



## Review article

# Chronic obstructive pulmonary disease as a risk factor for suicide: A systematic review and meta-analysis

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## ABSTRACT

**Background:** Patients living with chronic obstructive pulmonary disease (COPD) commonly present several limitations in their daily activities, high depression rates, and low quality of life, which makes this population a risk group for suicide. This study aims to systematically assess the literature on the association between COPD and the likelihood of suicide.

**Methods:** The protocol was registered in PROSPERO (CRD42018096618). The Latin-American and Caribbean Health Sciences Literature (LILACS), PubMed, SciELO, Scopus, LIVIVO, Web of Science, and PsychNET databases were used as primary study sources. OpenThesis and OpenGrey were used to partially capture the “grey literature”. A manual search was also performed through a systematized analysis of the references of eligible articles. The risk of bias among the studies included was assessed with the Joanna Briggs Institute Critical Appraisal Tools for Systematic Reviews. A random effects meta-analysis was performed to estimate the variation in odds ratio (OR) and 95% confidence intervals (95% CI).

**Results:** The search provided 4762 results, from which only seven met the eligibility criteria and were ultimately included in the qualitative assessment of the review. The studies were published from 2002 to 2015. All studies presented low risk of bias. The total sample included 1390 suicide cases of COPD patients. The meta-analysis, which was based on five eligible case control studies, found that people with history of COPD are more likely to commit suicide (OR = 1.90; 95% CI = 1.27–2.48;  $p = 0.002$ ).

**Conclusion:** COPD patients are 1.9 times more likely to commit suicide than people without COPD.

## 1. Introduction

Chronic obstructive pulmonary disease (COPD) is a common disease characterized by partial bronchial obstruction combined with an abnormal pulmonary inflammation that occurs as a reaction to significant exposures to harmful particles and gases [1,2]. It is especially caused by the exposure to tobacco and other environment pollutants [2]. There are around 175 million people with COPD worldwide in an increasing reporting curve [3].

Considering that COPD is a highly disabling disease, patients present great daily life limitations and low quality of life [1,4]. This implies a difficult adaptation process of individuals with COPD to their health

condition, especially concerning the challenges of performing routine tasks and nicotine withdrawal [5,6]. Hence, a high number of individuals with COPD develop anxiety or depression disorders [7–10], with a mean prevalence of 27.1% of patients [7]. In addition, depression increases COPD symptoms, revealing double and positive associations between COPD and depression [8].

Studies have reported a higher suicide tendency among patients who suffer from depression and anxiety [11–13], chronic diseases [3], mental disorders [14], asthma [3], chronic pain [15], cardiovascular diseases, ischemic heart diseases, cancer, diabetes, renal failure, and low quality of life [16]. In this regard, studies have also shown a higher tendency of individuals with COPD to present suicidal ideas or

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behaviours [17–20].

It is estimated that three million people diagnosed with COPD have died in 2015 [21]. Currently, this disease is among the three main causes of death over the last decade, especially affecting people older than 55 years [22,23].

Considering the extent and potential of the health impact caused by this disease, especially because it may be fatal, this systematic review aims to assess the likelihood of COPD patients to commit suicide. The authors tested the following working hypothesis: COPD patients have a different likelihood to commit suicide than individuals without COPD.

## 2. Method

### 2.1. Protocol and registration

This systematic review was performed according to the list of PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) recommendations [24] and the Cochrane guidelines [25]. The systematic review protocol was registered in the PROSPERO database under no. CRD42018096618.

### 2.2. Study design and eligibility criteria

This study was a systematic review that aimed to answer the following clinical question: “Are patients diagnosed with chronic obstructive pulmonary disease more likely to commit suicide than those without this disease?”

Only cohort or case-control observational studies were included, which specifically tested chronic obstructive pulmonary disease as a risk factor for suicide, without restrictions of year, language, or publication status. Additionally, only studies that selected patients by ICD-10 (or previous versions) for suicide (X60-X84) and COPD (J44) were included.

The exclusion criteria were: 1) Studies not related to the topic; 2) Review articles, letters to the editor/editorials, personal opinions, books/book chapters, textbooks, reports, conference abstracts, and patents; 3) Completely descriptive studies; and 4) Studies that grouped more than one pulmonary disease as a single risk factor; 4) Studies with high risk of bias.

