



Article

# Frequency and Associated Factors of Suicidal Ideation in Patients with Chronic Obstructive Pulmonary Disease

Carlos Roncero <sup>1,2,\*</sup>, José Pérez <sup>3</sup>, Jesús Molina <sup>4</sup>, José Antonio Quintano <sup>5</sup>, Ana Isabel Campuzano <sup>3</sup>, Javier Pérez <sup>1,2</sup> and Marc Miravittles <sup>6,7,\*</sup>

<sup>1</sup> Psychiatric Service, University of Salamanca Health Care Complex, 37007 Salamanca, Spain; jperezro@saludcastillayleon.es

<sup>2</sup> Institute of Biomedicine of Salamanca (IBSAL), University of Salamanca, 37007 Salamanca, Spain

<sup>3</sup> Medical Department, Grupo Ferrer, 08029 Barcelona, Spain; mjperetz@ferrer.com (J.P.); acampuzano@ferrer.com (A.I.C.)

<sup>4</sup> Centro de Salud Francia, Dirección Asistencial Oeste, 28993 Madrid, Spain; jmolinaparis@gmail.com

<sup>5</sup> Centro de Salud Lucena I, Lucena, 14900 Córdoba, Spain; quintanojimenez@gmail.com

<sup>6</sup> Department of Pneumology, Vall d'Hebron Institut de Recerca (VHIR), Hospital Universitari Vall d'Hebron, Vall d'Hebron Barcelona Hospital Campus, 08035 Barcelona, Spain

<sup>7</sup> Centro de Investigación Biomédica en Red de Enfermedades Respiratorias (CIBERES), 28029 Madrid, Spain

\* Correspondence: croncero@saludcastillayleon.es (C.R.); marcm@separ.es (M.M.)



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**Abstract:** We aimed to examine the prevalence of suicidal ideation in patients with chronic obstructive pulmonary disease (COPD) and the association between demographic and clinical variables and the occurrence of suicidal thoughts. This was a cross-sectional study. Sociodemographic and clinical data were recorded, and questionnaires were used to assess depressive symptoms (Beck Depression Inventory), comorbidities (Charlson Index), cognitive performance (Mini Mental State Examination), and quality of life (EuroQoL-5 dimensions and CAT). Specific questions about suicide-related behavior were included. Multivariate logistic regression analysis identified the significant factors associated with previous suicidal ideation and suicide attempts. The analysis included 1190 subjects. The prevalence of suicidal ideation and suicide attempts were 12.1% and 2.5%, respectively. Severely depressed patients had the highest prevalence of suicide-related behavior. The adjusted logistic model identified factors significantly associated with suicidal ideation: sex (odds ratio (OR) for women vs. men = 2.722 (95% confidence interval (CI) = 1.771–4.183)), depression score (OR = 1.163 (95% IC = 1.127–1.200)), and Charlson Index (OR 1.228 (95% IC 1.082–1.394)). Suicidal ideation is common in COPD patients, especially in women. While addressing suicidal ideation and suicide prevention, clinicians should first consider the management of depressive symptomatology and the improvement of coping strategies.

**Keywords:** depression; suicide; COPD; Beck Depression Inventory

## 1. Introduction

Chronic obstructive pulmonary disease (COPD) is a chronic and progressive respiratory disease that is frequently associated with multiple comorbidities [1]. Among these comorbidities, depression is one of the most frequent, with a prevalence of a clinical diagnosis ranging between 10% and 42% [2,3]. There is not a clear picture of all the associated factors with suicide ideation among COPD patients, but personality traits [4] and depression status [5] may be among them. It has also been suggested that the distress of suffering a severe physical disorder, the functional limitations, and the feelings of perceived burdensomeness may increase the risk of suicidal behaviors in older adults [6], and in fact, patients with severe and chronic physical disease carry a risk for committing suicide [7]. Few studies have examined the link between COPD and suicidality, but their results have consistently indicated an association between COPD and elevated suicide risk [8–10].

An optimal strategy for addressing psychiatric comorbidities is to appreciate the heightened risk in this specific clinical population and to recognize the risk factors for suicide, such as a history of self-harm [11]. However, it is not always easy for patients to spontaneously report self-injurious/suicidal behaviors, nor can their treating physicians make determinations by simply observing the patient's mood. The early identification of risk factors that could be associated with suicide-related behaviors may assist healthcare professionals to make appropriate treatment and referral decisions, with the final aim of preventing suicides among COPD patients. Therefore, the primary objective of this research was to examine the prevalence of suicidal ideation and suicide attempts in an unselected and representative group of patients with COPD; the secondary objective was to identify which major demographic and clinical variables were significantly associated factors, such as sex, depression, and quality of life.

## 2. Methods

### 2.1. Study Design and Sample

This was a cross-sectional and observational study (DeprEPOC or study of Depression in COPD patients). The design of the study has been described in detail previously [5,12]. Briefly, patients were included from primary care centers and pneumology services in Spain. Patients were included if they were 40 years of age or older, smokers or ex-smokers of at least 10 pack-years and had stable COPD (confirmed by post-bronchodilator spirometry showing FEV1/FVC <0.70 and absence of exacerbations for at least 3 months) [13]. All patients that correctly completed the Beck Depression Inventory (BDI) questionnaire and answered the questions about previous suicidal behaviors were included in this post-hoc analysis. The study was approved by the Ethics Committee of the Barcelona Clinic Hospital (Barcelona, Spain) and was conducted in accordance with the principles of the Declaration of Helsinki. All patients provided signed informed consent prior to their participation in the study.

### 2.2. Study Assessments

Information about patients' sociodemographics and clinical data were collected through face-to-face interviews with the patients and from medical records. Severity of respiratory disease was assessed with the modified Medical Research Council dyspnea scale (mMRC) [14] and the BODEx index (Body mass index, Obstruction, Dyspnea and Exacerbations) [15], the Charlson Index was used to quantify comorbidities [16], and information was obtained about the exacerbations suffered in the previous year [17]. The short Beck Depression Inventory (BDI) questionnaire was used to assess and quantify depressive symptoms [18]. The BDI is a 13-item self-administered questionnaire that assesses affective, motivational, cognitive, and vegetative symptoms of depression. Specific questions about suicidal ideation and suicide attempts were included: "Have you ever thought about ending your life?" and "Did you ever try to end your life?"

