

## DEPRESSION AND ANXIETY IN PATIENTS WITH COPD

<sup>1</sup>Saipova D.S., <sup>2</sup>Egamberdieva D.A., <sup>3</sup>Ruzmetova I.A.

<sup>1,2,3</sup>Tashkent Pediatric Medical Institute, Tashkent, Uzbekistan

<https://doi.org/10.5281/zenodo.10969501>

**Abstract.** *The incidence of COPD has increased worldwide and is a leading cause of morbidity and mortality. Common symptoms of the disease include shortness of breath, cough, sputum production, and changes in airway composition resulting from chronic exposure to cigarette smoke or pollutants. Depression and anxiety aggravate obesity and lead to exacerbation of COPD, and can also have a profound impact on health status, exercise capacity, lung function and mortality.*

**Keywords:** *chronic obstructive pulmonary disease (COPD), depression and anxiety*

**Introduction.** Chronic obstructive pulmonary disease (COPD) is an irreversible but treatable disease characterized primarily by shortness of breath, cough, and sputum production. Tobacco smoking is the main source of exposure, but air pollution and genetic or abnormal lung development may contribute for it [1].

In recent decades, it has been recognized that patients with chronic obstructive pulmonary disease (COPD) with three or more comorbidities are more likely to be hospitalized and have a high risk of premature death compared with patients with COPD without comorbidities. [2].

Untreated and unrecognized symptoms of depression and anxiety in patients with COPD negatively affect physical and social functioning, increasing fatigue and the needs for help [3, 4]. Depression and anxiety are difficult to identify and treat because their symptoms often overlap with COPD symptoms [5]. Identifying depression and anxiety and developing treatment strategies are important to improve the quality of life of patients with COPD and reduce health care utilization. This review examines the current understanding of the prevalence and potential mechanism of this association, and discusses implications for the treatment of patients with COPD with comorbid symptoms of depression and anxiety.

**Epidemiology.** The prevalence of COPD among people 30–79 years was 10.3% in 2019 using the GOLD criteria [8]. The frequency of depression among patients with stable COPD in a primary care setting ranging, from 10% to 57%, while the prevalence of anxiety varies widely, between 7% and 50% [6]. The variation stems from the patient population under focus and the clinic setting. In a recent longitudinal study [9] of 35,000 patients with COPD and with a follow-up of 10 years, the incidence of depression was 16.2 cases per 1000 person-years in the COPD group compared with 9.4 cases per 1000 person-years in the non-COPD control group. In addition, those with severe COPD were twice as likely to develop depression compared with patients with mild COPD. In patients with severe COPD (FEV1 < 50% predicted), the prevalence of depression was 25.0% compared with 17.5% in controls and 19.6% in patients with mild to moderate COPD [10]. Comorbid depression increased mortality risk by 1.83 (95% CI, 1.00–3.36) and anxiety raised the risk of mortality by 1.27; (95% CI, 1.02–1.58).

**Pathophysiology.** A systematic review and meta-analysis of 25 studies with long-term follow-up found that the association between COPD and depression is bidirectional [6], as depression can be both, a cause and a consequence of COPD. However, the precise mechanisms linking COPD to depression and anxiety have not been identified. Smoking increases the risk of

developing COPD, and the higher the severity of the disease, the higher the risk of depression and/or anxiety in patients with COPD. Nicotine dependence aggravates anxiety disorders in COPD [7]. Thus, these cross-sectional associations do not allow inference of cause and effect, and depression and anxiety lead to fear, panic and hopelessness, low self-esteem, social isolation and dependency on caregivers, thereby creating a vicious circle that perpetuates anxiety and depression.

There is emerging evidence to suggest that chronic pulmonary inflammation is partly a link between depressive symptoms and pulmonary function impairment, as elevated levels of inflammatory markers have been identified in patients with depression in older age [8] and COPD [9]. In a recent study, a sample of older adults with high levels of interleukin-6 and C-reactive protein showed an association of depressive symptoms with pulmonary obstruction [10].

