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Determinants of CAT (COPD Assessment Test) scores in a population of patients with COPD in central and Eastern Europe: The POPE study

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ABSTRACT

Background: The COPD Assessment Test (CAT) has been proposed to help guide therapy in chronic obstructive pulmonary disease (COPD). It is important to understand the distribution of scores in different COPD populations and their determinants.

Methods: The POPE study is an international, observational cross-sectional study of COPD subjects in 11 Central and Eastern European countries aimed at characterizing COPD phenotypes. Here we report the analysis of CAT scores with the objective of identifying their determinants, evaluating symptom load and investigating the distribution of scores among the participating countries. Additionally, we investigated the discrepancies between the CAT and modified Medical Research Council (mMRC) scores when used to classify patients according to the GOLD strategy.

Results: The study included 3452 patients (69.2% men, mean forced expiratory volume in 1 s (FEV1% predicted) 52.5%). The mean CAT score was 17.5 (SD = 7.8), ranging from 15.1 in Hungary to 21.2 in Bulgaria. Multiple linear regression analysis showed six variables significantly associated with CAT scores: depression, number of previous exacerbations, 6-min walking distance, FEV1(%), mMRC and country and explained 47.2% of the variance of CAT. According to either CAT or mMRC, up to 23.9% patients would be classified in different GOLD groups.

Conclusions: The CAT score may be predicted by factors related to COPD severity, depression and exercise capacity, with significant differences in the distribution of CAT scores in different countries. According to our results CAT > 10 is not equivalent to mMRC > 2 for assessing symptom burden.

Trial Registration: ClinicalTrials.gov, identifier NCT02119494;

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1. Introduction

Chronic obstructive pulmonary disease (COPD) is characterized by persistent respiratory symptoms [1]. The importance of symptoms has been recognized by the Global Initiative for Chronic Obstructive Lung Disease (GOLD), which established recommendations for pharmacologic treatment based on the assessment of risk and symptoms [2]. For the measurement of symptoms, the GOLD strategy suggests the use of either the modified Medical Research Council (mMRC) dyspnoea scale [3] or the COPD Assessment Test (CAT) [4]. Due to the relevance of CAT scores in the management of COPD, it is important to investigate their distribution and determinants in different populations as well as their correlation and possible equivalence with the mMRC.

Previous studies have evaluated the distribution of CAT scores in some populations [5], but data from Central and Eastern Europe (CEE) are scant. Studies performed in Western European countries have suggested little variability across countries [5] or regions [6]; however, differences among patients in CEE countries may be more notable due to greater differences in health care systems and socioeconomic conditions.

In this context, the Phenotypes of COPD in Central and Eastern Europe (POPE) study was developed to characterize a large population of patients of COPD in CEE [7,8]. In this article, we present the results of an analysis investigating the distribution of CAT scores, the differences among countries, the determinants of CAT scores and their concordance with mMRC degrees of dyspnoea for the classification of treatment groups according to the GOLD strategy.

2. Method

The POPE study is an international, multicentre, observational cross-sectional study of COPD subjects in 11 CEE countries: Austria, Bulgaria, Croatia, Czech Republic, Hungary, Latvia, Poland, Russia, Serbia, Slovakia, and Slovenia. The methodology of the POPE study has been reported in more detail elsewhere [7]. Briefly, patients aged ≥40 years, current and former smokers of more than 10 pack-years with a diagnosis of COPD confirmed by post-bronchodilator forced expired volume in 1 s/forced vital capacity (FEV1/FVC) < 0.7 were enrolled. Patients were recruited in a secondary care setting; either in hospital-based pulmonary outpatient clinics or at pulmonologists' offices Patient enrolment was consecutive and started in April 2014 and finished in July 2015. The study was submitted to the Ethic Committees in the respective countries and to regulatory agencies, where required [8]. All patients provided written informed consent. The POPE study was registered in ClinicalTrials.gov with the identifier NCT02119494.

2.1. Data collection

COPD symptoms, smoking status and other risk factors, history of exacerbations, and concomitant respiratory diseases were collected. Exacerbation was defined as a patient-reported event of increased symptoms requiring treatment with systemic steroids and/or antibiotics with (severe exacerbation) or without (moderate exacerbation) hospitalization [7]. Data on exacerbations were collected from the clinical records and interview with the patients during the inclusion visit.

Comorbidities were scored using the Charlson comorbidity index (CCI) [9]. Pulmonary function data were obtained using standard equipment according to the American Thoracic Society/European Respiratory Society (ATS/ERS) consensus guidelines [10].

Patients were stratified according to predefined phenotypes in line with the Spanish and Czech COPD guidelines [7,11,12]: non-Exacerbators (NON-Ex), asthma-COPD overlap (ACO), and frequent exacerbators with (FE-CB) and without chronic bronchitis (FE NON-CB). Chronic bronchitis was defined as a cough that occurred every day with sputum production and lasted for at least 3 months, for two consecutive years [7]. Asthma diagnosis before the age of 40 years or a positive bronchodilator test in the previous 12 months with a history of atopy and/or allergy was defined as ACO. NON-EX had a maximum of one acute exacerbation within the past 12 months (irrespective of severity), whereas FE-CB and FE NON-CB were required to have 2 or more moderate/severe exacerbations per year.