Cognitive status was evaluated by means of the Mini Mental State Examination (MMSE) [19], whereas quality of life was assessed by the generic EuroQoL-5 Dimensions (EQ-5D) questionnaire [20] and the specific COPD Assessment Test (CAT) questionnaire [21]. The EQ-5D consists of a five-item descriptive system (including usual activities, self-care, pain/discomfort, mobility, and anxiety/depression), and an overall score or tariff is calculated, ranging from zero (worst) to 100 (best). In addition, a visual analog scale (VAS) that ranges from zero to 100 was scored by the participants, where zero is the worst and 100 is the best health status possible. The validated Spanish version of the CAT questionnaire was used [22]. This is a short, respiratory-specific, quality of life questionnaire for patients with COPD. The CAT consists of eight items, with scores ranging from zero to five, providing a global score out of 40, where zero is the best and 40 the worst state possible. Physical activity was measured by patients' self-reported average minutes walked per day, as validated by our group in a previous publication [23].

### 2.3. Statistical Analysis

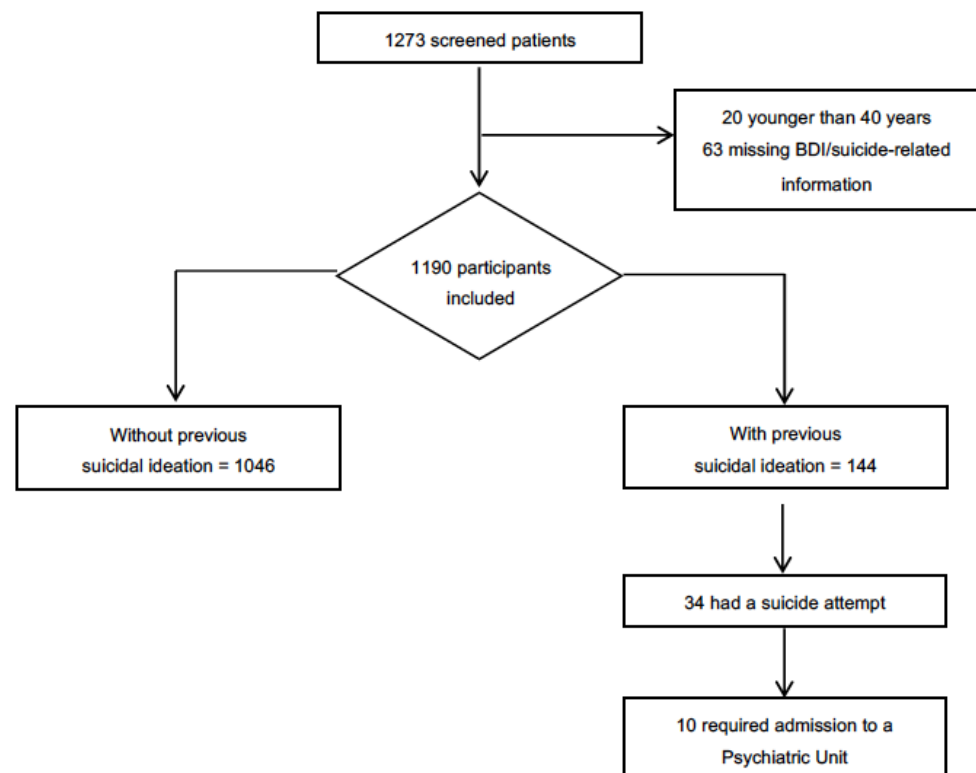
The mean and the standard deviation (SD) were used to describe continuous variables, whereas absolute and relative frequencies were used for categorical variables. No imputation was conducted for missing values. Pairwise comparisons of qualitative variables were performed by the Fisher's exact test, Bonferroni-corrected. In order to determine the relationship between quantitative variables by group, the Student's *t*-test was used. Stepwise multivariate logistic regression analysis with adjusted odds ratios (OR) were conducted to evaluate the different risks predefined in the study. In this analysis, we included all clinical, demographic, and questionnaire variables. The first model was developed with suicidal ideation/attempt history as a dependent variable, and independent variables were considered to be all variables that showed a significant association in the bivariate analysis (model 1). Model 2 was constructed with the same methodology but including only demographic and clinical variables among the independent variables, excluding the questionnaires. This model 2 was built with the objective of identifying the variables associated with suicidal ideation/attempt history that can be identified by physicians in everyday clinical practice without the administration of questionnaires. Finally, all multivariate analyses that showed significant results were studied by receiver operating characteristic (ROC) curve analysis.

A *p*-value <0.05 was considered significant. The statistical analysis was conducted with SAS software version 9.1.3 Service Pack 3 (Cary, NC, USA, EE.UU.). The investigators recruiting patients were different from the steering committee that conducted the analysis.

## 3. Results

### 3.1. Patients' Characteristics and Suicidal Behavior

Of 1273 patients screened by 343 investigators, 1190 were valid for the analysis (Figure 1). Included patients were predominantly male (80.2%), with a median age of 68.0 years (range: 40 to 90 years). A total of 144 patients (12.1%) confirmed the presence of previous suicidal ideation. Of them, 34 (23.6%) had at least one suicide attempt and 10 (29.4%) cases required admission to a psychiatric unit (Figure 1).



**Figure 1.** Flow diagram for the analysis and sample distribution according to previous suicidal ideation.

As shown in Table 2, suicidal ideation was more frequent in women, in younger patients, in current smokers, and in patients with longer disease duration, more severe dyspnea, and more COPD exacerbations in the previous year. In those receiving domiciliary oxygen, suicidal ideation was also more prevalent. Patients presenting with more depressive symptoms and patients with lower cognitive function more often reported suicidal thoughts, and high comorbidity burden and poor quality of life were also associated with suicidal ideation (Table 2). When patients were categorized into four groups according to BDI score (no depression, mild depression, moderate depression, and severe depression), frequencies of suicidal ideation were 9/301 (2.9%), 13/272 (4.9%), 57/430 (13.3%) and 65/178 (36.5%), respectively ( $p < 0.001$ ).