In addition, there are biological, behavioral and social factors that contribute to increased disability and social isolation among patients with COPD. A study on the prevalence of depression found that among 52,118 patients with COPD the prevalence of depression was 26%, among 5335 smokers without COPD it was 12%, and among 5243 non-smokers without COPD the prevalence of depression was 7% [11]. These results suggest that clinical and biological markers of disease are less important indicators for patients with COPD than disease symptoms and decreased quality of life, which lead to the development of depression.

**Clinical Features.** In one study, COPD exacerbations were associated with moderate to severe depression in nearly half of COPD survivors. exacerbation episodes during the previous year, moderate to severe anxiety. in more than two thirds of patients, and post-traumatic stress symptoms in one third of patients [12]. Symptoms of anxiety, depression and post-traumatic stress were more often observed in patients with frequent exacerbations of COPD ( $\geq 2$ ) compared with patients with  $< 1$  exacerbation of COPD in the previous year [13,18]. However, a study comparing patient interviews with physician ratings found that physicians may underestimate the psychological impact of exacerbations on patients [14], highlighting the importance of increasing physician awareness of these comorbid mental health problems. Based on this, depression and anxiety in patients with COPD are associated with decreased physical activity and worsened quality of life, increased respiratory symptoms, and the risk of hospitalization and mortality [14–16]. Patients have been found to have high levels of depression, even with mild exacerbation in patients with reduced physical activity.[17]

However, it has been suggested that time-limited symptoms of anxiety and depression occurring during an exacerbation of COPD do not require treatment [19], since the exacerbation may have resolved by the time these drugs begin to work. COPD does not only affect the mental health of patients: almost two thirds of people caring for patients with COPD report symptoms of anxiety and approximately one third report symptoms of depression [20]. Perceived caregiver burden and patient activity limitations have been identified as predictors of anxiety and depression symptoms in caregivers [ 21 ].

A randomized controlled trial found that PID-S resulted in higher rates of depression remission and greater reductions in depressive symptoms in dyspnea-related disability than treatment as usual at 28 weeks and 6 months after the last session [22]. Low severity of dyspnea disability and adherence to antidepressant medication predicted subsequent improvement in depression. Improvement in depression was not associated with antidepressant use and was associated with behavioral pulmonary rehabilitation interventions [23]. However, the long-term

benefit of pulmonary rehabilitation therapy in reducing anxiety and depression is unknown. In addition, further research is needed into the effectiveness of maintenance therapy to alleviate these symptoms and achieve complete remission.

Decreased physical activity following a COPD exacerbation may result in them staying home, which in turn may increase the patient's degree of depression, thereby creating a vicious cycle that will lead to further deterioration in the patient's physical activity. When studying the prescription of patients with end-stage COPD - having severe obstruction, serious condition and a high risk of exacerbations - it was shown that 58.5% of patients took anxiolytics, 42.4% - antipsychotics, 19.1% - antidepressants and 3.1% - non-depressants. -benzodiazepine hypnotics [24]. These data suggest that mental health problems are prevalent in patients with end-stage COPD, who are at high risk for exacerbations of COPD.

Exercise and low depression severity predicted improvements in dyspnea-related disability. A recent systematic review examined the effectiveness of comprehensive pulmonary rehabilitation (exercise plus education) in patients with COPD and found that the reduction in symptoms of depression and anxiety in the short term was comparable to usual care [25]. Additionally, a recent uncontrolled, intensive 3-week outpatient pulmonary rehabilitation program (6 hours per day for 5 days per week) showed significant improvements in depression and anxiety in patients with COPD [26]. Again, long-term benefits and their clinical implications require further study. Acute inpatient rehabilitation was followed by improvements in depressive symptoms and disability, even in older patients with severe COPD and major depression.

Zaimin Li et al. conducted a systematic review and meta-analysis of RCTs and found that exercise reduced both anxiety and depression in COPD patients with anxiety and depression. These scientists also studied the effect of various types of physical activity on the psycho-emotional state of patients with COPD. A mathematical analysis revealed that yoga classes for 30-60 minutes 2-3 times a week for 24 weeks had a greater effect on anxiety in patients with COPD over 70 years of age and older with a course of yoga therapy. disease for more than 10 years. And for depression, qigong exercises 2-3 times a week for 30-60 minutes each time had a greater effect in patients with COPD over 70 years of age and with a disease duration of less than 10 years. [12].