### 2.3. Sources of information and search

The Latin-American and Caribbean Health Sciences Literature (LILACS), PubMed (including MedLine), SciELO, Scopus, LIVIVO, Web of Science, and PsychNET databases were used as primary study sources. OpenThesis and OpenGrey were used to partially capture the “grey literature”. A manual search was also performed through a systematized analysis of the references of eligible articles. These steps aimed to minimize selection and publication biases.

The MeSH (Medical Subject Headings) and DeCS (Health Sciences Descriptors) were used to select the search descriptors. The Boolean operators “AND” and “OR” were used to enhance the search strategy through several combinations. (Table 1). The bibliographic research was performed in May 2018. The search strategy included the following keywords: “Suicide”, “Suicidal Ideation”, “Pulmonary Disease, Chronic Obstructive”, “Suicídio” [Portuguese], and their synonyms: “Suicides”, “Suicide rate”, “Fatal suicidal”, “COPD”, “Chronic Obstructive Pulmonary Disease”, “Chronic Obstructive Airway Disease”, “Chronic Obstructive Lung Disease”. The results obtained were exported to the EndNote Web™ software (Thomson Reuters, Toronto, Canada) and duplicates were removed. The remaining results were exported to Microsoft Word™ 2010 (Microsoft™ Ltd, Washington, USA) and the remaining duplicates were manually removed.

### 2.4. Study selection

The studies were selected in three phases. In the first phase, as a calibration exercise, the reviewers discussed the eligibility criteria and applied them to a sample of 20% of the studies retrieved to determine inter-examiner agreement. After achieving a proper level of agreement (Kappa  $\geq 0.81$ ), the two eligibility reviewers (MSS and WAV) performed a methodical analysis of all the titles of the studies, independently. The reviewers were not blind to the names of authors and journals. Titles not related to the topic and books/book chapters were eliminated in this phase. In the second phase, the reviewers (MSS and WAV) read all the remaining abstracts, independently. At this stage, the abstracts not related to the topic, review studies, and completely descriptive studies were eliminated. Titles that met the objectives of the study but did not have abstracts available were fully considered in the third phase.

The full texts of the eligible studies at this point were obtained and evaluated to verify whether they fulfilled the eligibility criteria. In all phases, when both reviewers disagreed, a third reviewer (LRP) was consulted to make a final decision. The studies rejected were registered separately, explaining the reasons for exclusion.

### 2.5. Data collection

After the selection, two authors (MSS and WAV) analysed the studies, which data were extracted for the following information: Identification of the study (author, year, research location, type of study), sample characteristics (number of patients in each study), data collection characteristics (assessment time, sources of information, confirmation methods for COPD diagnosis), and main results. In order to ensure the consistency among reviewers, a calibration exercise was performed with both reviewers (MSS and WAV), in which information were extracted jointly from an eligible study. Any disagreement between the reviewers was solved through discussions and when both reviewers could not agree, a third one (LRP) was consulted to make a final decision.

### 2.6. Risk of individual bias of the studies

Two authors (MSS and WAV) assessed the risk of bias and individual quality of the studies selected, independently, using the Joanna Briggs Institute Critical Appraisal Tools for use in JBI Systematic Reviews [26] for case-control and cohort studies. As a means of calibration, the authors analysed an eligible study jointly, with the presence of a third reviewer (LRP) in charge of solving divergences in case of doubts.

The following questions were used to assess the case-control studies: 1) Were the groups comparable other than the presence of disease in cases studies or the absence of disease in control studies? 2) Were cases and controls matched appropriately? 3) Were the same criteria used to identify cases and controls? 4) Was exposure measured in a standard, valid, and reliable way? 5) Was exposure measured in the same way for cases and controls? 6) Were confounding factors identified? 7) Were strategies to deal with confounding factors stated? 8) Were outcomes assessed in a standard, valid, and reliable way for cases and controls? 9) Was the exposure period of interest long enough to be significant? 10) Was appropriate statistical analysis used?