2.2. Study outcomes

The primary outcome of the POPE study was to assess the prevalence of phenotypes according to predefined criteria in patients with COPD. The results of the global population [8] and some individual countries have been reported elsewhere [13,14]. This study presents the results of one of the secondary outcomes, which was to evaluate symptom load by the CAT, and investigate the distribution of scores among the participating countries and the predictors of CAT scores [7]. Additionally, we investigated the discrepancies between CAT and mMRC scores when used to classify patients according to the GOLD strategy [2].

2.3. Statistical analysis

The CAT score was transformed into an ordinary variable (0–10, 11–20, 21–30 and 31–40) in order to compare sociodemographic and clinical variables. In the case of quantitative variables, linear regression analysis was used, and the Mantel-Haenszel test was employed for the comparison of categorical variables. Linear relationships were analyzed using the Pearson test.

Patients were classified into four groups according to CAT and mMRC scores: concordant groups 1) CAT < 10 and mMRC 0–1; 2) CAT ≥10 and mMRC 2–4; and discordant groups 3) CAT < 10 and mMRC 2–4; 4) CAT ≥10 and mMRC 0–1). These groups were compared using Chi-square, Kruskal-Wallis or Mann-Whitney tests, as appropriate.

A final model was developed using back stepwise linear regression analysis including the CAT score as a dependent variable. Variables with a significance < 0.1 in the univariate analysis were included as independent variables. The results are described with the coefficients of regression, 95% confidence interval (CI) and *p*-values. An adjusted coefficient of determination (R^2) was also calculated to assess the overall fit of the model. For all the tests *p*-values < 0.05 were considered statistically significant. The SPSS (V 23) statistical package was used for the statistical analyses.

3. Results

3.1. Study population

The majority of patients were recruited at hospital-based pulmonary outpatient clinics (n = 2445, 72.7%), whereas 27.3% of the study population (n = 917) were recruited at pulmonologists' offices. A total of 3745 patients from 11 countries were enrolled, of whom 3452 fulfilled the inclusion/exclusion criteria and had a recorded CAT score. The mean age was 66.1 years (SD = 8.6) and 2389 were men (69.2%). The mean FEV1(%) was 52.5% (SD = 18.4%). The majority of patients were NON-EX (63.3%) followed by FE-CB (20.4%).

3.2. Distribution of CAT scores

The mean CAT score was 17.5 (SD = 7.8), and up to 44.1% of patients had a CAT score between 11 and 20 (Fig. 1). The distribution of CAT scores showed significant differences among phenotypes, with patients with a NON-EX phenotype had the lowest value (15.8) compared with the highest value in FE-CB (21.2) (Fig. 2). The distribution of scores was significantly different by countries, with Hungary showing the lowest value (15.1) and Bulgaria the highest (21.2) (Fig. 3).

The age of the patients did not significantly differ in the different

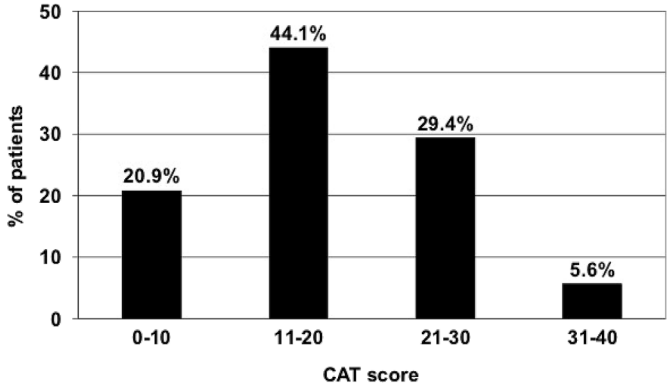

Fig. 1. Distribution of CAT scores.

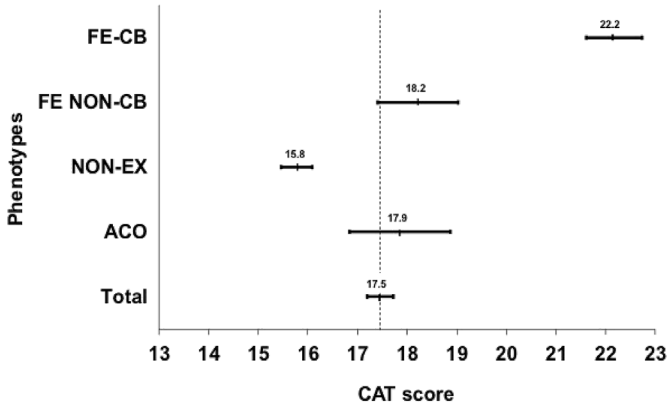

Fig. 2. CAT scores by phenotypes: mean and 95% confidence interval of the mean. Footnote: NON-EX: non exacerbators; FE-CB: frequent exacerbators with chronic bronchitis; FE NON-CB: frequent exacerbators without chronic bronchitis; ACO: asthma-COPD overlap.

