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*MINIREVIEWS*

# Depression and anxiety disorders in chronic obstructive pulmonary disease patients: Prevalence, disease impact, treatment

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## Abstract

Chronic obstructive pulmonary disease (COPD) is a common respiratory disorder that often co-occurs with depression and anxiety, worsening disease progression and reducing quality of life. A thorough review of the existing literature was conducted, including searches in PubMed, Embase, PsycINFO, and Cochrane Library databases up to 2024. This review encompasses a critical analysis of studies reporting on the prevalence, impact, and management of depression and anxiety in COPD patients. We found a high prevalence of psychological comorbidities in COPD patients, which were associated with worse disease outcomes, including increased exacerbations, hospitalizations, and reduced health-related quality of life. Diagnosing and managing these conditions is complex due to overlapping symptoms, necessitating a comprehensive patient care approach. While there has been progress in understanding COPD comorbidities, there is a need for more personalized and integrated treatments. This review emphasizes the need for increased awareness, tailored treatment plans, and further research for effective interventions.

**Key Words:** Chronic obstructive pulmonary disease; Depression; Anxiety; Comorbidities; Treatment strategies; Narrative review



**Core Tip:** Chronic obstructive pulmonary disease (COPD) is a global respiratory condition that affects public health. Depression and anxiety often accompany COPD, which can worsen the disease and lower patient quality of life. This narrative review examines COPD patients' depression and anxiety rates, their effects on disease progression, and current treatment options.

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## INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a prevalent respiratory disorder characterized by airflow obstruction, often stemming from chronic bronchitis or emphysema[1]. It poses a significant threat to public health, with a high prevalence rate of 9% to 10% among individuals over the age of 40 worldwide[2-4]. COPD diminishes patient quality of life and imposes a substantial economic burden on families and healthcare systems[5].

The etiology of COPD is not fully understood but is generally associated with chronic bronchitis and emphysema[5]. Risk factors include environmental exposures such as smoking, dust, chemicals, respiratory infections, air pollution, and lower socioeconomic status, as well as individual factors like genetic predispositions and developmental issues during critical periods. Patients exhibit a range of symptoms including chronic cough, sputum production, shortness of breath, chest tightness, wheezing, fatigue, and weight loss[6]. COPD is a complex disease primarily caused by exposure to toxic particles or gases, leading to abnormalities in the airways and/or alveoli. It affects the lungs, the cardiovascular, nervous, endocrine, and mental health systems, resulting in complications such as asthma, lung cancer, diffuse pulmonary fibrosis, pulmonary hypertension, right-sided heart failure, diabetes, gastroesophageal reflux disease, depression, and anxiety[7,8]. Among these, depression and anxiety are the most common comorbidities, often underdiagnosed due to overlapping symptoms[9]. The overlap between physical and mental symptoms complicates the diagnostic process and necessitates a comprehensive approach to patient care[10].

This review aims to delve into the prevalence of anxiety disorders in COPD patients and scrutinize the profound impact of depression and anxiety on disease progression. By synthesizing current research and treatment strategies, we aim to shed light on the importance of addressing these psychological comorbidities in clinical practice, thereby enhancing patient care and improving outcomes.

## CURRENT STATUS OF DEPRESSION AND ANXIETY DISORDERS IN COPD PATIENTS

### *Prevalence and symptoms of depression and anxiety*

Depression is a debilitating disorder that affects both the physiological and psychological well-being of individuals, often leading to a sense of helplessness and an increased risk of suicidal tendencies. Individuals with depression exhibit a loss of interest in activities they once enjoyed, impaired social relationships, and a range of other symptoms including sleep disturbances, fatigue, difficulty concentrating, and disordered eating patterns. The World Health Organization (WHO) recognizes major depressive disorder as one of the leading contributors to the global burden of disease[11]. In the context of comorbid physical illnesses, particularly chronic and severe conditions, the prevalence of major depressive disorder ranges from 10% to 20%[12-15]. Anxiety disorders, characterized by feelings of fear, avoidance, and restlessness, often co-occur with depression, exacerbating the complexity of the conditions[16,17]. The coexistence of depression and anxiety is more common than either disorder in isolation, and individuals with chronic illnesses such as COPD are 2 to 3 times more likely to experience depression compared to the general population matched for age and sex[12,18,19].

### *Prevalence of depression and anxiety in COPD patients*

Depression is a common comorbidity in adult COPD patients, with an estimated prevalence of 24.6%[20]. The incidence of anxiety and depressive disorders in COPD patients is significantly higher, primarily associated with damage to the central nervous system and the chronic experience of negative emotions in COPD[21]. The likelihood of a COPD patient developing comorbid depression is four times higher than that of an individual without COPD[21]. Furthermore, patients with other chronic conditions such as arthritis, cancer, diabetes, hypertension, and stroke are twice as likely to develop depression compared to those without these conditions[22]. Among many chronic diseases, the incidence of depression is significantly higher in women than in men[23], and this disparity is also observed in COPD patients, where the proportion of women with comorbid depression is notably higher than that of men[24].