**Table 1.** Comparison of patients with and without previous suicidal ideation.

Variable	"Have You Ever Thought about Ending Your Life?"		
	No (n = 1046)	Yes (n = 144)	p
Sex (n, %)			
Males	854 (82.2)	94 (65.7)	<0.001
Females	185 (17.8)	49 (34.3)	
Age (mean, SD)	68.0 (9.5)	65.7 (9.4)	0.007
Coexistence (n, %)			
Alone	136 (13.0)	24 (16.9)	0.002
With partner	736 (70.6)	78 (54.9)	
With family	146 (14.0)	34 (23.9)	
Institutionalized	9 (0.9)	3 (2.1)	
With professional caregiver	16 (1.5)	3 (2.1)	
Education level (n, %)			
Basic literacy	87 (8.4)	27 (19.0)	0.002
Primary level	619 (59.6)	75 (52.8)	
Secondary level	215 (20.7)	22 (15.5)	
Completed university	117 (11.3)	18 (12.7)	
Smoking habit (n, %)			
Ex-smoker	792 (78.3)	95 (68.3)	0.013
Active smoker	220 (21.7)	44 (31.7)	
Pack-years (mean, SD)	39.5 (21.6)	36.9 (22.3)	0.194
COPD duration (mean, SD)	11.1 (7.1)	12.9 (9.3)	0.009
Spirometry (mean, SD)			
FVC, mL	3028 (981)	3001 (933)	0.769
FVC, %	70.4 (17.7)	66.9 (20.4)	0.085
FEV1, mL	1864 (845)	1873 (856)	0.914
FEV1, %	55.2 (17.9)	53.3 (31.6)	0.346
FEV1/FVC	58.3 (20.7)	55.4 (15.1)	0.125
mMRC score (mean, SD)	2.76 (0.89)	3.29 (1.03)	<0.001
Exacerbations in the previous year (n, %)			
Yes	881 (84.2)	134 (93.1)	0.004
No	165 (15.8)	10 (6.9)	
Number of exacerbations in the previous year (mean, SD)	3.9 (3.3)	5.0 (4.8)	< 0.001
Number of ambulatory exacerbations (mean, SD)	2.6 (1.9)	3.2 (2.8)	<0.001
Number of admissions (mean, SD)	1.3 (2.0)	1.8 (2.4)	0.014
Home oxygen therapy (n, %)			
Yes	211 (21.6)	48 (33.8)	0.002
No	765 (78.4)	94 (66.2)	

**Table 1.** Cont.

	"Have You Ever Thought about Ending Your Life?"		
BODEx (mean, SD)	2.7 (1.8)	3.6 (2.0)	<0.001
BDI score (mean, SD)	8.1 (5.5)	16.0 (8.1)	<0.001
MMSE (mean, SD)	26.7 (3.8)	23.7 (5.1)	<0.001
Charlson Index (mean, SD)	1.3 (1.3)	2.5 (2.1)	<0.001
CAT score (mean, SD)	20.9 (8.1)	26.5 (7.6)	<0.001
EQ-5D VAS (mean, SD)	58.9 (18.1)	47.1 (19.6)	<0.001
EQ-5D Tariff (mean, SD)	64.8 (23.2)	41.1 (24.8)	<0.001
Minutes walked per day (mean, SD)	68.6 (58.2)	48.2 (39.4)	<0.001

Totals may not add up to the total number of patients due to missing values. Percentages are calculated without missing values. Comparisons were performed with the Fischer’s exact test for qualitative variables and the Student’s *t*-test for quantitative variables, Bonferroni-corrected. Abbreviations: SD, standard deviation; COPD, chronic obstructive pulmonary disease; BODEx, Body mass index, airflow Obstruction, Dyspnea and Exacerbations; BDI, Beck Depression Inventory; MMSE, Mini Mental State Examination; CAT, COPD Assessment Test; EQ-5D, EuroQoL-5 dimensions; VAS, visual analogic scale.

The description of patients that had and did not have a previous suicide attempt is shown in Table 2. In general, a similar pattern of associations was observed between suicide attempts and clinical and patient-reported measures. In this case, no difference in history of suicide attempts was found between female and male patients. Frequencies of suicide attempts in patients without depression and with mild, moderate or severe depression were 2/298 (0.7%), 6/264 (2.3%), 10/414 (2.4%), and 16/170 (9.4%), respectively ( $p < 0.001$ ).

**Table 2.** Comparison of patients with and without previous suicide attempts.

Variable	"Did You Ever Try to End Your Life?"		
	No ( <i>n</i> = 1112)	Yes ( <i>n</i> = 34)	<i>p</i>
Sex ( <i>n</i> , %)			
Males	894 (80.9)	24 (72.7)	0.261
Females	211 (19.1)	9 (27.3)	
Age (mean, SD)	67.9 (9.5)	63.2 (9.5)	0.005
Coexistence ( <i>n</i> , %)			
Alone	147 (13.6)	7 (21.2)	0.249
With partner	772 (69.6)	19 (57.6)	
With family	165 (14.9)	6 (18.2)	
Institutionalized	10 (0.9)	1 (3.0)	
With professional caregiver	15 (1.3)	0 (0)	
Education level ( <i>n</i> , %)			
Basic literacy	106 (9.6)	5 (15.1)	0.594
Primary level	649 (58.8)	19 (57.6)	
Secondary level	222 (20.1)	7 (21.2)	
Completed university	126 (11.4)	2 (6.1)	
Smoking habit ( <i>n</i> , %)			
Ex-smoker	843 (78.0)	19 (57.6)	0.010
Active smoker	238 (22.0)	14 (42.4)	
Pack-years (mean, SD)	38.9 (21.6)	43.3 (22.3)	0.263
COPD duration (mean, SD)	11.4 (7.5)	10.7 (7.2)	0.566

**Table 2.** *Cont.*

<b>“Did You Ever Try to End Your Life?”</b>				
Spirometry (mean, SD)				
FVC, mL	3014 (972)	3047 (890)	0.863	
FVC, %	70.0 (18.1)	73.5 (15.7)	0.397	
FEV1, mL	1852 (837)	2000 (886)	0.356	
FEV1, %	54.7 (18.1)	57.7 (22.3)	0.471	
FEV1/FVC	57.8 (20.4)	60.1 (15.9)	0.556	
mMRC score (mean, SD)	2.81 (0.91)	3.03 (1.00)	0.177	
Exacerbations in the previous year ( <i>n</i> , %)				
Yes	947 (85.2)	32 (94.1)	0.214	
No	165 (14.8)	2 (5.9)		
Number of exacerbations in the previous year (mean, SD)	4.0 (3.5)	6.0 (5.1)	0.001	
Number of ambulatory exacerbations (mean, SD)	2.6 (2.0)	3.9 (3.6)	<0.001	
Number of admissions (mean, SD)	1.4 (2.1)	2.2 (2.3)	0.038	
Home oxygen therapy ( <i>n</i> , %)				
Yes	238 (22.7)	8 (24.2)	0.834	
No	808 (77.3)	25 (75.8)		
BODEx (mean, SD)	2.7 (1.9)	3.4 (1.9)	0.099	
BDI score (mean, SD)	8.8 (6.1)	17.2 (10.1)	<0.001	
MMSE (mean, SD)	26.3 (4.0)	24.7 (5.6)	0.038	
Charlson Index (mean, SD)	1.4 (1.4)	2.4 (2.4)	<0.001	
CAT score (mean, SD)	21.5 (8.2)	26.3 (8.2)	<0.001	
EQ-5D VAS (mean, SD)	57.7 (18.4)	48.3 (24.2)	0.006	
EQ-5D tariff (mean, SD)	62.6 (24.1)	38.7 (27.5)	<0.001	
Minutes walked per day (mean, SD)	67.1 (57.5)	37.4 (25.4)	0.007	