The following questions were used to assess the cohort studies: 1) Were both groups similar and recruited from the same population? 2) Were the exposures measured similarly to assign people to both exposed and unexposed groups? 3) Was the exposure measured in a valid and reliable way? 4) Were confounding factors identified? 5) Were strategies to deal with confounding factors stated? 6) Were the groups/participants free of the outcome at the start of the study or at the time of exposure? 7) Were the outcomes measured in a valid and reliable way? 8) Was the follow-up time reported and long enough for outcomes to occur? 9) Was follow-up completed, and if not, were the reasons for

**Table 1**  
Strategies for database search.

Database	Search strategy (May 2018)	Results
<b>LILACS</b> <a href="http://lilacs.bvsalud.org/">http://lilacs.bvsalud.org/</a>	tw:((DPOC AND suicídio)) AND (instance:"regional") AND (db:("LILACS"))	0
	tw:((Pulmonary Disease, Chronic Obstructive and Suicide)) AND (instance:"regional") AND (db:("LILACS"))	0
	tw:((COPD and Suicide)) AND (instance:"regional") AND (db:("LILACS"))	0
	tw:((Chronic Disease and Suicide)) AND (instance:"regional") AND (db:("LILACS"))	35
	tw:((Doenças Crônicas and Suicídio)) AND (instance:"regional") AND (db:("LILACS"))	17
	tw:((Chronic Illness and Suicide)) AND (instance:"regional") AND (db:("LILACS"))	12
<b>SciELO</b> <a href="http://www.scielo.org/">http://www.scielo.org/</a>	DPOC AND Suicídio	0
	Pulmonary Disease, Chronic Obstructive and Suicide	0
	COPD and Suicide	0
	Chronic Disease and Suicide	15
	Chronic Illness and Suicide	2
	Doenças Crônicas and Suicídio	3
<b>PubMed</b> <a href="http://www.ncbi.nlm.nih.gov/pubmed">http://www.ncbi.nlm.nih.gov/pubmed</a>	((“Suicide” [MeSH Terms] OR “Suicide” [All Fields] OR “Suicides” [All Fields] OR “Suicide rate” [All Fields] OR “Suicidal Ideation” [MeSH Terms] OR “Suicidal Ideation” [All Fields] OR “Ideation, Suicidal” [All Fields] OR “Fatal suicidal” [All Fields]) AND (“Pulmonary Disease, Chronic Obstructive” [MeSH Terms] OR “Pulmonary Disease, Chronic Obstructive” [All Fields] OR “COPD” [All Fields] OR “Chronic Obstructive Pulmonary Disease” [All Fields] OR “COAD” [All Fields] OR “Chronic Obstructive Airway Disease” [All Fields] OR “Chronic Obstructive Lung Disease” [All Fields] OR “Airflow Obstruction, Chronic” [All Fields] OR “Airflow Obstructions, Chronic” [All Fields] OR “Chronic Disease” [MeSH Terms] OR “Chronic Disease” [All Fields] OR “Chronic Diseases” [All Fields] OR “Chronic Illness” [All Fields]))	1158
<b>Scopus</b> <a href="http://www.scopus.com/">http://www.scopus.com/</a>	((“Suicide” OR “Suicides” OR “Suicide rate” OR “Suicidal Ideation” OR “Ideation, Suicidal” AND (“Pulmonary Disease, Chronic Obstructive” OR “COPD” OR “Chronic Obstructive Pulmonary Disease” OR “Chronic Obstructive Airway Disease” OR “Chronic Disease”))	1685
<b>Web of Science</b> <a href="http://apps.webofknowledge.com/">http://apps.webofknowledge.com/</a>	((“Suicide” OR “Suicides” OR “Suicide rate” OR “Suicidal Ideation” OR “Ideation, Suicidal” OR “Fatal suicidal”) AND (“Pulmonary Disease, Chronic Obstructive” OR “COPD” OR “Chronic Obstructive Pulmonary Disease” OR “COAD” OR “Chronic Obstructive Airway Disease” OR “Chronic Obstructive Lung Disease” OR “Airflow Obstruction, Chronic” OR “Airflow Obstructions, Chronic” OR “Chronic Disease” OR “Chronic Diseases” OR “Chronic Illness”))	377
<b>LIVIVO</b> <a href="https://www.livivo.de">https://www.livivo.de</a>	((“Suicide” OR “Suicides” OR “Suicidal Ideation” OR “Ideation, Suicidal”) AND (“Pulmonary Disease, Chronic Obstructive” OR “COPD” OR “Chronic Obstructive Pulmonary Disease” OR “Chronic Obstructive Airway Disease”))	248
<b>PsychNET</b> <a href="http://psycnet.apa.org/">http://psycnet.apa.org/</a>	Any Field: “Suicide” OR “Suicides” OR “Suicide rate” OR “Suicidal Ideation” OR “Ideation, Suicidal” OR “Fatal suicidal” AND Any Field: “Pulmonary Disease, Chronic Obstructive” OR “COPD” OR “Chronic Obstructive Pulmonary Disease” OR “COAD” OR “Chronic Obstructive Airway Disease” OR “Chronic Obstructive Lung Disease” OR “Airflow Obstruction, Chronic” OR “Airflow Obstructions, Chronic” OR “Chronic Disease” OR “Chronic Diseases” OR “Chronic Illness”	734
<b>OpenThesis</b> <a href="http://www.openthesis.org/">http://www.openthesis.org/</a>	(“Suicide” or “Suicides” or “Ideation, Suicidal”) AND (“Pulmonary Disease, Chronic Obstructive” OR “Chronic Disease”)	474
<b>OpenGrey</b> <a href="http://www.opengrey.eu/">http://www.opengrey.eu/</a>	(“Suicide” OR “Suicides”) and “Pulmonary”	2
<b>TOTAL 4762</b>		