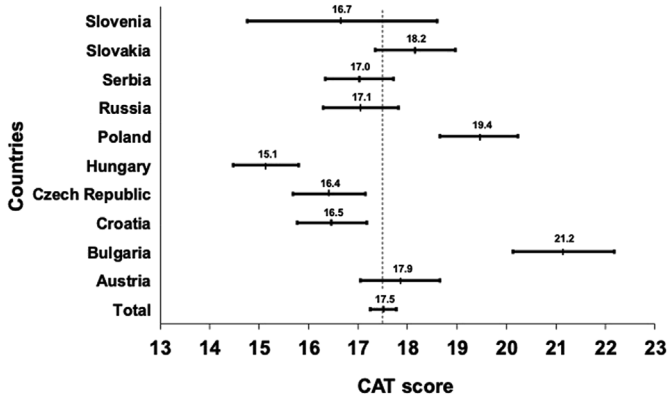

Fig. 3. CAT scores by countries: mean and 95% confidence interval of the mean.

CAT scores categories; however, patients with higher CAT scores had smoked more pack-years, had a higher CCI, more frequent exacerbations the previous year, more respiratory symptoms, worse lung function and a lower 6-MWD (Table 1, Fig. 4).

3.3. Correlations of CAT scores with other variables

The CAT scores showed a significant and negative correlation with FEV1(%) ($r = -0.34$; $p < 0.001$) and with the 6-MWD ($r = -0.43$; $p < 0.001$). CAT scores were also associated with higher degrees of dyspnoea and number of previous exacerbations (Fig. 5).

3.4. Determinant factors of CAT scores

Simple linear regression analysis identified a series of factors significantly associated with CAT scores, including the body mass index (BMI), comorbidities, phenotypes, frequency and severity of exacerbations, severity of dyspnoea, 6-MWD and FEV1(%). However, multiple linear regression analysis only found six variables to be significantly and independently associated with CAT scores: depression, number of previous exacerbations, 6-MWD, FEV1(%), mMRC score and country (Table 2). The model constructed with these variables obtained an adjusted coefficient of determination (R^2) of 47.2%.

3.5. Discrepancies between CAT and mMRC scores

A total of 2628 (76.1%) patients had concordant classifications; 412 (11.9%) were consistently classified as having a low level of symptoms (CAT < 10 and mMRC < 2), and 2216 (64.2%) were consistently classified as having a high level of symptoms. In contrast, 824 (23.9%) were discordant, with 157 (4.5%) classified with high symptom burden by mMRC and low by CAT, and 667 (19.3%) with low symptom scores by mMRC and high by CAT (Table 3). As expected, the characteristics of the patients classified in the two concordant and two discordant subgroups were significantly different, except for sex distribution and BMI. However, when comparing the two discordant subgroups, patients with high levels of dyspnoea but a CAT score < 10 were significantly older, with a lower percentage of active smokers, a higher BMI and worse FEV1 and FVC in absolute values but not percent predicted, compared with patients with low levels of dyspnoea but a CAT score > 10 (Table 3).

4. Discussion

The CAT questionnaire has been suggested as a tool to classify patients in order to direct treatment. Due to the relevant role of CAT scores in the therapy of COPD, it is important to understand the relationship of these scores with other demographic and clinical variables and identify the most relevant determinants of CAT scores in large populations of patients with COPD. In this international study, we observed a mean CAT score of 17.5 among a large group of patients of all degrees of severity managed mainly by lung specialists in CEE, with significant differences in scores between countries. There was a significant inverse correlation between CAT scores and FEV1(%), but a stronger correlation with the 6-MWD. In multiple regression analysis, the combination of variables identified explained 47.2% of the variability of the CAT scores.

The mean CAT scores observed in different populations are influenced by the characteristics of the patients analysed; however, despite these different characteristics, large studies can compare scores obtained in multiple countries. Two recent large studies in Spain in patients with a mean FEV1(%) of 52.3% and 61.6% observed mean CAT scores of 21.8 and 18.3, respectively [15,16]. An Italian study in milder patients with a mean FEV1(%) of 72% showed a mean CAT score of 16.6 [6]. A multicenter study in Latin America on 734 COPD patients with a mean FEV1(%) of 49% showed a mean CAT score of 15.3 [17]. However, there is limited information about the CAT scores in patients from CEE countries. A recent study on 1111 COPD patients in Russia with a mean FEV1(%) of 49% obtained a mean CAT score of 22.3 [18], and a large study in Czech Republic on 1335 patients observed a mean CAT score of 18.3 [19]. The POPE study included patients from 11 countries in CEE with all degrees of COPD severity, and the mean CAT score was 17.5. Interestingly there were significant differences in the mean CAT scores among countries. These differences among countries were not observed between different regions in Italy [6] or in a previous study including patients from 7 Western European countries, in which the lowest value was for the Netherlands with 14.6 and the highest for Belgium and Germany with 18.8 [5]. In contrast, our results concur

Table 1
Characteristics of the patients included in the study, categorized by CAT scores.

