

Anxiety and Depressive Symptoms among Patients with Chronic Obstructive Pulmonary Disease in Syria: A Cross-Sectional Study of Spirometric and Patient-Reported Correlates

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Abstract

Background

Anxiety and depression are common but often underrecognized comorbidities in chronic obstructive pulmonary disease (COPD). Evidence from low-resource settings remains limited. This study assessed the prevalence and correlates of anxiety and depressive symptoms among Syrian patients with COPD.

Methods

This cross-sectional analytical study included 249 patients with established COPD attending the pulmonary outpatient clinic at Damascus Hospital, Syria. Anxiety and depressive symptoms were assessed using validated Arabic versions of the Generalized Anxiety Disorder-7 scale (GAD-7) and Patient Health Questionnaire-9 scale (PHQ-9). Spirometry was performed before questionnaire administration, and FEV1% predicted was used for GOLD spirometric classification. Bivariate analyses and separate ordinal logistic regression models were conducted for GAD-7 and PHQ-9 severity.

Results

Clinically relevant anxiety was present in 30.9% of patients, while clinically relevant depression was present in 73.9%. In bivariate analyses, higher anxiety and depression severity were associated with lower FEV1% predicted, higher mMRC dyspnea score, GOLD group, smoking-related variables, physical activity, regular follow-up, and patient-reported challenges. In multivariable analysis, challenge burden score was the strongest independent correlate of anxiety severity (adjusted OR, 6.50; 95% CI, 4.02–10.51) and remained independently associated with depression severity (adjusted OR, 2.19; 95% CI, 1.52–3.17). Older age was independently associated with higher anxiety severity, while COPD duration shorter than 1 year was associated with lower depression severity compared with duration longer than 5 years. FEV1% predicted and GOLD category were not independently associated with either outcome.

Conclusion

Anxiety and depressive symptoms were highly prevalent among Syrian patients with COPD, especially depression. Patient-reported challenge burden was more consistently associated with psychological severity than spirometric impairment, supporting multidimensional COPD care that integrates psychological screening and symptom-burden assessment.

Introduction

Chronic obstructive pulmonary disease (COPD) is a preventable chronic respiratory disease characterized by persistent respiratory symptoms and airflow limitation, and it remains a major

contributor to global morbidity, mortality, disability, and healthcare burden [1–3]. Beyond airflow obstruction, COPD is increasingly recognized as a multidimensional systemic condition in which dyspnea, fatigue, sleep disturbance, reduced physical activity, impaired self-management, and functional limitation interact with psychological and social determinants of health [1, 2, 4]. Anxiety and depression are among the most common psychological comorbidities in COPD, although reported prevalence varies widely according to disease phase, clinical setting, population characteristics, and assessment method [1, 2]. These comorbidities are clinically important because they are associated with poorer quality of life, reduced adherence, lower participation in rehabilitation, increased exacerbations and hospitalization, greater healthcare utilization, and worse prognosis [2, 3, 5].

The relationship between COPD and psychological distress is complex and likely bidirectional. Breathlessness, functional limitation, social isolation, smoking, physical inactivity, poor sleep, comorbidities, and socioeconomic disadvantage may increase vulnerability to anxiety and depression, while psychological distress may worsen symptom perception, reduce coping capacity, impair adherence, and reinforce avoidance of activity [2–4]. Importantly, several studies suggest that psychological symptoms are not fully explained by spirometric severity. A Romanian study found that CAT-defined symptom burden predicted depression, anxiety, and stress more consistently than GOLD stage, while a Swedish primary-care study showed that dyspnea, current smoking, female sex, younger age, and comorbid asthma were associated with depression/anxiety, whereas FEV1 was not independently associated after adjustment [6, 7]. Evidence from Greece further indicates that anxiety and depression may already be present in mild and moderate COPD, supporting screening before advanced or oxygen-dependent disease stages [8].

Despite this burden, anxiety and depression in COPD often remain underrecognized because respiratory symptoms dominate clinical encounters and because fatigue, sleep disturbance, inactivity, and dyspnea overlap with psychological symptoms [2, 3]. This issue may be particularly relevant in low-resource settings, where financial constraints, limited healthcare access, family dependence, self-care difficulties, and fear about the future can intensify psychological distress among COPD patients [9]. However, context-specific data from Syria remain scarce. Therefore, this study aimed to assess the prevalence and severity of anxiety and depressive symptoms among Syrian patients with COPD using GAD-7 and PHQ-9, and to examine their sociodemographic, behavioral, clinical, spirometric, and patient-reported symptom-burden correlates.