interrupting follow-up described and explored? 10) Were there strategies to address incomplete follow-up? 11) Was appropriate statistical analysis used?

The risk of bias was ranked as **High** when the study reached up to 49% of “yes” score, **Moderate** when the study reached from 50% to 69% of “yes” score, and **Low** when the study reached over 70% of “yes” score. Studies characterized as “high risk of bias” were excluded [27].

## 2.7. Summary measures and syntheses of results

The primary summary measure was the likelihood of COPD patients to commit suicide. This summary was reported in odds ratio (OR) and 95% confidence intervals. A meta-analysis using a random effects model was performed to estimate the variation in odds ratio (OR) and 95% confidence intervals (95% CI) of the values reported by the individual studies [25,28]. The random model was used to minimize the heterogeneity effect among the studies [25], which was assessed using I<sup>2</sup> statistics and classified as follows: low (I<sup>2</sup> < 25%), moderate (I<sup>2</sup> = 50%), and high (I<sup>2</sup> > 75%) [29]. There was a high heterogeneity among the studies (I<sup>2</sup> = 95%). The analyses were performed with the Review Manager, version 5.3 (RevMan, Cochrane Collaboration) and Stata, version 15.0 (Stata Corp., College Station, USA) software.

## 2.8. Quality of evidence

The Grading of Recommendation, Assessment, Development, and Evaluation (GRADE) tool [30] assessed the quality of evidence and the grading of strength of recommendation. This assessment was based on study design, methodological limitations, inconsistency, indirectness,

imprecision, and other considerations. Quality of evidence was characterized as high, moderate, low, or very low [30].

## 3. Results

### 3.1. Study selection

During the first phase of study selection, 4762 results were found in the nine electronic databases, including the grey literature. After removing the duplicate results, 2582 articles remained for the analysis of titles and abstracts. After a detailed search process, only seven articles were eligible for the full text analysis. The references of these seven potentially eligible studies were carefully assessed and one more study was selected, resulting in eight studies for full text reading. Next, one study [31] did not fulfil the inclusion criteria and it was eliminated. Thus, only seven studies were selected for qualitative analysis and five were included in the meta-analysis. Fig. 1 reproduces the process of search, identification, inclusion, and exclusion of articles.

### 3.2. Characteristics of eligible studies

The studies were published between 2002 and 2015 and were performed in Canada [32–34], United Kingdom [35], Sweden [36], and Denmark [19,37]. Five studies were case-controls [19,32–35] and two were cohorts [36,37]. The assessment time ranged from eight years [35,36] to 26 years [19] and the studies were performed from 1981 [32] to 2009 [34,37].

