data are presented as beta value (SE). \* $p < 0.05$ , \*\* $p < 0.01$ , \*\*\* $p < 0.001$ . Model 1 only includes BDI and MMSE scores; Model 2 includes the whole set of variables, except FVC and FEV<sub>1</sub>/FVC due to collinearity; Model 3 stepwise automatic selection of variables with a  $p$ -value  $< 0.15$ .

**Abbreviations:** BDI, Beck Depression Inventory; CAT, COPD assessment test; FEV<sub>1</sub>, forced expiratory volume in 1 second; FVC, forced vital capacity; MMSE, Mini-Mental State Examination; NA, not assessed; SE, standard error.

such as FEV<sub>1</sub> (-0.15 in our study and between -0.17 and -0.23 in other large studies).<sup>1,23,24</sup>

The relationship between CAT and depression has also been investigated in a small case-control study in patients with COPD and mild hypoxemia. As in our study, the authors used the BDI and found a similar correlation between BDI and CAT in their selected population ( $r = 0.56$ ,  $p < 0.00001$ ).

**Table 3** Univariate regression analysis for CAT score variance

Variable	Beta value (SE)	R <sup>2</sup>
BDI score	0.80 (0.04)***	0.38
BODEx	2.06 (0.15)***	0.23
MMSE score	-0.70 (0.07)***	0.14
Charlson index	1.99 (0.19)***	0.13
Minutes walked per day	-0.04 (0.007)***	0.07
Post-bronchodilator FEV <sub>1</sub> (%)	-0.07 (0.02)***	0.02
Post-bronchodilator FEV <sub>1</sub> /FVC	-0.07 (0.02)**	0.01

**Note:** \*\* $p < 0.01$ , \*\*\* $p < 0.001$ .

**Abbreviations:** BDI, Beck Depression Inventory; BODEx, body mass index, airflow obstruction, dyspnea, and exacerbations; CAT, COPD assessment test; FEV<sub>1</sub>, forced expiratory volume in 1 second; FVC, forced vital capacity; MMSE, Mini-Mental State Examination; SE, standard error.

The BDI score alone explained 31% of the variance of CAT, and a cutoff of 20 units identified major depression with an odds ratio of 7.88.<sup>25</sup>

Models developed to try to identify demographic and clinical determinants of CAT scores have provided reasonably consistent results. Models including mMRC dyspnea scale, exacerbations rate/year, and either FEV<sub>1</sub> (% predicted) or total lung capacity (% predicted) explained 36% of the CAT variance.<sup>9</sup> The prediction of CAT scores at COPD diagnosis was associated with post-bronchodilator FEV<sub>1</sub> and exacerbations/year with an  $r^2$  of 0.49.<sup>26</sup> Similarly, our best model had an  $r^2$  of 0.45, but interestingly, the model including only the MMSE and BDI had already an  $r^2$  of 0.40.

The isolated impact of cognitive status on health status is not so clear. In our population, the relationship between cognitive status and CAT scores was weaker than that observed for depression. However, it was stronger than the association between CAT scores and spirometric parameters. Several studies using different methods to evaluate cognitive status did not find an impaired health-related quality of life associated with increased cognitive impairment,<sup>27–30</sup> although only one used the CAT to evaluate quality of life.<sup>30</sup> In a previous analysis of our population, we found a prevalence of cognitive impairment of 39.4%, and this impairment was significantly associated with lower educational level and impaired generic health-related quality of life measured by the EuroQol-5 dimensions questionnaire. CAT scores were not significant in the multivariate analysis, probably due to collinearity with the EuroQol-5 dimensions scores. In the univariate analysis, patients with cognitive impairment had significantly worse CAT scores (25.2 [SD =6.9] versus 19.3 [SD =8.7],  $p < 0.001$ ).<sup>31</sup> It is important to point out that patients with severe cognitive impairment that prevents them from understanding and completing the questionnaires were not included in the study.

The CAT questionnaire was developed to provide clinicians and patients with a simple and reliable measure of overall COPD-related health status for the assessment and long-term follow-up of individual patients; however, the GOLD strategy uses the CAT threshold of 10 units to differentiate patients into groups A, C or B, D, and as such, to guide the need to step up or step down COPD treatment. Although CAT scores are predictive of most COPD outcomes, it is important to be aware of the strong association between CAT scores and depression in order to make the appropriate conclusions and take the right course of action.

Our study has some limitations; since spirometry was not one of the main outcomes of the study, no formal validation of

spirometric values was conducted beyond the elimination of those values that were out of range or inconsistent. The results presented here are derived from a post hoc analysis of the original study,<sup>11</sup> and finally, the majority of patients included were men, consistent with the epidemiological characteristics of COPD in Spain,<sup>32,33</sup> and therefore, extrapolation of these results to women must be made with caution.

## Conclusion

Our results demonstrate the strong association between CAT scores and depression in COPD patients. Since the CAT is proposed as a tool to guide pharmacologic treatment in COPD, this association must be taken into account to help make the right therapeutic decisions in daily practice.

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## Author contributions

MM wrote the manuscript. All authors contributed toward the study design, planning and interpretation of data analysis, and critically revising the paper; they approved the final version to be published and agreed to be accountable for all aspects of the work.

## Disclosure

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