Methods

Study design and setting

This was a cross-sectional analytical, hospital-based, single-center study conducted among patients with chronic obstructive pulmonary disease (COPD) attending the pulmonary outpatient clinic at Damascus Hospital (Al-Mujtahid), Damascus, Syria. The present analysis was part of a larger COPD research dataset collected using a unified questionnaire; however, this manuscript focuses specifically

on anxiety and depressive symptoms and their associations with sociodemographic, behavioral, clinical, spirometric, and patient-reported symptom-burden factors. Data collection was conducted over 63 days, from 12 August 2025 to 14 October 2025.

Study population and eligibility criteria

The study population included adult patients with an established diagnosis of COPD who attended the pulmonary outpatient clinic during the study period. COPD had been previously diagnosed within the hospital pulmonary service and confirmed in routine clinical practice by post-bronchodilator spirometry. The investigators did not participate in establishing the original COPD diagnosis.

Patients were excluded if they had an acute COPD exacerbation at the time of assessment, respiratory failure, other underlying chest diseases, or explicit refusal to participate. All enrolled patients completed the anxiety and depression assessments, yielding a final analytic sample of 249 participants.

During data collection, spirometry was performed for all participants before questionnaire administration. The FEV1% predicted value measured at this study visit was used to classify current spirometric severity according to GOLD thresholds, rather than relying on previous spirometric records. GOLD spirometric grades were defined as grade 1, FEV1 $\geq$ 80% predicted; grade 2, 50%–79%; grade 3, 30%–49%; and grade 4, $<$ 30%.

Sampling and data collection

Participants were recruited using convenience sampling. Eligible patients who agreed to participate were enrolled after providing verbal informed consent. Although recruitment was carried out at a single tertiary hospital outpatient clinic, the sample included patients from different Syrian governorates.

Data were collected through face-to-face interviewer-administered interviews using a structured printed questionnaire. Questionnaire administration and data handling were performed by trained data collectors. Responses were first recorded on paper forms, then entered into Google Forms, exported as a CSV file, and subsequently analyzed statistically.

Anxiety and depression assessment

Anxiety symptoms were assessed using a validated Arabic version of the Generalized Anxiety Disorder-7 scale (GAD-7) [10]. The GAD-7 includes seven items scored from 0 to 3, producing a total score ranging from 0 to 21, with higher scores indicating greater anxiety symptom severity. For descriptive analyses, GAD-7 severity was presented using the original standard categories: minimal anxiety (0–4), mild anxiety (5–9), moderate anxiety (10–14), and severe anxiety (15–21). Clinically relevant anxiety was defined as GAD-7 $\geq$ 10.

For ordinal logistic regression, GAD-7 severity was collapsed into three ordered categories to improve model stability: minimal anxiety (0–4), mild anxiety (5–9), and moderate-to-severe anxiety (10–21).

Depressive symptoms were assessed using a validated Arabic version of the Patient Health Questionnaire-9 scale (PHQ-9) [10]. The PHQ-9 includes nine items scored from 0 to 3, producing a total score ranging from 0 to 27, with higher scores indicating greater depressive symptom severity. For descriptive analyses, PHQ-9 severity was presented using the original standard categories: minimal/no depression (0–4), mild depression (5–9), moderate depression (10–14), moderately severe depression (15–19), and severe depression (20–27). Clinically relevant depression was defined as PHQ-9 $\geq$ 10.

For ordinal logistic regression, PHQ-9 severity was collapsed into three ordered categories to improve model stability: minimal-to-mild depression (0–9), moderate depression (10–14), and moderately severe-to-severe depression (15–27).

Other study variables

The questionnaire also captured age, sex, place of residence, marital status, educational level, occupation, smoking status, smoking exposure in pack-years, occupational exposure, weekly physical activity level, COPD duration, chronic comorbidity, regular doctor follow-up, home oxygen use, mMRC dyspnea score, and self-rated current health status.