Totals may not add up to the total number of patients due to missing values. Percentages are calculated without missing values. Comparisons were performed with the Fischer’s exact test for qualitative variables and the Student’s *t*-test for quantitative variables, Bonferroni-corrected. Abbreviations: SD, standard deviation; COPD, chronic obstructive pulmonary disease; BODEx, Body mass index, airflow Obstruction, Dyspnea and Exacerbations; BDI, Beck Depression Inventory; MMSE, Mini Mental State Examination; CAT, COPD Assessment Test; EQ-5D, EuroQoL-5 dimensions; VAS, visual analogic scale.

### 3.2. Factors Associated with Previous Suicidal Behaviors

In the multivariate analysis including all the variables that were significant in the comparative analysis, suicidal ideation was associated with female sex, more depressive symptoms, and higher comorbidity burden (Table 3). The c index (area under the ROC curve) from this multivariable model was 0.81 (confidence interval (CI) 95%, 0.77 to 0.85). With the best discriminating Youden’s Index of 0.16, sensitivity and specificity of the model were 0.65 and 0.85, respectively. When we excluded from the analysis all the variables derived from the questionnaires and included only the demographic and clinical variables available in the routine clinical visit, only sex and degree of dyspnea were significant in the multivariate analysis (Table 3). The c index from this multivariable model was 0.68 (CI 95%, 0.63 to 0.73). With the best discriminating Youden’s Index of 0.17, sensitivity and specificity of the model were 0.52 and 0.73, respectively.

**Table 3.** Multivariate associations with suicidal ideation.

<b>MODEL 1: Multivariate Analysis Including All The Variables</b>	<b>Odds Ratio</b>	<b>95%CI</b>	<b>p-Value</b>
Sex (women vs men)	2.722	1.771–4.183	<0.001
BDI score	1.163	1.127–1.200	<0.001
Charlson Index	1.228	1.082–1.394	0.001
<b>MODEL 2: Multivariate Analysis Excluding Questionnaires</b>	<b>Odds Ratio</b>	<b>CI 95%</b>	<b>p-Value</b>
Sex (women vs. men)	2.537	1.713–3.757	<0.001
Dyspnea grade	1.885	1.550–2.291	<0.001

Abbreviations: CI, confidence interval; BDI, Beck Depression Inventory.

The predictive models for suicide attempts are shown in Table 4. Those variables that were statistically significant in the bivariate analysis were selected for multivariate logistic regression analysis, of which only age and BDI score were independently associated with previous suicide attempt(s). The corresponding values of c index, Youden's Index, sensitivity, and specificity were 0.80 (CI 95%, 0.72–0.88), 0.019, 0.63, and 0.82. In the second model that included only demographic and clinical variables, the significant factors were age and number of outpatient exacerbations (Table 4). The c index from this multivariable model was 0.71 (CI 95%, 0.61 to 0.81). With the best discriminating Youden's index of 0.039, sensitivity and specificity of the model were 0.59 and 0.76, respectively.

**Table 4.** Multivariate associations with suicide attempts.

<b>MODEL 1: Multivariate Analysis Including All The Variables</b>	<b>Odds Ratio</b>	<b>95%CI</b>	<b>p-Value</b>
Age	0.945	0.912–0.980	0.001
BDI Score	1.160	1.112–1.210	<0.001
<b>MODEL 2: Multivariate Analysis Excluding Questionnaires</b>	<b>Odds ratio</b>	<b>CI 95%</b>	<b>p-value</b>
Age	0.945	0.912–0.980	0.002
Number of outpatient exacerbations	1.213	1.087–1.354	<0.001

Abbreviations: CI, confidence interval; BDI, Beck Depression Inventory.

#### 4. Discussion

Up to 11% of adults in Spain have COPD [24], and previous reports about the high incidence of comorbidities, particularly depression and anxiety, have contributed to the growing attention to mental health in this population [25,26]. In this study, we found that 12% of the sample of unselected COPD patients reported previous suicidal ideation, and almost 3% had experienced at least one suicide attempt.

It is recognized that people with COPD are more likely to commit suicide [27]. The frequencies of suicidal ideation and suicide attempts in patients with COPD observed in our study are similar to those reported in previous studies [8,28,29]. According to a large case-control study [8], the relative risk of suicide was significantly elevated among patients with COPD compared with patients without major chronic illnesses (3.1% versus 1.9%, respectively). A national survey conducted in Korea showed even higher numbers, with suicidal thoughts reported by 16.0% of patients in GOLD stages I and II and by 23.8% of those in stages III and IV [30].

Some authors suggested that different types or degrees of suicidal ideation represent different levels of risk for suicide, ranging from passive death wishes, to active thoughts of committing suicide, to having a specific suicidal plan with a real intention to carry it out [31]. Although suicidal ideation is a risk factor for completed suicide, thoughts of death may

be common among older adults and can represent normative reflections on mortality [32]. In the USA general population, there are 25 attempts for every death by suicide, whereas in the older population (65+ years) the rate is 1:4 [33]. In our study, the specific questions about suicidal ideation and suicide attempts were intended to search for active thoughts/actions of committing suicide, but patients' incorrect interpretation cannot be ruled out. However, the fact that suicidal behaviors were more common among severely depressed patients indicates that suicidality was correctly identified in the study population. This finding was also observed in a Chinese study, in which suicidal ideation was significantly associated with the severity of depressive symptoms in COPD patients [34] and in Taiwanese COPD patients, depression was associated with a 13.6 percent higher risk of suicidal attempts compared to patients without depression [35]. In a population with psychiatric disorders, the comorbidity of depression and anxiety was the most important risk factor for suicide attempts [36]. Unfortunately, however, no information regarding anxiety was collected in our study.