### *Analysis of anxiety factors in patients with COPD*

COPD causes organ damage but also inflicts psychological harm on patients, who can often exhibit various psychological abnormalities, predominantly characterized by anxiety, irritability, and depression[25]. Studies have indicated that the incidence of comorbid anxiety in COPD patients ranges from 50% to 75%[26]. Psychological disorders significantly impair patient recovery and quality of life and are one of the major factors leading to patient mortality[27]. Consequently, numerous clinical researchers are dedicated to analyzing the causes of anxiety in COPD patients. Through the analysis and summary of patient onset factors, effective measures can be taken to intervene, thereby improving the psychological state of patients and promoting faster recovery to health. For instance, Song *et al*[28] conducted a study on elderly patients with COPD to explore the best psychological nursing plan using anxiety and depression scales to identify the main factors affecting patient anxiety and depressive emotions. The study found that factors influencing anxiety in COPD

patients include occupation, education level, economic status, family relationships, and disease severity. Effective psychological nursing interventions based on these factors have been developed to improve patient psychological conditions, leading to a significant improvement in anxiety and depressive symptoms and promoting faster patient recovery.

Lokesh *et al*[29] selected 100 patients with COPD for anxiety and depression scale assessment and found that the incidence of anxiety and depression in COPD patients was 65% and 54%, respectively. Patients who were more aware of their condition had poorer quality of life and more severe anxiety and depression. Living alone was identified as a significant factor contributing to patient anxiety, with males being more prone to anxiety than females. Therefore, if patients are diagnosed with symptoms of anxiety or depression, timely diagnosis and effective treatment measures should be taken to improve patient quality of life and prognosis.

Wu *et al*[30] studied related factors of patients with COPD and comorbid anxiety and depression disorders and found that the higher the quality of life assessment test score, the higher the probability of comorbid anxiety and depression. Patients without medical insurance and with longer disease courses had a higher probability of anxiety, more hospital admissions, and lower quality of life. Therefore, the clinical treatment of COPD patients with comorbid anxiety should be emphasized.

Cao *et al*[31] found that due to the chronic and protracted nature of COPD, patients experience a continuous decline in lung function and activity tolerance, reduced labor capacity, and decreased quality of life. The long-term medical treatment places a heavy economic burden on patients, often leading to negative psychological states such as hopelessness, apathy, inferiority, self-blame, and anxiety. Psychological counseling is an effective measure in treating anxiety and depression, and pharmacological treatment (*e.g.*, with Dailixin) is also noteworthy for its ability to alleviate anxiety and depressive emotions and control the disease.

## IMPACT OF DEPRESSION AND ANXIETY ON COPD

### *Influence on disease course*

A comprehensive meta-analysis by Atlantis *et al*[32] examined 22 studies, substantiating the bidirectional relationship between depression, anxiety, and COPD. Sixteen of these studies, encompassing 28759 patients followed for 1 year to 8 years, were utilized to predict the impact of depression and anxiety on COPD outcomes. Conversely, six studies, including 7439159 patients, investigated the influence of COPD on the incidence of depression and anxiety. The findings indicate that depression and anxiety significantly increase the risk of adverse COPD outcomes [relative risk (RR) = 1.43; 95%CI: 1.22-1.68], with a pronounced effect in patients under the age of 66. Comorbid depression augments the risk of mortality in COPD (RR = 1.83; 95%CI: 1.00-3.36), particularly among males. In the majority of studies, anxiety (or psychological stress) raised the risk of COPD exacerbation or death (RR = 1.27; 95%CI: 1.02-1.58). Furthermore, COPD elevated the risk of developing depression (RR = 1.83; 95%CI: 1.00-3.36).

Pooler *et al*[33] conducted a systematic review and meta-analysis of 24 studies, revealing that 17 studies (70.9%) provided evidence linking comorbid depression and anxiety with higher hospitalization and readmission rates due to COPD exacerbations. The analysis demonstrates that patients with comorbid depression and anxiety, once hospitalized, have longer hospital stays and a higher risk of mortality post-discharge[34].