Other sources of information regarding suicide (year, location, method) and the demographic characteristics of the population (age,

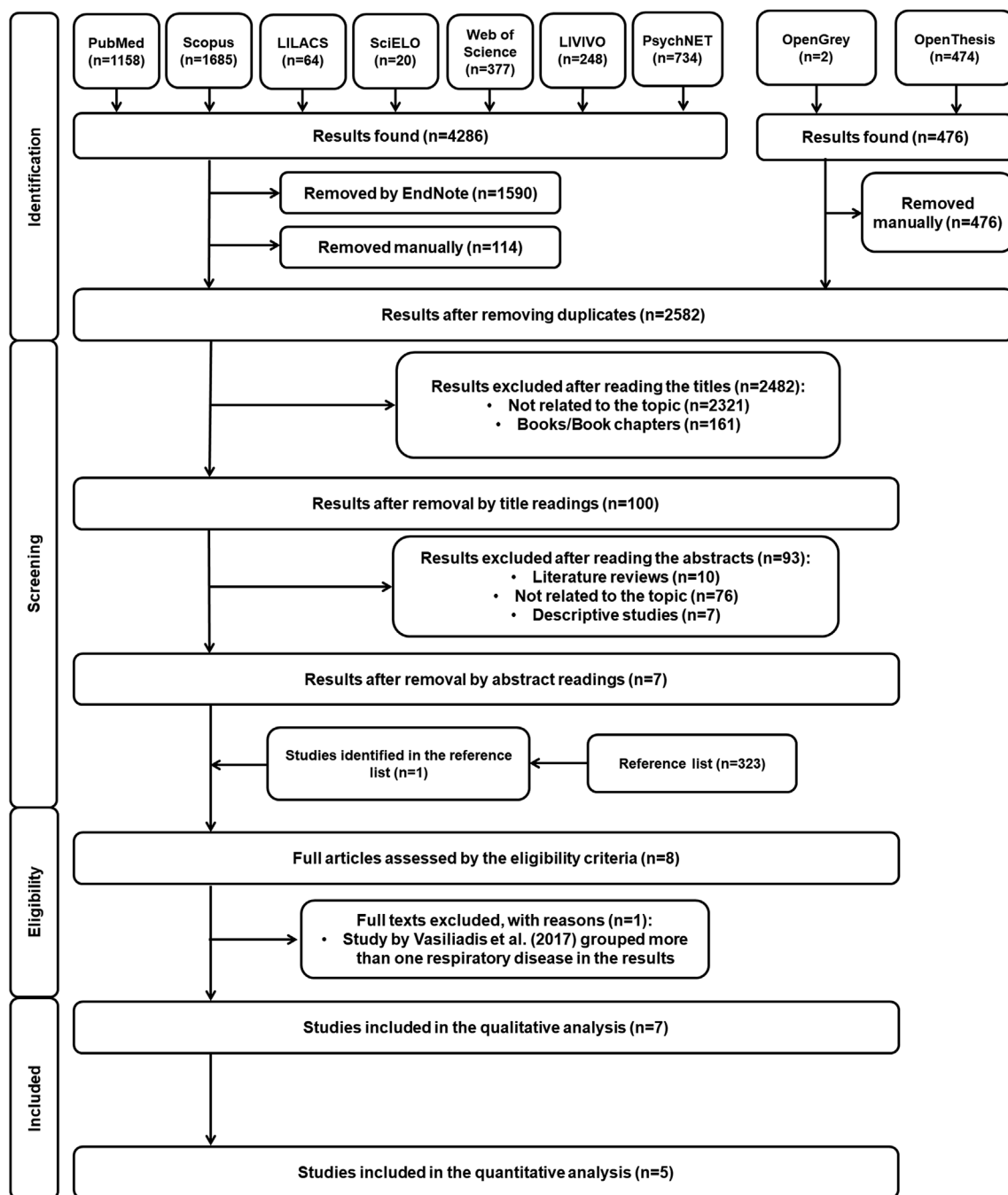


Fig. 1. - Flowchart of the process of literature search and selection, adapted from the PRISMA statement.

income, housing, sex) of all studies [19,32–37] were obtained from secondary data of local databases maintained by government agencies. The total sample included 1390 suicide cases of people diagnosed with COPD. In order to determine the COPD diagnosis, all studies [19,32–37] used government databases with data regarding the health conditions of the population, identifying people diagnosed with COPD by the ICD code (J44). Table 2 shows details of the eligible studies.