Screening and Diagnosis D.L. Matte et al in their meta-analysis found that one study [27] used self-completed depression questionnaires. three studies [29,33,34] used the CES-D, two [28,29] used the Geriatric Depression Score (GDS); one [30,32] used the Hospital Anxiety and Depression Scale (HADS-D) and only one study [31] the Structured Clinical Interview for DSM-I (SCID-DSMIV) was used by a psychiatrist to determine the presence of depression. The authors also identified that the disease severity was associated with higher prevalence of depression in five studies.

Management. There is currently evidence that the effectiveness of treating depression or anxiety with selective serotonin reuptake inhibitors (SSRIs) in patients with COPD is questionable. This is partly due to patient concerns that antidepressants are addictive and have side effects, as well as cognitive impairment associated with depression. In addition, the lack of adequate support and explanation from health professionals about the causes and effectiveness of treatment for depression leads to patients refusing treatment. The patient-family collaborative care model has been found to be beneficial in the treatment of depression in patients with chronic illness [12]. A recent Cochrane review [13] examined studies that examined the benefits of pharmacological interventions in treating anxiety in patients with COPD. Their results show that studies were

heterogeneous and treatment effectiveness was inconclusive. Therefore, well-controlled randomized studies are needed. Recently, a personalized nine-session intervention for depression and COPD (PID-S) was developed for patients with major depression and severe COPD [17]. PID-S is offered by care managers who, through support and targeted interventions, help patients adhere to exercise and antidepressant medications. Care managers also collaborate with patients' physicians to monitor patients' treatment and progress.

There is some evidence to suggest that psychological therapies, including cognitive behavioral therapy and counseling, may improve symptoms of depression and anxiety in patients with COPD [5, 6]. However, there is currently uncertainty regarding the "dosage" and duration of therapy for even mild cases of anxiety and depression. In addition, the availability of psychological therapy in primary care settings for this group of patients is limited. It is worth considering the possibility of providing access to psychological therapy resources through Internet technologies as a complementary therapy.

WALTERS et al. [22] examined the effectiveness of telephone health coaching using cognitive behavioral therapy (n580) compared with usual care (n574) in a 12-month treatment program. The experimental group received 16 30-minute phone calls over 12 months, with increasing time between calls. The control group received usual care from general practitioners and monthly telephone calls from a research nurse. Anxiety decreased in both groups after 12 months. Health coaching improved self-management ability, but both groups had similar quality of life scores at the end of the treatment phase. Moreover, there was no difference in depression scores between the two groups. BUCKNALL et al [23] reported that the minority of patients with COPD who were able to learn effective self-management were younger and more likely to live with others. These patients had a significantly reduced risk of COPD readmission.

Conclusions. COPD patients with comorbid conditions and anxiety or depression experience frequent exacerbations and hospital readmissions within a year. The mortality rate among patients with comorbidities is higher than in patients with COPD without comorbidities. Adequate and effective methods for screening, diagnosing and treating anxiety and depression in patients with COPD are needed to reduce the negative impact on quality of life and also reduce the incidence of readmission and mortality.

## **REFERENCES**

1. Vogelmeier CF, Criner GJ, Martinez FJ, et al. Global strategy for the diagnosis, management, and prevention of chronic obstructive lung disease 2017 report. *Am J Respir Crit Care Med.* 2017;195 (5):557–582. doi:10.1164/rccm.201701-0218PP
2. Sode BF, Dahl M, Nordestgaard BG. Myocardial infarction and other comorbidities with chronic obstructive pulmonary disease: a Danish Nationwide study of 7.4 million individuals. *Eur Heart J* 2011; 32: 2365–2375.
3. Doyle T, Palmer S, Johnson J, et al. Association of anxiety and depression with pulmonary-specific symptoms in chronic obstructive pulmonary disease. *Int J Psychiatry Med* 2013; 45: 189–202.
4. Dalal AA, Shah M, Lunacsek O, et al. Clinical and economic burden of depression/anxiety in chronic obstructive pulmonary disease patients within a managed care population. *COPD* 2011; 8: 293–299.