Patient-reported challenge indicators were recorded as binary variables for dyspnea, sleep difficulty, fatigue, anxiety/depression-related challenge, and difficulty performing daily tasks. Each reported challenge was coded as 1, and each absent challenge was coded as 0. A cumulative challenge burden score was then generated by summing these five indicators, with higher scores indicating greater patient-reported symptom and functional burden.

Statistical analysis

Data were analyzed using IBM SPSS Statistics version 26. Categorical variables were summarized as frequencies and percentages. Age and PHQ-9 score were summarized as mean and standard deviation, whereas skewed or ordinal continuous variables, including GAD-7 score, smoking exposure in pack-years, and FEV1% predicted, were summarized as median and interquartile range.

The main outcomes were GAD-7 anxiety severity and PHQ-9 depression severity. For bivariate analyses, the original GAD-7 and PHQ-9 severity categories were used. Associations between severity categories and continuous or ordinal predictors were assessed using Jonckheere–Terpstra tests. Associations with categorical predictors were evaluated using chi-square or exact tests as appropriate. Effect sizes were reported as r for Jonckheere–Terpstra tests and Cramer's V for categorical associations.

Separate ordinal logistic regression models were constructed for GAD-7 anxiety severity and PHQ-9 depression severity using the three-category outcome variables. Predictors were selected based on

clinical relevance and bivariate findings. Adjusted odds ratios (ORs) with 95% confidence intervals (CIs) were reported, with ORs greater than 1 indicating higher odds of being in a more severe anxiety or depression category.

For the GAD-7 model, predictors included age, FEV1% predicted, challenge burden score, smoking status, and GOLD spirometric category. For the PHQ-9 model, predictors included age, challenge burden score, FEV1% predicted, sex, COPD duration, home oxygen use, and GOLD spirometric category. Model performance was assessed using model-fitting chi-square statistics, Pearson and deviance goodness-of-fit tests, pseudo-R² measures, and the test of parallel lines for the proportional odds assumption. The proportional odds assumption was met for both models. A two-sided p value < 0.05 was considered statistically significant.

Ethical considerations

The study protocol was approved by the Research Ethics Committee of the Syrian Private University (MD-30032026-131). Verbal informed consent was obtained from all participants before enrollment.

Results

A total of 249 patients with established COPD and complete GAD-7 and PHQ-9 data were included. The mean age was 60.2 ± 9.5 years, and most participants were male (82.7%), rural residents (69.1%), and currently married (84.3%). More than half had below-secondary education (55.4%), and the largest occupational group was manual, industrial, or high-exposure service work (60.6%). Most participants were current smokers (80.3%), with a median smoking exposure of 35.0 pack-years among current smokers with available pack-year data (IQR, 20.0–60.0). Occupational exposure was reported by 76.3% of patients, and most reported light weekly physical activity (71.1%) (Table 1).

Table 1
Sociodemographic, behavioral, and exposure characteristics among patients with COPD

Variable	Category / summary	Overall
Sociodemographic characteristics		
Age, years	Mean (SD)	60.2 (9.5)
Sex	Female	43 (17.3%)
	Male	206 (82.7%)
Place of residence	Rural	172 (69.1%)
	Urban	77 (30.9%)
Marital status	Currently not married	39 (15.7%)
	Currently married	210 (84.3%)
Educational level	Below secondary education	138 (55.4%)
	Secondary education or above	111 (44.6%)
Occupation	Not working / out of the labor force	47 (18.9%)
	Office / professional / low-exposure service work	26 (10.4%)
	Manual / industrial / high-exposure service work	151 (60.6%)
	Agriculture / herding / livestock raising	25 (10.0%)
Behavioral and exposure characteristics		
Smoking status	Never smoked	13 (5.2%)
	Previous smoker	36 (14.5%)
	Current smoker	200 (80.3%)
Smoking exposure, pack-years	Median (IQR)	35.0 (20.0–60.0)
Occupational exposure	No	59 (23.7%)
	Yes	190 (76.3%)
Weekly physical activity level	No physical activity	42 (16.9%)
	Light physical activity	177 (71.1%)

Note. Overall sample N = 249. Categorical variables are presented as n (%). Age is presented as mean (SD); other continuous variables are presented as median (IQR). Percentages are based on valid responses. Smoking exposure was available for current smokers with pack-year data (n = 200). Abbreviations: COPD, chronic obstructive pulmonary disease; IQR, interquartile range; SD, standard deviation.