### 3.3. Risk of individual bias of the studies

All eligible studies, both case-controls [19,32–35] and cohorts [36,37], presented 100% of “yes” answers to the Joanna Briggs Institute Critical Appraisal Tools for use in JBI Systematic Reviews [26], which means that all studies presented a low risk of bias/high methodological

quality.

### 3.4. Results of individual studies

The studies by Crump et al. (2014) [36] and Erlangsen et al. (2015) [37] were removed from the meta-analysis of this review for presenting distinct study designs and analysis models (Hazard Ratios and Rates Ratios, respectively). However, the results of both studies [36,37] showed a positive association between people with COPD and suicide. The studies [19,32–35] included in the quantitative analysis presented results ranging from 1.62 to 4.75 of likelihood of people with COPD to commit suicide. Table 2 shows the specific results of each study.

**Table 2**  
Summary of the main characteristics and outcomes of the eligible studies.

Author, year	Location	Assessment time	Source of information (suicide)	Source of information (population)	Sample (n)	COPD confirmation method	Main results
Quan et al., 2002 [32]	Alberta, Canada	11 years (1984–1995)	Office of the Chief Medical Examiner of the Province of Alberta	Demographic and Income Statistics for Postal Address; Alberta Health and Wellness database	113 (controls) 133 (cases)	Information collected by the medical records in the Manitoba Health Registry Alberta Health and Wellness database, using the ICD code for COPD	Elderly men with COPD are more likely to commit suicide, especially when married (OR, 1.86; 95% CI, 1.22–2.83).
Juurlink et al., 2004 [33]	Ontario, Canada	9 years (1992–2000)	Office of the Chief Coroner for Ontario	Registered Persons Database	583 (controls) 220 (cases)	Information from the Ontario Benefit Program	COPD is directly associated with suicide (OR, 1.62; 95% CI, 1.37–1.92).
Webb et al., 2012 [35]	United Kingdom	8 years (2001–2008)	Office for National Statistics and General Register Offices	General Practice Research Database	329 (controls) 27 (cases)	Information from the General Practice Research Database, using the ICD code for COPD	COPD is directly associated with suicide (OR, 1.80; 95% CI, 1.18–2.76), and it is more prevalent among women (OR, 3.23; 95% CI, 1.57–6.66) than men (OR, 1.41; 95% CI, 0.83–2.39)
Grump et al., 2014 [36]	Sweden	8 year (2001–2008)	Swedish Death Registry (National Board of Health and Welfare)	Swedish Population Registry	89 suicides of people with COPD	Information from the Swedish Out-patient Registry or Swedish Hospital Registry, using the ICD code for COPD	COPD is associated with a higher rate of suicide among both women (HR, 3.05; 95% CI, 2.46–3.79) and men (HR, 2.26; 95% CI, 1.92–2.65)
Bolton et al., 2014 [34]	Manitoba, Canada	14 years (1996–2009)	Population Health Research Data Repository at the Manitoba Centre for Health Policy	Population Health Research Data Repository at the Manitoba Centre for Health Policy	101 (controls) 65 (cases)	Information from the Manitoba Health Registry, using the ICD code for COPD	COPD increases the risk of suicide (OR, 2.06; 95% CI, 1.48–2.86) and it is more prevalent among women (OR, 4.75; 95% CI, 1.84–12.22) than men (OR, 1.12; 95% CI, 0.70–1.79)
Srivid et al., 2014 [19]	Denmark	26 years (1981–2006)	Cause-of-Death Registry	Danish Civil Population System	3087 (controls) 592 (cases)	Information from the Danish National Patient Registry, using the ICD code for COPD	Patients diagnosed with COPD and with history of hospitalization are more likely to commit suicide (OR 2.6; 95% CI, 2.3–2.8)
Erlangsen et al., 2015 [37]	Denmark	20 years (1990–2009)	Cause of Death Registry	Danish Civil Population Registry	264 suicides of people with COPD	Information from the Danish National Patient Registry, using the ICD code for COPD	People with COPD are more likely to commit suicide (RR, 1.73; 95% CI, 1.52–1.96)

Abbreviations: COPD - Chronic Obstructive Pulmonary Disease; ICD - International Classification of Diseases; OR - Odds Ratio; CI - Confidence Interval; RR - Relative Risk; HR - Hazard Ratios.