	Total (n = 3452)	CAT scores 0–10 (n = 720)	CAT scores 11–20 (n = 1522)	CAT scores 21–30 (n = 1016)	CAT scores 31–40 (n = 194)	*P*-value[a]
Age, years	66.1 (8.7)	65.4 (8.9)	66.4 (8.7)	66.2 (8.5)	66.2 (8.7)	0.135
Age at COPD diagnosis	58.5 (8.9)	59.2 (9.2)	58.9 (9.0)	57.6 (8.6)	57.1 (8.6)	< **0.001**
Sex, male % total	2389 (69.2%)	493 (68.5%)	1099 (72.2%)	667 (65.6%)	130 (67.0%)	0.080
BMI, Kg/m^2	27.1 (5.7)	27.5 (5.0)	27.3 (5.8)	26.9 (5.9)	26 (6.1)	**0.001**
Smoking status						0.281
Ex-smoker	2179 (63.1%)	461 (64.0%)	956 (62.9%)	635 (62.5%)	127 (65.5%)	
Current smoker	1220 (35.4%)	245 (34.0%)	539 (35.4%)	370 (36.4%)	66 (34.0%)	
Pack-years of smoking	41.2 (23.2)	38.8 (22.1)	41.1 (22.8)	42.2 (23.7)	44.6 (26.1)	< **0.001**
Comorbidities						
Coronary Artery Disease	786 (22.8%)	110 (15.3%)	335 (22%)	281 (27.7%)	60 (30.9%)	< **0.001**
Hypertension	2199 (63.7%)	451 (62.6%)	962 (63.2%)	661 (65.1%)	125 (64.4%)	0.300
Osteoporosis	362 (10.5%)	50 (6.9%)	149 (9.8%)	129 (12.7%)	34 (17.5%)	< **0.001**
Depression	373 (10.8%)	33 (4.6%)	124 (8.1%)	170 (16.7%)	46 (23.7%)	< **0.001**
Anxiety	334 (9.7%)	36 (5%)	119 (7.8%)	135 (13.3%)	44 (22.7%)	< **0.001**
Insomnia	455 (13.2%)	39 (5.4%)	165 (10.8%)	200 (19.7%)	51 (26.3%)	< **0.001**
Gastroesophageal reflux disease	408 (11.8%)	66 (9.2%)	184 (12.1%)	125 (12.3%)	33 (17.0%)	**0.005**
Anemia	113 (3.3%)	10 (1.4%)	46 (3%)	37 (3.6%)	20 (10.3%)	< **0.001**
Charlson comorbidity index	2.01 (1.38)	1.76 (1.16)	1.98 (1.38)	2.17 (1.46)	2.21 (1.58)	< **0.001**
Symptoms and exacerbations						
mMRC	2.02 (1.01)	1.16 (0.79)	1.91 (0.87)	2.58 (0.84)	3.12 (0.83)	< **0.001**
Chronic cough	2256 (65.4%)	378 (52.5%)	940 (61.8%)	771 (75.9%)	167 (86.1%)	< **0.001**
Chronic sputum production	1957 (56.7%)	291 (40.4%)	800 (52.6%)	703 (69.2%)	163 (84.0%)	< **0.001**
Purulent sputum expectoration	365 (18.7%)	29 (10%)	133 (16.6%)	148 (21.1%)	55 (33.7%)	< **0.001**
CAT score	17.5 (7.8)	7.2 (2.4)	15.5 (2.8)	24.7 (2.7)	33.4 (2.3)	< **0.001**
Moderate exacerbations the previous year	0.91 (1.3)	0.55 (0.86)	0.8 (1.20)	1.17 (1.34)	1.68 (2.21)	< **0.001**
Severe exacerbations the previous year	0.35 (0.73)	0.14 (0.45)	0.26 (0.61)	0.49 (0.86)	1 (1.15)	< **0.001**
Total exacerbations the previous year	1.25 (1.61)	0.69 (1.02)	1.07 (1.40)	1.66 (1.72)	2.68 (2.64)	< **0.001**
Exercise capacity and spirometry						
6-MWD, meters	371.5 (116.7)	427.2 (107.5)	387.6 (107.8)	325.3 (103.2)	260.4 (118.3)	< **0.001**
Post-bronchodilator FEV1, liters	1.42 (0.58)	1.70 (0.59)	1.46 (0.57)	1.24 (0.49)	1.05 (0.46)	< **0.001**
Post-bronchodilator FEV1, % predicted	52.5 (18.4)	61.8 (17.6)	53.4 (17.9)	47.01 (17.1)	40.4 (15.6)	< **0.001**
Post-bronchodilator FVC, liters	2.75 (0.89)	3.07 (0.88)	2.81 (0.88)	2.52 (0.83)	2.23 (0.79)	< **0.001**
Post-bronchodilator FVC, % predicted	80.1 (20.5)	88.1 (19.1)	81 (20.1)	75.3 (19.9)	67.9 (19.1)	< **0.001**
FEV1/FVC	0.52 (0.12)	0.56 (0.11)	0.52 (0.12)	0.49 (0.12)	0.47 (0.12)	< **0.001**
Phenotypes						< **0.001**
ACO	222 (6.7%)	45 (6.4%)	100 (6.8%)	61 (6.3%)	16 (8.6%)	
Non-exacerbator	2103 (63.2%)	564 (80.1%)	988 (67.5%)	492 (50.7%)	59 (31.6%)	
Exacerbator without chronic bronchitis	320 (9.6%)	50 (7.1%)	151 (10.3%)	103 (10.6%)	16 (8.6%)	
Exacerbator with chronic bronchitis	680 (20.5%)	45 (6.4%)	225 (15.4%)	314 (32.4%)	96 (51.3%)	
Country						< **0.001**
Austria	347 (10.0%)	63 (8.8%)	157 (10.3%)	109 (10.7%)	18 (9.3%)	
Bulgaria	264 (7.6%)	31 (4.3%)	89 (5.8%)	103 (10.1%)	41 (21.1%)	
Croatia	349 (10.1%)	74 (10.3%)	190 (12.5%)	72 (7.1%)	13 (6.7%)	
CzechRepublic	403 (11.7%)	90 (12.5%)	199 (13.1%)	102 (10%)	12 (6.2%)	
Hungary	374 (10.8%)	103 (14.3%)	194 (12.7%)	73 (7.2%)	4 (2.1%)	
Poland	451 (13.1%)	82 (11.4%)	159 (10.4%)	163 (16%)	47 (24.2%)	
Russia	346 (10%)	69 (9.6%)	173 (11.4%)	87 (8.6%)	17 (8.8%)	
Serbia	524 (15.2%)	125 (17.4%)	216 (14.2%)	155 (15.3%)	28 (14.4%)	
Slovakia	328 (9.5%)	66 (9.2%)	115 (7.6%)	137 (13.5%)	10 (5.2%)	
Slovenia	66 (1.9%)	17 (2.4%)	30 (2%)	15 (1.5%)	4 (2.1%)	