Patients with suicidal ideation presented with higher COPD severity according to longer disease duration, higher intensity of dyspnea, more exacerbations in the previous year, and the need for oxygen therapy. They also had a higher comorbidity burden and more severely impaired quality of life, with the same pattern observed in suicide attempters, and all these variables are presumably associated with frequent hospitalizations [37]. It has been shown that having required medical attention for several different physical diseases [38] or having been recently hospitalized [39] is linked to elevated risk of suicidal behaviors. Strid et al. [40] demonstrated that there was a substantially increased risk of suicide among patients previously hospitalized for COPD compared with non-hospitalized patients, and the relative risk of suicide increased with the number of hospitalizations and recentness of the last hospital stay.

The identification of suicidal ideation in COPD is particularly important because these patients are candidates for specialized care that can result in improved outcomes. By means of multivariate logistic regression analysis which combined demographic, clinical, and patient questionnaire scores (model 1), female sex, more severe depressive symptoms and high comorbidity levels were significantly and independently associated with the presence of suicidal ideation, with good values of sensitivity and specificity. As the use of questionnaires is not a routine practice by most primary care physicians or even respiratory specialists, we explored an alternative multivariate model including only demographic and clinical variables (model 2). In this model, suicidal ideation was associated with female sex and more severe dyspnea, but the sensitivity and the specificity of the model were lower.

On the other hand, the results for the multivariate associations with suicide attempts showed that age and depression were the only significant risk factors, with good predictive accuracy. After excluding the questionnaires, suicide attempts were associated with age and higher number of exacerbations, but the model lost sensitivity. The high specificity and low sensitivity found using the combination of clinical and demographic variables suggests that their utility may be in confirmatory testing among already selected high-risk individuals, rather than for initial screening.

Our results concur with previous investigations that reported more frequent suicidal ideation in women and smokers [25,41,42]. Active smokers also had more suicidal ideation and suicide attempts than former smokers, which is in line with several reports on independent associations between suicide attempts and nicotine dependence [43] and tobacco use [44,45], and between completed suicide and smoking [46]. Decreased brain serotonin synthesis associated with the hypoxia present in COPD patients, and aggravation in active smokers may be a possible underlying mechanism of the elevated risk of suicide-related behaviors in these populations [47], somehow supported by the finding that suicide rates are also elevated among people living at higher altitudes [48]. However, in our study, active smoking was no longer significant in multivariate analysis.

COPD is a chronic, progressive and debilitating disease; the functional decline that leads to increased dependence on help [49] and the disconnection from social networks



interferes with quality of life as well as adherence to medication [50]. During the clinical consultation, asking COPD patients about how they are getting on with managing their medicines and activities needed for their medical condition may provide clues to these patients' suicidal thoughts. Effective prevention of suicide requires a multifaceted approach in both respiratory medicine and primary care settings, targeting depression and indicators of social support. Involving family members in the development and implementation of treatment plans is essential [51,52]. Patients with high risk should be referred to intensive programs from mental health resources [53].

Our study has some limitations; firstly, the cross-sectional design of this study precludes any type of causal inferences, and the directionality between COPD or its severity and suicidal behavior remains unclear. Life stressors can impact both tobacco use and suicidality, but the social, emotional, and medical contexts of suicidal ideation episodes and suicide attempts were not investigated. Secondly, since conducting non-intervention studies that may influence prescription is prohibited by Spanish legislation, we did not collect any information about prescribing habits to make sure that no interference existed. As treatment may impact the mental health of COPD patients [54], such information should be available in the future. Thirdly, a large multicenter study with the participation of many investigators is subjected to the possibility of missing values in some variables, as occurred in our study. In any case, our results in a large sample of unselected COPD patients confirm previous evidence indicating that chronic medical illness resulting in functional disability may be associated with an increased risk of suicidal thoughts and suicidal attempts even in the absence of previous mental illness [55].

## 5. Conclusions

Suicidal ideation was not uncommon in COPD and was associated with female sex, more severe depressive symptoms, active smoking, more frequent exacerbations, increased comorbidity burden, and low health status. Health professionals should be aware of and discuss suicidality with their patients, as they may need a more individualized intervention to help them cope with their chronic illness. COPD patients who show any signs of depression or distress should be asked about psychological symptoms, including suicidal ideation.

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Sancho Villanova, Fernando Marco Cardona, Fernando Martí-Vivaldi Martínez, Fernando Mayo Ferreiro, Fernando Sánchez-Toril López, Francisco De Pablo Cillero, Francisco Durán Hernández, Francisco Javier Balda Jauregui, Francisco Javier Bartolomé Resano, Francisco Javier Fernández De Frutos, Francisco Javier Guerra Ramos, Francisco Javier Rodríguez Argüeso, Francisco Javier Tamayo Sicilia, Francisco Luis Gil Muñoz, Francisco Manuel Balaguer Montesinos, Francisco Martos Torres, Francisco Risco Sánchez, Francisco Samuel Fernández Escribano, Francisco Sanguis Biosca, Francisco Vaques Arias, Froilan Sánchez Sánchez, Gador Ramos Villalobos, Gemma Martínez Almagro, Gerardo Estruch Catalá, Germán Fernández López, German Saez Roca, Gonzalo Carles Hueso, Guadalupe Fernández Esteve, Guillermo Pérez Toledo, Gustavo Solince Gallardo, Hugo Dante García Ibarra, Ignacio Abascal Carey, Ignacio J. 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Navarro González, Juan Barón Carrillo, Juan Carles Clara Riart, Juan Carlos Martín La Foz, Juan Enrique Luces Macias, Juan Francisco Andrade Bellido, Juan Francisco De Vega García, Juan Gil Carbonell, Juan Guallar Ballester, Juan Guijo Castro, Juan Hilanderas Jiménez, Juan Jiménez Guillén, Juan José Linares Linares, Juan José Martínez De La Torre, Juan Luis De La Torre Alvaro, Juan Luis García Rivero, Juan Manuel Acosta Méndez, Juan Manuel Meseguer Gil, Juan Manuel Nieto Somoza, Juan Manuel Verdeguez Miralles, Juan Miguel Sampol Company, Juan Ortiz De Saracho Y Boho, Juan Pablo García Muñoz, Juan Ramis Alemany, Juan Suárez Antelo, Juan Viles Valentí, Julia Vazquez Vazquez, Julián Ramón Garrido Jiménez, Julio Antonio García Cañizares, Julio Aurelio Gorriz Nuñez, Julio Portela Carreiro, Justo Grau Delgado, Khaled A Bdeir Egnem, Larraitz Garcia Echeberria, Lirios Sacristán Bou, Lorenzo Jiménez Alfonso, Lucia Díaz Cañaverall, Lucia Díaz Cañaverall, Luis Antonio González Rodríguez, Luis Camara Cabrerizo, Luis Carlos Aguilar Martínez, Luis Emilio Delgado Torices, Luis M Entrenas Costa, Luis Rodríguez Pascual, Luis Toca Enrique, Luisa Valladares Rodríguez, Maite Andreu Sabdell, Maite Gómara Urdiain, Manuel Carlos Barreiro Mourentan, Manuel Castilla Martínez, Manuel Cervera Del Pino, Manuel Cervera Del Pino, Manuel M<sup>o</sup> Liñares Stolle, Manuel Martínez Riaza, Manuel Miquel Palasi, Manuel Ocaña Torres, Manuel Pastor Rull, Manuel Salcedo Espinosa, Manuel Torres Pascual, Manuel Vicente Chincilla, Manuel Vila Justríbó, Marc Bonnin Vilapalan, María Begoña Salinas Lasa, María Belén Alonso Ortiz, María