Mathew *et al*[35] performed a single laboratory assessment of 37 COPD patients, including 17 current daily smokers and 20 former smokers. Participants completed self-report measures of psychological factors, impact of COPD symptoms, symptom response, and symptoms of anxiety and depression. Three psychological factors were evaluated: Anxiety sensitivity (AS), distress intolerance (DI), and anhedonia (Anh). In univariate regression models, AS, DI, and Anh were all correlated with severe COPD dyspnea symptoms. After adjusting for symptoms of generalized depression and anxiety, AS remained a significant predictor of dyspnea symptoms in COPD[36].

### *Impact on health-related quality of life*

Enhancing health-related quality of life (HRQL) is a critical goal in the treatment of patients with chronic respiratory failure (CRF) undergoing long-term oxygen therapy and/or home non-invasive ventilation. A systematic review and meta-analysis included six studies to examine the association between comorbid depression and anxiety in COPD and HRQL[37]. The results indicate that comorbid depression at the 1-year follow-up is significantly correlated with HRQL (pooled $r = 0.48$, 95%CI: 0.37-0.57, $P < 0.001$). Similarly, comorbid anxiety at the 1-year follow-up was also significantly related to HRQL (pooled $r = 0.36$, 95%CI: 0.23-0.48, $P < 0.001$). A multicenter prospective cross-sectional study involving 80 severe COPD patients with an average age of 66 years and 93% male participants selected depression status, dyspnea, exacerbation frequency, and exercise capacity as predictors for the total St. George's Respiratory Questionnaire score. The findings suggest that the presence of comorbid depression is the strongest predictor of disease-specific and general HRQL. Screening and early intervention for depression in severe COPD patients can improve HRQL[38].

Recent evidence underscores the importance of comprehensive care in addressing the psychological comorbidities in COPD[16,19,31]. The use of remote patient monitoring (RPM) technologies has shown promise in helping patients self-manage and reducing COPD-related hospital readmissions[28]. These technologies, which include devices like pulse oximeters and spirometers, can aid in the early recognition of COPD exacerbations, potentially leading to better disease management and improved HRQL[30]. Pulmonary rehabilitation, a key non-pharmacological intervention, has been shown to improve not only physical capacity but also mood symptoms in COPD patients. This holistic approach can be particularly beneficial in enhancing HRQL by reducing symptoms, optimizing functional status, and increasing patient participation. The integration of psychological support with medical management is crucial in enhancing HRQL for COPD patients. The adoption of RPM technologies and participation in pulmonary rehabilitation programs can provide

additional benefits beyond traditional pharmacological treatments, offering a more comprehensive approach to care. The impact of depression and anxiety on COPD are summarized in Table 1.

## TREATMENT STRATEGIES

When comorbid with COPD, depression and anxiety significantly impact patients' quality of life and functional outcomes. The WHO advocates for chronic disease patients, such as those with COPD, to receive patient-centered, comprehensive care plans that extend beyond disease-specific treatments[39]. Therapeutic approaches for psychological symptoms in COPD patients typically include cognitive-behavioral therapy, pharmacological interventions, pulmonary rehabilitation, relaxation techniques, and palliative care.

### *Pharmacological interventions*

The National Institute for Health and Care Excellence (NICE) guidelines for the treatment of depression in older adults recommend the use of antidepressant medications for moderate to severe depression, including in patients with COPD. Selective serotonin reuptake inhibitors (SSRIs) are suggested as the first-line treatment for depression and should be accompanied by appropriate depression rating scales, such as the Patient Health Questionnaire-9 or the Hospital Anxiety and Depression Scale[40]. A subset of randomized clinical trials has confirmed the benefits of antidepressant treatment for patients with COPD and comorbid depression, not only reducing depressive symptoms but also decreasing tobacco dependence, improving subjective breathlessness, enhancing appetite, preventing weight loss, and alleviating anxiety symptoms[41]. Current pharmacological research for depression and anxiety in COPD patients primarily focuses on SSRIs and tricyclic antidepressants (TCAs). An evaluation of antidepressants, mainly SSRIs and TCAs, has shown significant improvement for patients with depression or depressive symptoms comorbid with physical illnesses. This assessment also demonstrated that SSRIs have a higher degree of long-term improvement compared to TCAs[42]. Therefore, SSRIs are the preferred treatment for depression and anxiety[43].

In a randomized controlled trial[44] involving 120 patients with stable COPD and moderate to severe depression, there was no statistically significant difference in lung function test parameters between the placebo and intervention groups treated with sertraline ($P > 0.05$). However, patients in the sertraline group showed a greater change in the Hamilton Depression Scale scores and the COPD Assessment Test after treatment ($P < 0.05$), and they also walked a longer distance in the 6-minute walk test compared to the placebo group ($P < 0.05$). A single-blind study[45] followed 14 COPD patients with comorbid depression who took fluoxetine 20 mg daily for 6 months, with 7 completing the study. Among those who completed the study, 4 responded to fluoxetine (a 50% reduction in the Geriatric Mental State Schedule scores). After 6 months of fluoxetine treatment, there were no significant improvements in forced expiratory volume in 1 second or physical activity scores. A study[46] compared the efficacy of paroxetine (20 mg/day) with placebo in 28 COPD patients over 6 weeks. There were no statistically significant differences in exercise capacity, lung function, and quality of life between the two groups. After the 6-week open-label phase with paroxetine, both groups continued to take 20 mg paroxetine for an additional 3 months, resulting in significant improvements in depression scores, walking distance, and quality of life.