Footnote: COPD: chronic obstructive pulmonary disease; BMI: body-mass index; mMRC: modified Medical research Council dyspnea scale; CAT: COPD Assessment Test; 6-MWD: 6-min walking distance; FEV1: forced expiratory volume in 1 s; FVC: forced vital capacity; ACO: asthma-COPD overlap.
Data presented as mean (standard deviation) or absolute patient numbers (% of total population).

with those obtained in a multicenter study in 7 Latin American countries, where CAT scores ranged from 11.8 in Argentina to 22.2 in Chile, while the patient characteristics were quite similar except for a larger percentage of patients with exacerbations in Chile [17]. Similarly, the differences in scores observed in our study may be explained, at least in part, by the differences in the distribution of clinical phenotypes, with worse CAT scores in countries with a larger proportion of frequent exacerbators.

The impact of exacerbations on health-related quality of life and symptom intensity in COPD is well known [1]. The relationship between CAT scores and different aspects of COPD exacerbations, such as frequency, severity, time to resolution and relapse has been described in previous studies [20–22], but other determinants may also significantly influence CAT scores. The results of multiple linear regression analysis showed that the combination of six factors: depression, number of previous exacerbations, the 6-MWD, FEV1(%), the mMRC dyspnoea scale and country explained close to 50% of the variability of the CAT scores in our population. This observation concurs with the systematic review by Karloh et al. [23] that demonstrated that the models to predict the CAT score were able to explain less than half of their variance. It is important to note the impact of the different determinants on the CAT score; a recent work demonstrated that depression alone explained 38% of the CAT variance [15]. This finding may explain, at least in part, the discrepancies between impairment in CAT scores and the different physiologic parameters of COPD. The correlation between CAT and FEV1(%) in our study was r = −0.34, being within the range of other studies [24], and increased to r = −0.43 for the 6-MWD, which was higher compared to the range of −0.37 to −0.27 observed

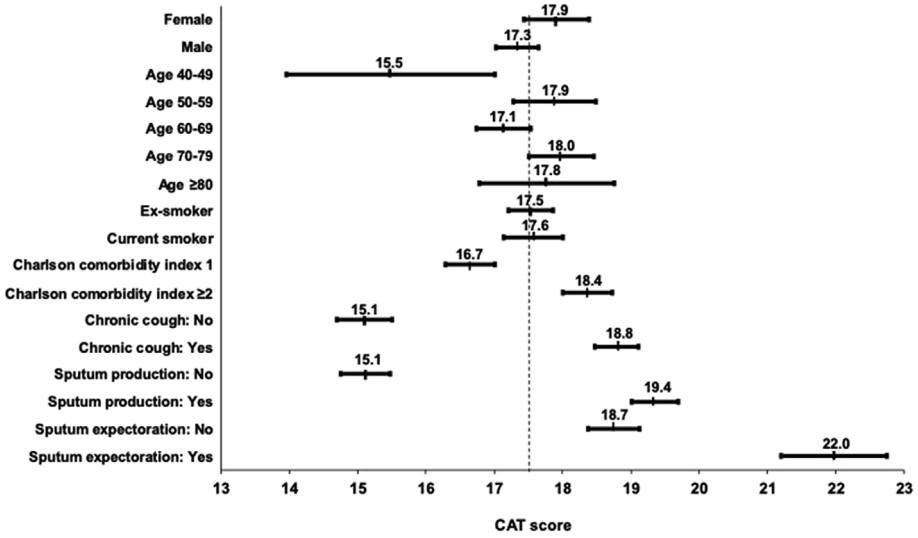

Fig. 4. Determinants of CAT scores: mean and 95% confidence interval of the mean . Footnote: Scores for sputum expectoration correspond only to patients who answered "yes" to sputum expectoration.

in the systematic review by Gupta et al. [24].