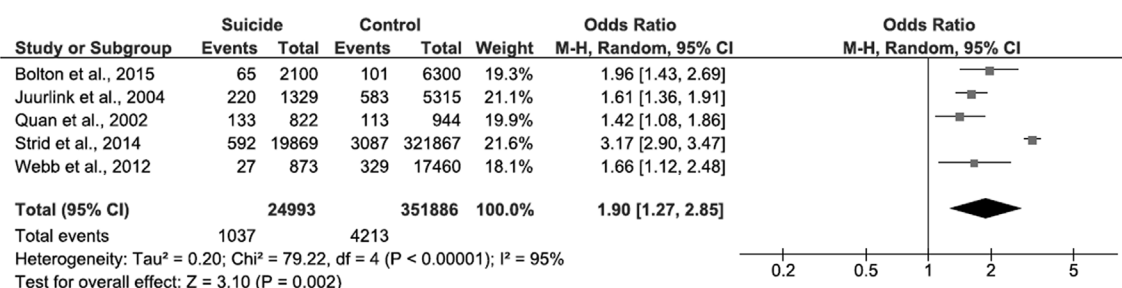


Fig. 2. - Forest plot of the case-control studies, showing a higher likelihood of suicide in the presence of COPD.

### 3.5. Synthesis of results and meta-analysis

Fig. 2 shows the meta-analysis of case-control studies assessing the likelihood of suicide in the presence of COPD. History of COPD provided a higher likelihood of suicide (OR = 1.90; 95% CI = 1.27–2.48;  $p = 0.002$ ). The heterogeneity among studies was  $I^2 = 95\%$ , characterizing high heterogeneity.

### 3.6. Quality of evidence

Overall, the quality of evidence from the outcomes evaluated by the GRADE [30] system was assessed as moderate (Table 3).

## 4. Discussion

The results of the present systematic review confirmed a positive association between COPD and suicide. Moreover, a person with COPD is 90% more likely to commit suicide than a person without COPD.

Suicide is related to several factors, including social organization, family history, limitation of daily life activities, personality traits, and mental disorders [38,39]. Regarding mental disorders, depression has been strongly associated with suicide and suicidal behavior [39]. Some characteristics of people with depression aggravate the suicide outcome, such as the male sex, family history of psychiatric disorder, hopelessness, comorbid disorders, anxiety, and misuse of alcohol and drugs [39]. Additionally, a higher prevalence of suicide has been observed among older people [11,40–42], which is related to isolation, loss of a loved one, feeling of uselessness to the family, or even loss of autonomy [43–46]. Besides risk factors directly associated with suicide, it is observed that suicidal ideation is strongly associated with the presence of moderate limitations in routine activities and the presence of severe pain [42,47].

Risk factors for suicide have been observed in people with COPD, which could help understanding the outcome of the meta-analysis developed in this study. The diagnosis of COPD is a major factor for developing depression and anxiety, and the presence of psychological disorders increases the likelihood of worsening COPD conditions [8].

Moreover, great daily life limitations and low quality of life resulting from COPD have an influence on the development of psychological disorders [1,4]. People with COPD are more likely to present suicidal behaviours such as ideation or previous attempts [20,48]. This potential relationship between risk factor for suicide and COPD may guide further studies, considering the link among such conditions has been rarely investigated [49]. The performance of prospective cohort studies following patients correctly diagnosed with COPD, either exposed to depression or not, is encouraged.

Despite this confluence between risk factors for suicide and factors related to COPD, three eligible studies [34–36] showed that women with COPD have a higher risk of committing suicide than men with COPD. These results contradict the international literature, which has shown that men are more related to suicide [50,51]. Therefore, the relationship between sex and suicide is not clear and further studies are required to explain the binding mechanism between these variables.

Acknowledging the rate of suicide of people with COPD shows a remarkable need for intervention. However, suicide intervention is not a simple task, because it is considered a complex and multifactorial phenomenon which occurrence cannot be attributed to one single characteristic or event [52]. Thus, family support through a multi-professional team is essential to improve the quality of life of these patients. Moreover, aiming to implement suicide surveillance policies, public agencies, especially in developing countries, should invest in the creation and development of databases for reporting this type of health event.