Variable	Category / summary	Overall
Sociodemographic characteristics		
	Moderate or higher physical activity	30 (12.0%)
Note. Overall sample N = 249. Categorical variables are presented as n (%). Age is presented as mean (SD); other continuous variables are presented as median (IQR). Percentages are based on valid responses. Smoking exposure was available for current smokers with pack-year data (n = 200). Abbreviations: COPD, chronic obstructive pulmonary disease; IQR, interquartile range; SD, standard deviation.		

Regarding clinical characteristics, 58.6% of patients had COPD duration shorter than 1 year, while 34.9% had a disease duration of 1–5 years. Chronic comorbidity was present in 52.6% of participants, and only 35.3% reported regular doctor follow-up. Home oxygen use was uncommon (3.6%). The median FEV1% predicted was 59.0% (IQR, 50.0–67.0). Most patients were classified as GOLD 2 (73.9%), followed by GOLD 3 (20.1%). The most frequent mMRC dyspnea grade was grade I (62.2%). Patient-reported challenges were common, particularly dyspnea (97.2%) and sleep difficulty (71.9%) (Table 2).

Table 2
Clinical severity, respiratory status, and symptom burden among patients with COPD

Variable	Category / summary	Overall
Clinical characteristics		
COPD duration	< 1 year	146 (58.6%)
	1–5 years	87 (34.9%)
	> 5 years	16 (6.4%)
Chronic disease	No	118 (47.4%)
	Yes	131 (52.6%)
Regular doctor follow-up	No	161 (64.7%)
	Yes	88 (35.3%)
Home oxygen use	No	240 (96.4%)
	Yes	9 (3.6%)
Lung function and disease severity		
FEV1% predicted	Median (IQR)	59.0 (50.0–67.0)
GOLD spirometric grade	GOLD 1	5 (2.0%)
	GOLD 2	184 (73.9%)
	GOLD 3	50 (20.1%)
	GOLD 4	10 (4.0%)
mMRC dyspnea score	0	13 (5.2%)
	I	155 (62.2%)
	II	39 (15.7%)
	III	30 (12.0%)
	IV	12 (4.8%)
Self-rated current health status	Very bad	12 (4.8%)
	Bad	52 (20.9%)
	Moderate	169 (67.9%)

Note. Overall sample N = 249. Categorical variables are presented as n (%). Continuous variables other than age and PHQ-9 score are presented as median (IQR). Percentages are based on valid responses. Abbreviations: COPD, chronic obstructive pulmonary disease; FEV1, forced expiratory volume in 1 second; GOLD, Global Initiative for Chronic Obstructive Lung Disease; IQR, interquartile range; mMRC, modified Medical Research Council; SD, standard deviation.

Variable	Category / summary	Overall
Clinical characteristics		
	Good	15 (6.0%)
	Very good	1 (0.4%)
Patient-reported challenge indicators		
Dyspnea challenge	No	7 (2.8%)
	Yes	242 (97.2%)
Sleep difficulty challenge	No	70 (28.1%)
	Yes	179 (71.9%)
Fatigue challenge	No	209 (83.9%)
	Yes	40 (16.1%)
Anxiety/depression challenge	No	211 (84.7%)
	Yes	38 (15.3%)
Daily tasks difficulty challenge	No	212 (85.1%)
	Yes	37 (14.9%)
Note. Overall sample N = 249. Categorical variables are presented as n (%). Continuous variables other than age and PHQ-9 score are presented as median (IQR). Percentages are based on valid responses. Abbreviations: COPD, chronic obstructive pulmonary disease; FEV1, forced expiratory volume in 1 second; GOLD, Global Initiative for Chronic Obstructive Lung Disease; IQR, interquartile range; mMRC, modified Medical Research Council; SD, standard deviation.		