More interesting is the correlation between the CAT score and the mMRC dyspnoea scale, because they have been proposed as equivalent for classifying patients in different treatment groups according to the GOLD strategy. The range of correlation observed between these measurements is 0.29–0.62, and the k agreement between these scores ranges from 0.13 to 0.77 [6,24]. Thus, the distribution of patients in the GOLD groups using either the CAT or mMRC will be on average 13% different [23]. In our population we found that almost one in four patients would be classified differently using either the CAT or mMRC, which is consistent with a study by Rieger-Reyes et al. [25]. The most frequent discrepancy was to have a low level of dyspnea but a high CAT score, which may be explained by variables impacting quality of life but with little impact on (or association with) dyspnea, such as depression, anxiety or frequent exacerbations [15,22,23,26]. This discrepancy can be illustrated with an example derived from a large observational study in Spain, where patients with an mMRC 0 had a mean CAT score of 13 [16]. The different classification of patients in GOLD categories according to the use of CAT or mMRC has already been described in multiple studies [27–29], and does not support using these cut offs as

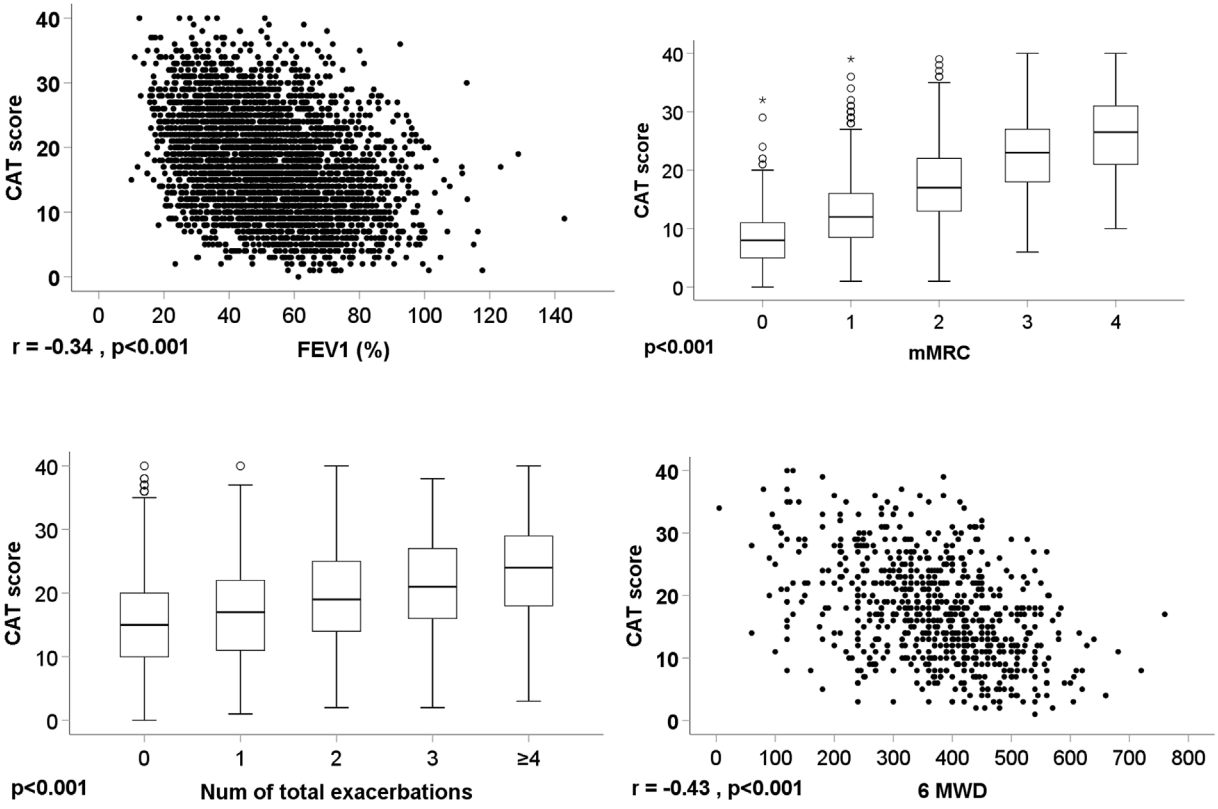

Fig. 5. Relationship between CAT scores and post-bronchodilator FEV1(%), mMRC, total exacerbations and 6-MWD Footnote: In each scatter plot, r indicates the Pearson's correlation coefficient. In each box plot, the median value is indicated by the center horizontal line, and the 25th and 75th percentiles are indicated by the lower and upper box horizontal lines. Whiskers above and below the box indicate the 90th and 10th percentiles. Circles represent outliers.

Table 2
Simple and multiple linear regression analyses to determine factors associated with the CAT score.

	Simple			Multiple[c] [d]		
	β	95% CI	*P*-value	β	95% CI	*P*-value
Age at inclusion	0.025	−0.005 to 0.055	0.103			
Sex, male	−0.576	−1.139 to −0.014	0.045			
Smoking status	0.021	−0.031 to 0.072	0.433			
Pack-years	0.023	0.012 to 0.034	< 0.001			
Depression	4.763	3.942 to 5.585	< 0.001	1.785	0.329 to 3.241	0.016
Number of moderateexacerbations the previous year[e]	1.418	1.223 to 1.613	< 0.001			
Number of severe exacerbations the previous year[e]	2.880	2.538 to 3.221	< 0.001			
Number of total exacerbations the previous year	1.520	1.366 to 1.673	< 0.001	0.569	0.289 to 0.848	< 0.001
Charlson comorbidity index	0.700	0.513 to 0.887	< 0.001			
BMI, Kg/m^2	−0.071	−0.116 to −0.026	0.002			
6-MWD	−0.030	−0.035 to −0.025	< 0.001	−0.009	−0.014 to −0.005	< 0.001
Post-bronchodilator FEV1, % predicted	−0.144	−0.157 to −0.131	< 0.001	−0.029	−0.057 to −0.001	0.044
mMRC	4.577	4.372 to 4.783	< 0.001	3.760	3.239 to 4.281	< 0.001
Phenotypes[a]	2.507	2.221 to 2.793	< 0.001			
Country[b]	0.511	0.422 to 0.599	< 0.001	0.409	0.233 to 0.586	< 0.001