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## References

1. Divo, M.; Cote, C.; de Torres, J.P.; Casanova, C.; Marin, J.M.; Pinto-Plata, V.; Zulueta, J.; Cabrera, C.; Zagaceta, J.; Hunninghake, G.; et al. Comorbidities and risk of mortality in patients with chronic obstructive pulmonary disease. *Am. J. Respir. Crit. Care Med.* **2012**, *186*, 155–161. [[CrossRef](#)]
2. Maurer, J.; Rebbapragada, V.; Borson, S.; Goldstein, R.; Kunik, M.E.; Yohannes, A.M.; Hanania, N.A. Anxiety and depression in COPD: Current understanding, unanswered questions, and research needs. *Chest* **2008**, *134*, 43s–56s. [[CrossRef](#)]
3. Martínez Rivera, C.; Costan Galicia, J.; Alcazar Navarrete, B.; Garcia-Polo, C.; Ruiz Iturriaga, L.A.; Herrejon, A.; Ros Lucas, J.A.; Garcia-Sidro, P.; Tirado-Conde, G.; Lopez-Campos, J.L.; et al. Factors Associated with Depression in COPD: A Multicenter Study. *Lung* **2016**, *194*, 335–343. [[CrossRef](#)] [[PubMed](#)]
4. Han, D.; Zhang, Y.; Li, B.; Lv, Z.; Huo, X.; Li, Y.; Zhong, Y. Alexithymia in Chinese chronic obstructive pulmonary disease (COPD) patients: The prevalence and related factors of alexithymia. *Psychiatr. Res.* **2012**, *198*, 274–278. [[CrossRef](#)] [[PubMed](#)]