Anxiety and depression burden

The median GAD-7 score was 7.0 (IQR, 6.0–10.0). Minimal anxiety was observed in 17.3% of participants, mild anxiety in 51.8%, moderate anxiety in 22.1%, and severe anxiety in 8.8%. Clinically relevant anxiety, defined as GAD-7 $\geq$ 10, was present in 30.9% of patients. The mean PHQ-9 score was 12.2 ± 4.6 . Minimal or no depression was reported by 4.4% of participants, while 21.7% had mild depression, 47.8% had moderate depression, 19.3% had moderately severe depression, and 6.8% had severe depression. Clinically relevant depression, defined as PHQ-9 $\geq$ 10, was present in 73.9% of patients (Table 3).

Table 3
Anxiety and depression measures among patients with COPD

Variable	Category / summary	Overall
Anxiety and depression measures		
GAD-7 score	Median (IQR)	7.0 (6.0–10.0)
GAD-7 severity category	Minimal anxiety (0–4)	43 (17.3%)
	Mild anxiety (5–9)	129 (51.8%)
	Moderate anxiety (10–14)	55 (22.1%)
	Severe anxiety (15–21)	22 (8.8%)
Clinically relevant anxiety (GAD-7)	GAD-7 ≥ 10	77 (30.9%)
PHQ-9 score	Mean (SD)	12.2 (4.6)
PHQ-9 severity category	Minimal/no depression (0–4)	11 (4.4%)
	Mild depression (5–9)	54 (21.7%)
	Moderate depression (10–14)	119 (47.8%)
	Moderately severe depression (15–19)	48 (19.3%)
	Severe depression (20–27)	17 (6.8%)
Clinically relevant depression (PHQ-9)	PHQ-9 ≥ 10	184 (73.9%)
Note. GAD-7 and PHQ-9 scores were available for all 249 patients included in this analysis. Categorical variables are presented as n (%). PHQ-9 score is presented as mean (SD); GAD-7 score is presented as median (IQR). Clinically relevant anxiety and depression were defined as GAD-7 ≥ 10 and PHQ-9 ≥ 10, respectively. Abbreviations: COPD, chronic obstructive pulmonary disease; GAD-7, Generalized Anxiety Disorder 7-item scale; IQR, interquartile range; PHQ-9, Patient Health Questionnaire 9-item scale; SD, standard deviation.		

Bivariate associations with anxiety and depression severity

In bivariate analyses, higher GAD-7 anxiety severity was significantly associated with older age, greater smoking exposure, lower FEV1% predicted, and higher mMRC dyspnea score. Among continuous and ordinal predictors, the strongest associations were observed for mMRC dyspnea score ($r = 0.612$, $p < 0.001$) and FEV1% predicted ($r = -0.503$, $p < 0.001$). Anxiety severity also differed significantly by educational level, marital status, COPD duration, smoking status, chronic comorbidity, weekly physical activity, regular doctor follow-up, patient-reported sleep difficulty, fatigue, difficulty performing daily tasks, and GOLD group (**Table S1**).

Similarly, higher PHQ-9 depression severity was significantly associated with older age, greater smoking exposure, lower FEV1% predicted, and higher mMRC dyspnea score. Among continuous and ordinal predictors, the strongest associations were observed for mMRC dyspnea score ($r = 0.568$, $p < 0.001$), FEV1% predicted ($r = -0.452$, $p < 0.001$), and smoking exposure in pack-years ($r = 0.320$, $p < 0.001$). Depression severity also differed significantly by marital status, educational level, COPD duration, smoking status, chronic comorbidity, weekly physical activity, regular doctor follow-up, sleep difficulty, fatigue, difficulty performing daily tasks, and GOLD group (**Table S2**).

Multivariable predictors of anxiety severity

In the ordinal logistic regression model for GAD-7 anxiety severity, the overall model was statistically significant ($\chi^2(5) = 166.159$, $p < 0.001$), and the proportional odds assumption was satisfied (test of parallel lines: $\chi^2(5) = 8.042$, $p = 0.154$). Older age was independently associated with higher anxiety severity, with each additional year increasing the odds of being in a more severe GAD-7 category by 5% (adjusted OR, 1.05; 95% CI, 1.02–1.08; $p = 0.002$). The challenge burden score was the strongest independent predictor; each one-point increase was associated with markedly higher odds of greater anxiety severity (adjusted OR, 6.50; 95% CI, 4.02–10.51; $p < 0.001$). FEV1% predicted, smoking status, and GOLD category were not independently associated with anxiety severity after adjustment (Table 4).