Footnote: β, coefficient of regression; CI, confidence interval; BMI, body mass index; 6-MWD, 6-min walking distance; mMRC,modified Medical Research Council dyspnea scale; FEV1: forced expiratory volume in 1 s.
All risk factors showing an association in the simple linear regression models ($p < 0.10$) were added to the multiple linear regression model; a stepwise selection ($p_{in} \leq 0.05$, $p_{out} \geq 0.10$) was used to determine factors associated with the CAT score, using the probability of F criterion.

[a] Phenotype has been included as an ordinal variable according to the CAT score (lower to higher value): NON AE, ACOS, AE NON-CB, AE-CB. β means the increase in the CAT score when changing phenotype.

[b] Country has been included as an ordinal variable according to the CAT score (lower to higher value): Hungary, Czech Republic, Croatia, Serbia, Russia, Austria, Slovakia, Poland, Bulgary. β means the increase in the CAT score when changing country.

[c] Adjusted R^2 coefficient of determination: 47.2%.

[d] Multiple linear regression model: CAT score = β_0 + β_1 x Country + β_2 x Depression + β_3 x Number of total exacerbations (in the last 12 months) + β_4 x 6 MWD + β_5 x Post-bronchodilator FEV1 - relative value + β_6 x mMRC = 11.530 + 0.409 x Country + 1.785 x Depression + 0.569 x Number of moderate exacerbations (in the last 12 months) - 0.009 × 6 MWD - 0.029 x Post-bronchodilator FEV1 - relative value + 3.760 x mMRC.

[e] Highly correlated with other variable/s; therefore, it was excluded from the multiple analysis.

equivalent [23]. Our results showed that patients with high levels of dyspnea and a CAT score < 10 were older, less frequently active smokers and with a higher BMI, while FEV1(%) and FVC(%) were not significantly different. These data suggest that other causes of dyspnoea different from COPD should also be explored in this population.

Another way of establishing equivalent values for the CAT and mMRC is to investigate the predictive value for clinical outcomes of the cut offs proposed for these questionnaires. Jo et al. [30] demonstrated that a CAT > 15 had a better prognostic value than CAT > 10 for future exacerbations. Similarly, a CAT > 13 together with history of previous exacerbations showed an area under the curve of 0.864 to predict future events [20]. Regarding mortality, the predictive value of a CAT score ≥17 was similar to an mMRC ≥2 for the event [27], and likewise, a CAT score of 17 was demonstrated to significantly reduce the discrepancies with mMRC ≥2 regarding classification into GOLD groups [29].

Our study has some limitations, due to the cross-sectional design, it was not possible to evaluate the reproducibility of the questionnaires used. In addition, the lack of follow-up to investigate the evolution and predictive value of the CAT scores. However, this is the first study to analyse the distribution of CAT scores and their determinants in a large population of COPD patients from different countries of CEE using a standardised protocol. The results demonstrate that some aspects not linked to COPD, such as depressive symptoms and country significantly influence CAT scores and CAT scores do not always correspond with degree of dyspnoea. These findings must be taken into account when using CAT to decide treatment strategies for COPD. These results add to the current knowledge about the usefulness of this tool in the daily clinical management of patients with COPD.

Declaration of interests

Marc Miravitlles has received speaker or consulting fees from AstraZeneca, Bial, Boehringer Ingelheim, Chiesi, Cipla, CSL Behring, Laboratorios Esteve, Ferrer, Gebro Pharma, GlaxoSmithKline, Grifols, Menarini, Mereo Biopharma, Novartis, pH Pharma, Rovi, TEVA, Verona Pharma and Zambon, and research grants from GlaxoSmithKline and Grifols. Cristina Esquinas has received personal fees for consulting and scientific collaboration from Bayer and speaker fees from CSL Behring. Attila Somfay has received speaker fees from AstraZeneca, Boehringer Ingelheim, Chiesi, Berlin-Chemie Menarini, Novartis, Sandoz and consulting fees from AstraZeneca, Boehringer Ingelheim, GSK, Berlin-Chemie/Menarini, Chiesi, Novartis, Orion Pharma. Vladimir Koblizek has received speaker fees from Angelini, Boehringer Ingelheim, Chiesi, CSL Behring, and Novartis, and consulting fees from Boehringer Ingelheim, Chiesi, GlaxoSmithKline, and Novartis. Adam Barczykhas received speaker fees from Boehringer Ingelheim, Chiesi, Novartis, AstraZeneca, Roche, Takeda, Polpharma and Pfizer and consulting fees from Boehringer Ingelheim, Chiesi, GlaxoSmithKline, Teva and Novartis. Neven Tudoric has received speaker fees from Astra-Zeneca, Berlin-Chemie, Boehringer Ingelheim, Chiesi, Cipla, GlaxoSmithKline, Krka, Novartis, Pliva, and Sanofy, consulting fees from Astra-Zeneca, Berlin-Chemie, Boehringer Ingelheim, Chiesi, GlaxoSmithKline, Novartis, Pliva and Sanofy. Kirill Zykov has received speaker and consulting fees from AstraZeneca, Boehringer Ingelheim, Novartis, KRKA, Berlin Chemie and Thermo Fisher Scientific. Branislava Milenkovic has no conflicts of interest to disclose. Kosta Kostov has nothing to disclose. Alvils Krams has received speaker fees from AstraZeneca, Berlin-Chemie/Menarini, Boehringer Ingelheim, GlaxoSmithKline, Merck Serono, Novartis, Pfizer and consulting fees from AstraZeneca, Boehringer Ingelheim, GlaxoSmithKline and Novartis. Arschang Valipour has received speaker fees from Astra Zeneca, Boehringer Ingelheim, Chiesi, Novartis, Pulmonx, PneumRx and Olympus.