5. Miravittles, M.; Molina, J.; Quintano, J.A.; Campuzano, A.; Perez, J.; Roncero, C. Factors associated with depression and severe depression in patients with COPD. *Respir. Med.* **2014**, *108*, 1615–1625. [[CrossRef](#)] [[PubMed](#)]
6. Erlangsen, A.; Stenager, E.; Conwell, Y. Physical diseases as predictors of suicide in older adults: A nationwide, register-based cohort study. *Soc. Psychiatr. Psychiatr. Epidemiol.* **2015**, *50*, 1427–1439. [[CrossRef](#)]
7. Fegg, M.; Kraus, S.; Graw, M.; Bausewein, C. Physical compared to mental diseases as reasons for committing suicide: A retrospective study. *BMC Palliat. Care* **2016**, *15*, 14. [[CrossRef](#)]
8. Webb, R.T.; Kontopantelis, E.; Doran, T.; Qin, P.; Creed, F.; Kapur, N. Suicide risk in primary care patients with major physical diseases: A case-control study. *Arch. Gen. Psychiatr.* **2012**, *69*, 256–264. [[CrossRef](#)]
9. Crump, C.; Sundquist, K.; Sundquist, J.; Winkleby, M.A. Sociodemographic, psychiatric and somatic risk factors for suicide: A Swedish national cohort study. *Psychol. Med.* **2014**, *44*, 279–289. [[CrossRef](#)]
10. Bolton, J.M.; Walld, R.; Chateau, D.; Finlayson, G.; Sareen, J. Risk of suicide and suicide attempts associated with physical disorders: A population-based, balancing score-matched analysis. *Psychol. Med.* **2015**, *45*, 495–504. [[CrossRef](#)]
11. Hawton, K.; Zahl, D.; Weatherall, R. Suicide following deliberate self-harm: Long-term follow-up of patients who presented to a general hospital. *Br. J. Psychiatr.* **2003**, *182*, 537–542. [[CrossRef](#)] [[PubMed](#)]
12. Roncero, C.; Campuzano, A.I.; Quintano, J.A.; Molina, J.; Perez, J.; Miravittles, M. Cognitive status among patients with chronic obstructive pulmonary disease. *Int. J. Chronic Obstr. Pulm. Dis.* **2016**, *11*, 543–551. [[CrossRef](#)] [[PubMed](#)]
13. Miravittles, M.; Calle, M.; Molina, J.; Almagro, P.; Tomás Gómez, J.; Trigueros, J.A.; Cosío, B.; Casanova, C.; López-Campos, J.L.; Riesco, J.A.; et al. Spanish COPD guidelines (GesEPOC) 2021: Updated pharmacological treatment of stable COPD. *Arch. Bronconeumol.* **2022**, *58*, 68–91. [[CrossRef](#)] [[PubMed](#)]
14. Bestall, J.; Paul, E.; Garrod, R.; Garnham, R.; Jones, P.; Wedzicha, J. Usefulness of the Medical Research Council (MRC) dyspnoea scale as a measure of disability in patients with chronic obstructive pulmonary disease. *Thorax* **1999**, *54*, 581–586. [[CrossRef](#)]
15. Soler-Cataluña, J.J.; Martínez-García, M.Á.; Sánchez, L.S.; Tordera, M.P.; Sánchez, P.R. Severe exacerbations and BODE index: Two independent risk factors for death in male COPD patients. *Respir. Med.* **2009**, *103*, 692–699. [[CrossRef](#)]
16. Charlson, M.E.; Pompei, P.; Ales, K.L.; MacKenzie, C.R. A new method of classifying prognostic comorbidity in longitudinal studies: Development and validation. *J. Chronic Dis.* **1987**, *40*, 373–383. [[CrossRef](#)]
17. Soler-Cataluña, J.J.; Piñera, P.; Trigueros, J.A.; Calle, M.; Casanova, C.; Cosío, B.; Lopez-Campos, J.L.; Molina, J.; Almagro, P.; Gomez, J.T.; et al. Spanish COPD Guidelines (GesEPOC) 2021 Update Diagnosis and Treatment of COPD Exacerbation Syndrome. *Arch. Bronconeumol.* **2022**, *58*, 159–170. [[CrossRef](#)]
18. Beck, A.T.; Steer, R.A.; Carbin, M.G. Psychometric properties of the Beck Depression Inventory: Twenty-five years of evaluation. *Clin. Psychol. Rev.* **1988**, *8*, 77–100. [[CrossRef](#)]
19. Folstein, M.F.; Folstein, S.E.; McHugh, P.R. “Mini-mental state”. A practical method for grading the cognitive state of patients for the clinician. *J. Psychiatr. Res.* **1975**, *12*, 189–198. [[CrossRef](#)]
20. Badia, X.; Roset, M.; Montserrat, S.; Herdman, M.; Segura, A. The Spanish version of EuroQol: A description and its applications. European Quality of Life scale. *Med. Clin.* **1999**, *112*, 79–85.
21. Jones, P.W.; Harding, G.; Berry, P.; Wiklund, I.; Chen, W.H.; Kline Leidy, N. Development and first validation of the COPD Assessment Test. *Eur. Respir. J.* **2009**, *34*, 648–654. [[CrossRef](#)] [[PubMed](#)]
22. Miravittles, M.; Molina, J.; Quintano, J.A.; Campuzano, A.; Pérez, J.; Roncero, C. Depressive status explains a significant amount of the variance in COPD assessment test (CAT) scores. *Int. J. Chronic Obstr. Pulm. Dis.* **2018**, *13*, 823–831. [[CrossRef](#)] [[PubMed](#)]
23. Ramon, M.A.; Esquinas, C.; Barrecheguren, M.; Pleguezuelos, E.; Molina, J.; Quintano, J.A.; Roman-Rodríguez, M.; Naberan, K.; Llor, C.; Roncero, C.; et al. Self-reported daily walking time in COPD: Relationship with relevant clinical and functional characteristics. *Int. J. Chronic Obstr. Pulm. Dis.* **2017**, *12*, 1173–1181. [[CrossRef](#)] [[PubMed](#)]
24. Soriano, J.B.; Alfageme, I.; Miravittles, M.; de Lucas, P.; Soler-Cataluña, J.J.; García-Río, F.; Casanova, C.; Rodríguez González-Moro, J.M.; Cosío, B.G.; Sánchez, G.; et al. Prevalence and Determinants of COPD in Spain: EPISCAN II. *Arch. Bronconeumol.* **2021**, *57*, 61–69. [[CrossRef](#)] [[PubMed](#)]
25. Yohannes, A.M.; Willgoss, T.G.; Baldwin, R.C.; Connolly, M.J. Depression and anxiety in chronic heart failure and chronic obstructive pulmonary disease: Prevalence, relevance, clinical implications and management principles. *Int. J. Geriatr. Psychiatr.* **2010**, *25*, 1209–1221. [[CrossRef](#)] [[PubMed](#)]
26. Tselebis, A.; Pachi, A.; Ilias, I.; Kosmas, E.; Bratis, D.; Moussas, G.; Tzanakis, N. Strategies to improve anxiety and depression in patients with COPD: A mental health perspective. *Neuropsychiatr. Dis. Treat.* **2016**, *12*, 297–328. [[CrossRef](#)]
27. Sampaio, M.S.; Vieira, W.A.; Bernardino, Í.M.; Herval, Á.M.; Flores-Mir, C.; Paranhos, L.R. Chronic obstructive pulmonary disease as a risk factor for suicide: A systematic review and meta-analysis. *Respir. Med.* **2019**, *151*, 11–18. [[CrossRef](#)]
28. Fleehart, S.; Fan, V.S.; Nguyen, H.Q.; Lee, J.; Kohen, R.; Herting, J.R.; Matute-Bello, G.; Adams, S.G.; Pagalilauan, G.; Borson, S. Prevalence and correlates of suicide ideation in patients with COPD: A mixed methods study. *Int. J. Chronic Obstr. Pulm. Dis.* **2015**, *10*, 1321–1329.
29. Goodwin, R.D. Is COPD associated with suicide behavior? *J. Psychiatr. Res.* **2011**, *45*, 1269–1271. [[CrossRef](#)]
30. Chung, J.H.; Han, C.H.; Park, S.C.; Kim, C.J. Suicidal ideation and suicide attempts in chronic obstructive pulmonary disease: The Korea National Health and Nutrition Examination Survey (KNHANES IV, V) from 2007–2012. *NPJ Prim. Care Respir. Med.* **2014**, *24*, 14094. [[CrossRef](#)]