In this review, all the studies included [19,32–37] were found in databases of developed countries. However, it is known that the highest prevalence of suicide is found in low or medium income countries [53], which often do not have a database on suicide [54]. Thus, it is essential to invest in the creation and improvement of databases, especially in developing countries, because according to Lozano et al. (2012) [23], the effects of the massive use of tobacco observed among men in such countries at the end of the last century will start to emerge and tends to increase COPD diagnoses.

Another question related to secondary data is the criteria for diagnosing COPD, considering subtypes of this disease are acknowledged

Table 3

Summary of findings by the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) for the outcomes of the systematic review and meta-analysis.

Quality Assessment							Summary of Results			Importance
Number of studies	Study Design	Methodological limitations	Inconsistency	Indirectness	Imprecision	Publication biases	Number of participants		Effects	General Quality
							Case group	Control group	Random (95%CI)	
5	Case control studies	Not serious	Serious <sup>a</sup>	Not serious	Not serious	Not serious	1119	3884	(OR = 1.90; 95%CI = 1.27–2.48)	+++ MODERATE

GRADE factors: = √, not serious limitations; X, serious limitation; General quality of evidence: +, very low; ++, low; +++, moderate; +++++, high.

<sup>a</sup> Heterogeneity  $I^2 > 75\%$ .

and characterize COPD as a heterogeneous disease [55,56], but the studies included did not consider these differences. Pinto et al. (2015) [56] considered the existence of two COPD phenotypes: one is observed in younger people and it is more prevalent in women, presenting no other comorbidities and a rapid decline in lung function. The other is associated with comorbidities (obesity, cardiovascular and metabolic alterations), and people with this phenotype appear to have worse health outcomes. Esteban et al. (2016) [55] also considered a third phenotype with lower levels of dyspnea and comorbidities.

Considering COPD is a complex disease [55], it is essential to analyse these differences and their relationships with the suicide outcome. This heterogeneity varies from younger participants, lower dyspnea scores, higher lung capacity and level of physical activity, lower comorbidities, and better quality of life (subtype A) to higher dyspnea scores, lower pulmonary function, lower quality of life and level of physical activity (subtype C), and higher rates of hospitalization (subtype D) [55].

This is an important synthesis study that contributes to the overall cumulative knowledge from the following three points: It is the first systematic review in the literature to observe the likelihood of suicide in COPD patients, the high methodological quality observed in the eligible studies provides credibility to the results obtained, presenting evidence level 3 according to the Oxford Centre for Evidence Based Medicine [57] and moderate quality of evidence according to GRADE [30].

#### 4.1. Limitations

Summarizing information from secondary data requires the awareness of the accuracy of such data, as observed in all the eligible studies of this systematic review [19,32–37]. Besides the underreporting commonly associated with secondary data on suicide, there are also contextual issues (esteem and pressures in legal, religious, and political environments), diagnosis difficulties in some cases (self-starvation, falls, drownings, motor vehicle accidents, opiate overdose, euthanasia), and the lack of an internationally standardized procedure for suicide reporting [58]. Another limitation related to secondary data is not considering the heterogeneity of COPD, which subtypes could be related to the suicide outcome, but are not informed separately [55,56].

This study is not free of limitations, including the low number of eligible studies and the heterogeneity among them, which is common in systematic reviews of observational studies. Moreover, the absence of studies performed in developing countries may have limited the external validity of the results of our meta-analysis for the global reality.

#### 5. Conclusion

The findings of the present review allow concluding that COPD patients have a higher likelihood of suicide (1.9 times) than non-carriers of the disease. It is worth noting that COPD is a heterogeneous disease, which may delay diagnoses and treatment. Similarly, risk factors associated with suicide, such as mental disorders, are underdiagnosed and undertreated.

Patients living with COPD form a group that requires attention from health teams and policymakers to prevent the suicide outcome. Implementing suicide prevention measures in this group of patients is of utmost importance, including psychological care and the adaptation of daily life activities, which should start along with the COPD diagnosis.

#### Conflicts of interest

None.

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