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Table 3
Characteristics of patients with concordant and discordant GOLD classification according to the CAT scores or mMRC.

	Concordant classification		Discordant classification		*P*-value[a]	*P*-value[b]
	CAT score < 10 and mMRC 0–1 (n = 412)	CAT score ≥10 and mMRC 2–4 (n = 2216)	CAT score < 10 and mMRC 2–4 (n = 157)	CAT score ≥10 and mMRC 0–1 (n = 667)		
Age at inclusion	64 (8.8)	66.9 (8.5)	68.3 (8.4)	64.4 (8.6)	< **0.001**	< **0.001**
Age at COPD diagnosis	57.9 (8.9)	58.6 (8.8)	61.5 (9.8)	57.7 (8.8)	< **0.001**	< **0.001**
Sex, male	283 (68.7%)	1550 (69.9%)	105 (66.9%)	451 (67.6%)	0.613	0.859
Current smokers	148 (35.9%)	749 (33.8%)	42 (26.8%)	281 (42.1%)	< **0.001**	**0.001**
Pack-years	37.2 (21.8)	42.5 (23.6)	40.8 (22.9)	39.1 (22.4)	< **0.001**	0.386
Depression	16 (3.9%)	305 (13.8%)	6 (3.8%)	46 (6.9%)	< **0.001**	0.154
Anxiety	20 (4.9%)	259 (11.7%)	7 (4.5%)	48 (7.2%)	< **0.001**	0.216
Total exacerbations the previousyear	0.56 (0.83)	1.53 (1.8)	0.9 (1.27)	0.83 (1.02)	< **0.001**	0.893
Charlson comorbidity index	1.67 (1.11)	2.13 (1.43)	1.98 (1.32)	1.82 (1.3)	< **0.001**	0.052
BMI	27.3 (4.6)	27.1 (6)	27.9 (5.4)	26.9 (5.4)	0.104	**0.042**
6-MWD	455.1 (103)	333.4 (108.1)	388.9 (116.8)	422.3 (100.7)	< **0.001**	0.142
Post-bronchodilator FEV1, liters	1.82 (0.63)	1.28 (0.52)	1.5 (0.48)	1.64 (0.58)	< **0.001**	**0.017**
Post-bronchodilator FEV1, % predicted	64.6 (17.7)	48 (17.3)	56.9 (16.4)	59.2 (17.6)	< **0.001**	0.166
Post-bronchodilator FVC, liters	3.21 (0.92)	2.58 (0.84)	2.81 (0.76)	3.02 (0.9)	< **0.001**	**0.011**
Post-bronchodilator FVC, % predicted	90.4 (19.2)	76.1 (20)	83.9 (18.7)	85.9 (19.5)	< **0.001**	0.248
FEV1/FVC	0.57 (0.1)	0.5 (0.12)	0.54 (0.11)	0.54 (0.11)	< **0.001**	0.550
CAT score	6.2 (2.2)	20.9 (6.4)	7.2 (1.9)	15.6 (4.9)	< **0.001**	< **0.001**
mMRC	0.69 (0.46)	2.6 (0.69)	2.1 (0.29)	0.89 (0.32)	< **0.001**	< **0.001**
Phenotypes					< **0.001**	**0.194**
ACO	32 (7.9%)	148 (7%)	4 (2.6%)	38 (5.9%)		
Non exacerbator	331 (82.1%)	1181 (55.5%)	118 (77.6%)	473 (73.8%)		
Exacerbator without chronic bronchitis	24 (6%)	234 (11%)	15 (9.9%)	47 (7.3%)		
Exacerbator with chronic bronchitis	16 (4%)	566 (26.6%)	15 (9.9%)	83 (12.9%)		

Footnote: [a] *P*-values for comparing the four groups. Chi-square test or Kruskal-Wallis test.[b] *P*-values for discordant classification groups, i.e. comparing the CAT score < 10 and mMRC 2–4 group vs. CAT score ≥10 and mMRC 0–1 group. Chi-square test or Mann-Whitney test.
COPD: chronic obstructive pulmonary disease; BMI: body-mass index; mMRC: modified Medical Research Council dyspnea scale; CAT: COPD Assessment Test; 6-MWD: 6-min walking distance; FEV1: forced expiratory volume in 1 s; FVC: forced vital capacity; ACO: asthma-COPD overlap.
Data presented as mean (standard deviation) or absolute patient numbers (% of total population).

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