Table 4
Ordinal logistic regression model for GAD-7 anxiety severity

Predictor	Estimate (B)	SE	Wald chi-square	p value	Adjusted OR (95% CI)
Age, years	0.050	0.016	9.837	0.002	1.05 (1.02–1.08)
FEV1% predicted	-0.030	0.018	2.769	0.096	0.97 (0.94–1.01)
Challenge burden score	1.872	0.245	58.537	< 0.001	6.50 (4.02–10.51)
Never smoker vs ever smoker	-0.091	0.648	0.020	0.888	0.91 (0.26–3.25)
GOLD 1–2 vs GOLD 3–4	-0.878	0.573	2.351	0.125	0.42 (0.14–1.28)

Note. Dependent variable: GAD-7 three-category severity. Link function: logit. Adjusted ORs > 1 indicate higher odds of being in a more severe anxiety category. Threshold/cut-point parameters were omitted from the main table. Model diagnostics: $N = 249$; model fitting chi-square(5) = 166.159, $p < 0.001$; Pearson goodness-of-fit chi-square(471) = 506.484, $p = 0.125$; Deviance chi-square(471) = 323.155, $p = 1.000$; Cox and Snell R-squared = 0.487, Nagelkerke R-squared = 0.562, McFadden R-squared = 0.331; test of parallel lines chi-square(5) = 8.042, $p = 0.154$. Reference categories: ever smoker for smoking and GOLD 3–4 for GOLD category. 474 zero-frequency cells (66.1%); categorical estimates should be interpreted cautiously.

Multivariable predictors of depression severity

In the ordinal logistic regression model for PHQ-9 depression severity, the overall model was statistically significant ($\chi^2(8) = 110.074$, $p < 0.001$), and the proportional odds assumption was satisfied (test of parallel lines: $\chi^2(8) = 6.406$, $p = 0.602$). The challenge burden score remained independently associated with depression severity; each one-point increase was associated with higher odds of being in a more severe PHQ-9 category (adjusted OR, 2.19; 95% CI, 1.52–3.17; $p < 0.001$). Compared with patients with COPD duration longer than 5 years, those with disease duration shorter than 1 year had lower odds of more severe depression (adjusted OR, 0.05; 95% CI, 0.004–0.65; $p = 0.022$). Age, FEV1% predicted, sex, home oxygen use, and GOLD category were not independently associated with depression severity after adjustment (Table 5).

Table 5
Ordinal logistic regression model for PHQ-9 depression severity

Predictor	Estimate (B)	SE	Wald chi-square	p value	Adjusted OR (95% CI)
Age, years	0.022	0.014	2.344	0.126	1.02 (0.99–1.05)
Challenge burden score	0.785	0.189	17.336	< 0.001	2.19 (1.52–3.17)
FEV1% predicted	-0.017	0.017	1.028	0.311	0.98 (0.95–1.02)
Female vs male	-0.326	0.353	0.854	0.355	0.72 (0.36–1.44)
COPD duration < 1 year vs > 5 years	-2.927	1.274	5.279	0.022	0.05 (0.004–0.65)
COPD duration 1–5 years vs > 5 years	-2.292	1.247	3.378	0.066	0.10 (0.009–1.16)
No home oxygen use vs home oxygen use	0.995	1.099	0.820	0.365	2.70 (0.31–23.29)
GOLD 1–2 vs GOLD 3–4	-0.818	0.507	2.601	0.107	0.44 (0.16–1.19)
Note. Dependent variable: PHQ-9 three-category severity. Link function: logit. Adjusted ORs > 1 indicate higher odds of being in a more severe depression category. Threshold/cut-point parameters were omitted from the main table. Model diagnostics: N = 249; model fitting chi-square(8) = 110.074, $p < 0.001$; Pearson goodness-of-fit chi-square(474) = 485.212, $p = 0.351$; Deviance chi-square(474) = 402.708, $p = 0.992$; Cox and Snell R-squared = 0.357, Nagelkerke R-squared = 0.407, McFadden R-squared = 0.210; test of parallel lines chi-square(8) = 6.406, $p = 0.602$. Reference categories: male for sex, COPD duration > 5 years, home oxygen use, and GOLD 3–4. 480 zero-frequency cells (66.1%); categorical estimates, especially home oxygen use, should be interpreted cautiously.					