### *Potential drug interactions*

In the management of COPD, β2-agonists and anticholinergic medications are frequently utilized. Notably, β2-agonists such as salbutamol, indacaterol, and salmeterol can lead to dose-dependent prolongation of the QT interval and potassium loss. The co-administration of these medications with certain SSRIs known to prolong the QT interval, such as escitalopram, citalopram, and fluoxetine, and TCAs like nortriptyline and dothiepin, may result in additive effects and an increased risk of ventricular arrhythmias[47]. Furthermore, TCAs have the potential to exacerbate cardiovascular adverse effects associated with β2-agonists, including hypertension, tachycardia, and chest pain. Additionally, the anticholinergic properties of TCAs can intensify the effects of anticholinergic bronchodilators used in COPD, such as tiotropium and ipratropium, leading to side effects like dry mouth, urinary retention, constipation, mydriasis, blurred vision, and fever, and potentially worsening glaucoma.

### *Non-pharmacological interventions*

The NICE guidelines for depression in adults highlight the importance of psychosocial interventions for patients with chronic health conditions, including those with clinical or subthreshold depression. These interventions can range from low to high intensity, tailored to the severity of mood symptoms[48]. A systematic review of randomized controlled trials involving psychological and/or lifestyle interventions for adult COPD patients indicates that complex interventions, including an exercise component, significantly improve depressive and anxiety symptoms. Importantly, multi-component exercise training can effectively alleviate anxiety and depressive symptoms in all COPD patients, irrespective of the severity of these conditions[49].

## CONCLUSION

Current studies on treating depression and anxiety in COPD patients face limitations such as small sample sizes, diverse patient populations, and inconsistent assessment tools. These issues necessitate more rigorous validation through larger

**Table 1 Impact of depression and anxiety on chronic obstructive pulmonary disease**

| Disease impact | Details |
|---|---|
| Bidirectional relationship | A significant bidirectional relationship between depression, anxiety, and COPD[32] |
| Impact on COPD outcomes | Depression and anxiety significantly increase the risk of adverse COPD outcomes and mortality in COPD. Anxiety raises the risk of COPD exacerbation or death[32] |
| Hospitalization and readmission rates | Higher hospitalization and readmission rates due to COPD exacerbations in patients with comorbid depression and anxiety[33] |
| Psychological factors and dyspnea | Anxiety sensitivity to be a significant predictor of dyspnea symptoms in COPD, even after adjusting for generalized depression and anxiety[35] |
| HRQL | Comorbid depression and anxiety at the 1-year follow-up are significantly correlated with HRQL in COPD[35] |
| Predictors of HRQL | Comorbid depression as the strongest predictor of disease-specific and general HRQL in severe COPD patients[38] |

COPD: Chronic obstructive pulmonary disease; HRQL: Health-related quality of life.

randomized controlled trials to confirm treatment effectiveness. For patients with mild to moderate depression, non-pharmacological interventions like psychological therapy and lifestyle changes are recommended. These methods have shown efficacy in managing symptoms without medication-related risks. In severe cases where non-pharmacological approaches are inadequate, cautious use of antidepressants like SSRIs may be necessary. Regular ECG assessments are recommended to monitor for potential QT interval prolongation[30]. Patients should be informed about the importance of immediate medical attention for symptoms like palpitations or syncope, which could signal cardiac side effects. Regular monitoring of electrolyte levels is also crucial to prevent arrhythmias. The use of antidepressants requires careful consideration of potential drug interactions. Balancing the benefits of symptom relief against treatment risks is key, emphasizing the need for personalized treatment strategies tailored to each patient's specific needs. The findings highlight the importance of a multifaceted approach to managing depression and anxiety in COPD patients. This includes the development of more robust research methodologies, the promotion of non-pharmacological interventions, and the cautious application of pharmacological treatments with comprehensive patient education and monitoring.

## FOOTNOTES

**Author contributions:** Wu S wrote the main manuscript; Qiu CJ performed data collection; All authors analyzed and interpreted results, reviewed the results and approved the final version of the manuscript, and were informed of each step of manuscript processing including submission, revision, revision reminder, *etc*.

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