5. Willgoss TG, Yohannes AM. Anxiety disorders in patients with COPD: a systematic review. *Respir Care* 2013; 58: 858–866.
6. Atlantis E, Fahey P, Cochrane B, et al. Bidirectional associations between clinically relevant depression or anxiety and COPD: a systematic review and meta-analysis. *Chest* 2013; 144: 766–777.
7. Goodwin RD, Lavoie KL, Lemeshow AR, et al. Depression, anxiety, and COPD: the unexamined role of nicotine dependence. *Nicotine Tob Res* 2012; 14: 176–183.
8. Alexopoulos GS, Morimoto SS. The inflammation hypothesis in geriatric depression. *Int J Geriatr Psychiatry* 2011; 26: 1109–1118.
9. Huerta A, Crisafulli E, Mene´ndez R, et al. Pneumonic and non-pneumonic exacerbations of COPD: inflammatory response and clinical characteristics. *Chest* 2013; 144: 1134–1142.
10. Lu Y, Feng L, Feng L, et al. Systemic inflammation, depression and obstructive pulmonary function: a populationbased study. *Respir Res* 2013; 14: 53.
11. Selzler, Cindy Ellerton, Lauren Ellerton, Razanne Habash, Erica Nikolaichuk, Roger Goldstein & Dina Brooks (2023) The Relationship between Physical Activity, Depression and Anxiety in People with COPD: A Systematic Review and Meta-analyses, *COPD: Journal of Chronic Obstructive Pulmonary Disease*, 20:1, 167-177, DOI: 10.1080/15412555.2023.2200826
12. Zaimin Li 1 , Shijie Liu 2 , Lin Wang 3,\* and Lee Smith 4 Mind–Body Exercise for Anxiety and Depression in COPD Patients: A Systematic Review and Meta-Analysis *Int. J. Environ. Res. Public Health* 2020, 17, 22; doi:10.3390/ijerph17010022
13. Darlan L. Matte a, b , Marcia M.M. Pizzichini a, c, \* , Andrea T.C. Hoepers a , Alexandre P. Diaz a , Manuela Karloh a , Mirella Dias a , Emilio Pizzichini a Prevalence of depression in COPD: A systematic review and metaanalysis of controlled studies *Respiratory Medicine* 117 (2016) 154e161 <http://dx.doi.org/10.1016/j.rmed.2016.06.006>
14. T.S. Wong, Y.T. Xiang, J. Tsoh, et al., Depressive disorders in older patients with chronic obstructive pulmonary disease (COPD) in Hong Kong: a controlled study, *Aging & Ment. health* 18 (5) (2014) 588e592
15. J.G. van Manen, P.J. Bindels, F.W. Dekker, et al., Risk of depression in patients with chronic obstructive pulmonary disease and its determinants, *Thorax* 57 (5) (2002) 412e416
16. N.A. Hanania, H. Mullerova, N.W. Locantore, et al., Determinants of depression in the ECLIPSE chronic obstructive pulmonary disease cohort, *Am. J. Respir. Crit. Care Med.* 183 (5) (2011) 604e611.
17. L.J. Persson, M. Aanerud, P.S. Hiemstra, et al., Chronic obstructive pulmonary disease is associated with low levels of vitamin D, *PloS one* 7 (6) (2012) e38934
18. T.P. Ng, M. Niti, C. Fones, et al., Co-morbid association of depression and COPD: a population-based study, *Respir. Med.* 103 (6) (2009) 895e901.
19. T.A. Omachi, P.P. Katz, E.H. Yelin, et al., Depression and health-related quality of life in chronic obstructive pulmonary disease, *Am. J. Med.* 122 (8) (2009) 778
20. Quaderi, S.A.; Hurst, J.R. The unmet global burden of COPD. *Glob. Health Epidemiol. Genom.* 2018, 3, e4. [CrossRef]
21. Press, V.G.; Konetzka, R.T.; White, S.R. Insights about the economic impact of chronic obstructive pulmonary disease readmissions post implementation of the hospital readmission reduction program. *Curr. Opin. Pulm. Med.* 2018, 24, 138–146. [CrossRef] [PubMed]