Estimated marginal means showed a stepwise increase in the challenge burden score across PHQ-9 depression categories, with higher values observed in more severe depression categories, visually supporting the positive association between cumulative patient-reported challenges and depressive symptom severity (Fig. 1).

Discussion

Principal findings

This study found a substantial burden of psychological symptoms among Syrian patients with COPD, with clinically relevant anxiety present in 30.9% and clinically relevant depression in 73.9% of participants. Although several sociodemographic, behavioral, clinical, and respiratory variables were

associated with anxiety and depression severity in bivariate analyses, the multivariable models showed a more focused pattern. Older age and challenge burden score remained independently associated with anxiety severity, whereas challenge burden score and longer COPD duration were the main independent correlates of depression severity. In contrast, FEV1% predicted and GOLD spirometric category were not independently associated with either anxiety or depression after adjustment. These findings suggest that psychological distress in this cohort was more closely linked to cumulative patient-reported symptom and functional burden than to spirometric severity alone.

Demographic and socioeconomic context

The demographic profile of our cohort reflects a socially and occupationally vulnerable COPD population, with predominance of males, rural residence, low educational attainment, current smoking, and occupational exposure. This pattern is broadly consistent with regional COPD studies from Egypt, Türkiye, and Pakistan, where COPD samples were also frequently characterized by male predominance, smoking, low education, and environmental or occupational exposures [9, 11, 12]. In the Syrian context, these characteristics may have particular relevance. Rural residence, limited income, lower health literacy, transportation barriers, and medication costs may reduce access to regular follow-up, pulmonary rehabilitation, smoking-cessation services, and mental-health support; notably, only 35.3% of patients in our cohort reported regular physician follow-up. Similar contextual influences were emphasized in the Pakistani mixed-methods study, where financial constraints, dependence on family decision-making, self-care difficulties, and fear about the future contributed to psychological distress among COPD patients [9]. Therefore, the high psychological burden observed in our study should be interpreted not only as a clinical consequence of COPD, but also within a broader socioeconomic and healthcare-access context.

Burden and under-recognition of psychological symptoms

The prevalence of clinically relevant depression in our cohort was strikingly high. Although estimates vary widely across studies because of differences in setting, disease phase, and screening tools, our depression prevalence was close to that reported in an American study of patients hospitalized for severe COPD exacerbations, where clinical depression was found in 73.0% of patients [13]. This similarity is notable because our study excluded patients with acute exacerbation at the time of assessment. Lower estimates have been reported in other settings, including 42.01% among hospitalized Chinese patients with AECOPD using PHQ-9 and 23.0% self-reported depression/anxiety in a large Swedish primary-care COPD cohort [7, 14]. These differences may reflect variation in disease acuity, healthcare access, cultural expression of distress, and the use of screening scales versus self-reported diagnosis or symptoms.

A particularly important finding was the gap between standardized screening and patient-reported recognition of psychological distress. Although 73.9% met the PHQ-9 threshold for clinically relevant depression and 30.9% met the GAD-7 threshold for clinically relevant anxiety, only 15.3% directly reported anxiety/depression as a challenge. This discrepancy may reflect under-recognition, stigma, or somatic

expression of distress. Anxiety and depression in COPD are often missed because respiratory symptoms dominate clinical encounters and overlap with fatigue, sleep disturbance, reduced activity, and dyspnea [2]. This supports the need for routine screening using brief tools such as GAD-7 and PHQ-9, particularly in settings where psychological symptoms may be underreported or culturally minimized [2, 8, 9].

Symptom burden versus spirometric severity

In bivariate analyses, both anxiety and depression severity were associated with markers of respiratory disease burden. The strongest associations were observed for mMRC dyspnea score with both anxiety severity ($r = 0.612$, $p < 0.001$) and depression severity ($r = 0.568$, $p < 0.001$), followed by FEV1% predicted with anxiety severity ($r = -0.503$, $p < 0.001$) and depression severity ($r = -0.452$, $p < 0.001$). GOLD group also differed significantly across anxiety and depression severity categories. However, after adjustment, FEV1% predicted and GOLD category were no longer independently associated with either outcome. Instead, challenge burden score was the most consistent independent predictor, with each one-point increase associated with substantially higher anxiety severity (adjusted OR = 6.50, $p < 0.001$) and depression severity (adjusted OR = 2.19, $p < 0.001$). This suggests that the psychological impact of COPD may be better captured by the patient's lived symptom and functional experience than by airflow limitation alone.