31. Raue, P.J.; Ghesquiere, A.R.; Bruce, M.L. Suicide Risk in Primary Care: Identification and Management in Older Adults. *Curr. Psychiatr. Rep.* **2014**, *16*, 466. [CrossRef]
32. Scocco, P.; Meneghel, G.; Caon, F.; Dello Buono, M.; De Leo, D. Death ideation and its correlates: Survey of an over-65-year-old population. *J. Nerv. Ment. Dis.* **2001**, *189*, 210–218. [CrossRef]
33. Drapeau, C.W.; McIntosh, J.L. *Suicidology. U.S.A. Suicide 2016: Official Final Data.*. Available online: [https://suicideprevention.nv.gov/uploadedFiles/suicidepreventionnv.gov/content/SP/CRSF/Mtgs/2018/2016\\_AAS\\_USA\\_data.pdf](https://suicideprevention.nv.gov/uploadedFiles/suicidepreventionnv.gov/content/SP/CRSF/Mtgs/2018/2016_AAS_USA_data.pdf) (accessed on 8 November 2021).
34. Lin, C.Y.; Harnod, T.; Lin, C.L.; Kao, C.H. Suicide Attempt and Suicidal Drug Overdose in Chronic Obstructive Pulmonary Disease Patients With or Without Depression. *Front. Psychiatr.* **2020**, *11*, 270. [CrossRef]
35. Wong, T.S.; Xiang, Y.T.; Tsoh, J.; Ungvari, G.S.; Ko, F.W.; Hui, D.S.; Chiu, H.F. Suicidal ideation in Chinese patients with chronic obstructive pulmonary disease: A controlled study. *Psychogeriatrics* **2016**, *16*, 172–176. [CrossRef]
36. Baca García, E.; Aroca, F. Suicide risk factors related to depressive and anxiety disorders. *Salud Ment.* **2014**, *37*, 373–380. [CrossRef]
37. Fernández-García, S.; Represas-Represas, C.; Ruano-Raviña, A.; Mosteiro-Añón, M.; Mouronte-Roibas, C.; Fernández-Villar, A. Social Profile of Patients Admitted for COPD Exacerbations. A Gender Analysis. *Arch. Bronconeumol.* **2020**, *56*, 84–89. [CrossRef]
38. Juurlink, D.N.; Herrmann, N.; Szalai, J.P.; Kopp, A.; Redelmeier, D.A. Medical illness and the risk of suicide in the elderly. *Arch. Intern. Med.* **2004**, *164*, 1179–1184. [CrossRef]
39. Erlangsen, A.; Vach, W.; Jeune, B. The effect of hospitalization with medical illnesses on the suicide risk in the oldest old: A population-based register study. *J. Am. Geriatr. Soc.* **2005**, *53*, 771–776. [CrossRef]
40. Strid, J.M.; Christiansen, C.F.; Olsen, M.; Qin, P. Hospitalisation for chronic obstructive pulmonary disease and risk of suicide: A population-based case-control study. *BMJ Open* **2014**, *4*, e006363. [CrossRef]
41. Lapierre, S.; Boyer, R.; Desjardins, S.; Dube, M.; Lorrain, D.; Preville, M.; Brassard, J. Daily hassles, physical illness, and sleep problems in older adults with wishes to die. *Int. Psychogeriatr.* **2012**, *24*, 243–252. [CrossRef]
42. Saias, T.; Beck, F.; Bodard, J.; Guignard, R.; du Roscoat, E. Social participation, social environment and death ideations in later life. *PLoS ONE* **2012**, *7*, e46723. [CrossRef] [PubMed]
43. Rodríguez-Cintas, L.; Daigre, C.; Braquehais, M.D.; Palma-Alvarez, R.F.; Grau-Lopez, L.; Ros-Cucurull, E.; Rodríguez-Martos, L.; Abad, A.C.; Roncero, C. Factors associated with lifetime suicidal ideation and suicide attempts in outpatients with substance use disorders. *Psychiatr. Res.* **2018**, *262*, 440–445. [CrossRef] [PubMed]
44. Berlin, I.; Hakes, J.K.; Hu, M.-C.; Covey, L.S. Tobacco Use and Suicide Attempt: Longitudinal Analysis with Retrospective Reports. *PLoS ONE* **2015**, *10*, e0122607. [CrossRef] [PubMed]
45. Riala, K.; Taanila, A.; Hakko, H.; Rasanen, P. Longitudinal smoking habits as risk factors for early-onset and repetitive suicide attempts: The Northern Finland 1966 Birth Cohort study. *Ann. Epidemiol.* **2009**, *19*, 329–335. [CrossRef]
46. Li, D.; Yang, X.; Ge, Z.; Hao, Y.; Wang, Q.; Liu, F.; Gu, D.; Huang, J. Cigarette smoking and risk of completed suicide: A meta-analysis of prospective cohort studies. *J. Psychiatr. Res.* **2012**, *46*, 1257–1266. [CrossRef] [PubMed]
47. Young, S.N. Elevated incidence of suicide in people living at altitude, smokers and patients with chronic obstructive pulmonary disease and asthma: Possible role of hypoxia causing decreased serotonin synthesis. *J. Psychiatr. Neurosci.* **2013**, *38*, 423–426. [CrossRef]
48. Haws, C.A.; Gray, D.D.; Yurgelun-Todd, D.A.; Moskos, M.; Meyer, L.J.; Renshaw, P.F. The possible effect of altitude on regional variation in suicide rates. *Med. Hypotheses* **2009**, *73*, 587–590. [CrossRef]
49. Miravittles, M.; Peña-Longobardo, L.M.; Oliva-Moreno, J.; Hidalgo-Vega, A. Caregivers' burden in chronic obstructive pulmonary disease. *Int. J. Chronic Obstr. Pulm. Dis.* **2015**, *10*, 347–356. [CrossRef]
50. Grenard, J.L.; Munjas, B.A.; Adams, J.L.; Suttrop, M.; Maglione, M.; McGlynn, E.A.; Gellad, W.F. Depression and medication adherence in the treatment of chronic diseases in the United States: A meta-analysis. *J. Gen. Intern. Med.* **2011**, *26*, 1175–1182. [CrossRef]
51. Lindner, R.; Foerster, R.; von Renteln-Kruse, W. Physical distress and relationship problems: Exploring the psychosocial and intrapsychic world of suicidal geriatric patients. *Gerontol. Geriatr.* **2014**, *47*, 502–507. [CrossRef]
52. Garcia-Sanz, M.T.; Gonzalez-Barcala, F.J. COPS is more than just lung function: Let's not forget depression. *Arch. Bronconeumol.* **2021**, *57*, 519–520. [CrossRef] [PubMed]
53. Reijas, T.; Ferrer, E.; Gonzalez, A.; Iglesias, F. Evaluation of an intensive intervention program in suicidal behaviour. *Actas Esp. Psiquiatr.* **2013**, *41*, 279–286. [PubMed]
54. Celli, B.; Divo, M.; Plata, V.P. Pharmacotherapy Impacts on COPD Mortality. *Arch. Bronconeumol.* **2021**, *57*, 5–6. [CrossRef] [PubMed]
55. De Santiago-Díaz, A.I.; Pérez-Herrera, M.; Medina-Blanco, R.; Díaz-de Santiago, I.; López-García, E.; Artal-Simón, J. Suicidal behaviour: Emergency department attendance for suicidal recurrence and other psychiatric or medical reasons in the 6 months following the index episode. *Actas Esp. Psiquiatr.* **2021**, *49*, 244–252.