22. Safiri, S.; Carson-Chahhoud, K.; Noori, M.; Nejadghaderi, S.A.; Sullman, M.J.M.; Ahmadian Heris, J.; Ansarin, K.; Mansournia, M.A.; Collins, G.S.; Kolahi, A.A.; et al. Burden of chronic obstructive pulmonary disease and its attributable risk factors in 204 countries and territories, 1990–2019: Results from the Global Burden of Disease Study 2019. *BMJ* 2022, 378, e069679. [CrossRef] [PubMed]
23. Zareifopoulos, N.; Bellou, A.; Spiropoulou, A.; Spiropoulos, K. Prevalence, Contribution to Disease Burden and Management of Comorbid Depression and Anxiety in Chronic Obstructive Pulmonary Disease: A Narrative Review. *J. Obstr. Pulm. Dis.* 2019, 16, 406–417. [CrossRef]
24. Atlantis, E.; Fahey, P.; Cochrane, B.; Smith, S. Bidirectional associations between clinically relevant depression or anxiety and COPD: A systematic review and meta-analysis. *Chest* 2013, 144, 766–777. [CrossRef]
25. Pumar, M.I.; Gray, C.R.; Walsh, J.R.; Yang, I.A.; Rolls, T.A.; Ward, D.L. Anxiety and depression-Important psychological comorbidities of COPD. *J. Thorac. Dis.* 2014, 6, 1615–1631. [CrossRef] [PubMed]
26. Schuler, M.; Wittmann, M.; Faller, H.; Schultz, K. The interrelations among aspects of dyspnea and symptoms of depression in COPD patients—A network analysis. *J. Affect. Disord.* 2018, 240, 33–40. [CrossRef]
27. Adeloye, D.; Song, P.; Zhu, Y.; Campbell, H.; Sheikh, A.; Rudan, I. Global, regional, and national prevalence of, and risk factors for, chronic obstructive pulmonary disease (COPD) in 2019: A systematic review and modelling analysis. *Lancet. Respir. Med.* 2022, 10, 447–458. [CrossRef]
28. Schneider, C.; Jick, S.S.; Bothner, U.; Meier, C.R. COPD and the risk of depression. *Chest* 2010, 137, 341–347. [CrossRef]
29. Van Manen, J.G.; Bindels, P.J.; Dekker, F.W.; CJ, I.J.; van der Zee, J.S.; Schadé, E. Risk of depression in patients with chronic obstructive pulmonary disease and its determinants. *Thorax* 2002, 57, 412–416. [CrossRef]
30. Blakemore, A.; Dickens, C.; Guthrie, E.; Bower, P.; Kontopantelis, E.; Afzal, C.; Coventry, P.A. Depression and anxiety predict health-related quality of life in chronic obstructive pulmonary disease: Systematic review and meta-analysis. *Int. J. Chron. Obstruct. Pulmon. Dis.* 2014, 9, 501–512. [CrossRef]
31. Martucci, V.L.; Richmond, B.; Davis, L.K.; Blackwell, T.S.; Cox, N.J.; Samuels, D.; Velez Edwards, D.; Aldrich, M.C. Fate or coincidence: Do COPD and major depression share genetic risk factors? *Hum. Mol. Genet.* 2021, 30, 619–628. [CrossRef] [PubMed]
32. Xu, K.; Li, X. Risk Factors for Depression in Patients with Chronic Obstructive Pulmonary Disease. *Med. Sci. Monit.* 2018, 24, 1417–1423. [CrossRef] [PubMed]
33. Chatila, W.M.; Thomashow, B.M.; Minai, O.A.; Criner, G.J.; Make, B.J. Comorbidities in chronic obstructive pulmonary disease. *Proc. Am. Thorac. Soc.* 2008, 5, 549–555. [CrossRef]
34. Gunasekaran, K.; Murthi, S.; Elango, K.; Rahi, M.S.; Thilagar, B.; Ramalingam, S.; Voruganti, D.; Paramasivam, V.K.; Kolandaivel, K.P.; Arora, A.; et al. The Impact of Diabetes Mellitus in Patients with Chronic Obstructive Pulmonary Disease (COPD) Hospitalization. *J. Clin. Med.* 2021, 10, 235. [CrossRef]
35. Yohannes, A.M.; Alexopoulos, G.S. Depression and anxiety in patients with COPD. *Eur. Respir. Rev.* 2014, 23, 345–349. [CrossRef] *Adv. Respir. Med.* 2023, 91 132