This interpretation is strongly supported by previous studies. A Romanian study using DASS-21 found that CAT-defined symptom burden predicted depression, anxiety, and stress more consistently than GOLD stage [6]. Similarly, a Turkish study reported that CAT and mMRC were more closely related to psychological symptoms and quality-of-life impairment than FEV1 [12]. A Swedish primary-care study also found that mMRC dyspnea ≥ 2 was independently associated with depression/anxiety, whereas FEV1% predicted was not significant after adjustment [7]. Evidence from Greece further shows that anxiety and depression can be present even in mild and moderate COPD, supporting screening before patients reach advanced or oxygen-dependent stages [8]. Together, these findings reinforce the central message of our study: spirometry is essential for COPD diagnosis and staging, but it does not fully capture the psychological burden experienced by patients.

Modifiable behavioral and functional factors

Several modifiable factors were associated with anxiety and depression severity in bivariate analyses, including smoking exposure, physical activity, sleep difficulty, fatigue, daily-task difficulty, and regular follow-up. The most clinically meaningful associations were observed for functional and symptom-related variables: fatigue was strongly associated with both anxiety severity (Cramer's $V = 0.556$, $p < 0.001$) and depression severity (Cramer's $V = 0.573$, $p < 0.001$), as was difficulty performing daily tasks (anxiety: Cramer's $V = 0.518$, $p < 0.001$; depression: Cramer's $V = 0.569$, $p < 0.001$). Weekly physical activity and regular physician follow-up were also significantly related to both outcomes. Although these variables lost independent significance after adjustment, this likely reflects their overlap with challenge burden rather than lack of clinical importance. Sleep disturbance is especially relevant, as 71.9% of patients reported sleep difficulty and it was significantly associated with both anxiety and depression

severity. Previous studies have linked poor sleep in COPD to depression, functional impairment, and reduced quality of life [13, 15]. A multinational study also found that sleep duration was associated with depression in obstructive airway disease populations, with physical activity partly mediating this relationship in some cohorts [16].

Physical inactivity and smoking may further reinforce psychological distress through a dyspnea–avoidance–deconditioning cycle. A scoping review identified dyspnea, reduced exercise capacity, disease burden, age, and depression as major barriers to physical activity in COPD [4]. The NHANES Life’s Essential 8 study found that each 10-point increase in LE8 score was associated with lower odds of depression among adults with COPD, with physical activity, nicotine exposure, and sleep health among the most relevant components [17]. Current smoking was also independently associated with depression/anxiety in the Swedish primary-care study and was identified as a modifiable risk factor for depression in a Chinese AECOPD biomarker study [7, 18]. These findings support practical, low-cost interventions in Syria focused on smoking cessation, sleep improvement, gradual activity plans, and symptom-guided self-management.

Follow-up, self-management, and Syrian care implications

Only a minority of patients reported regular physician follow-up, and this variable was associated with both anxiety and depression severity in bivariate analyses. In a resource-limited setting, irregular follow-up may increase uncertainty, delay treatment adjustment, reduce adherence, and limit opportunities for education and reassurance. Evidence from Germany suggests that COPD may be associated with medication underuse, highlighting the importance of treatment review and continuity of care [19]. A Turkish study of pulse oximeter use among COPD patients receiving long-term oxygen therapy suggested that home monitoring may reduce some non-exacerbation-related healthcare use without increasing anxiety or symptom severity [20]. While home monitoring may not be feasible for all Syrian patients, structured follow-up, inhaler review, education about exacerbation warning signs, and family involvement are realistic and clinically relevant strategies.

Family-supported and self-management approaches may be particularly suitable in Syria, where family members often play a central role in patient care. A Thai randomized trial showed that a self- and family-management intervention improved dyspnea, exercise tolerance, and family function in older COPD patients [21]. A U.S. trial protocol also reflects growing interest in remotely delivered, family-partnered coping-skills interventions for COPD-related depressive symptoms [22]. These approaches support adapting COPD care toward a more integrated model that combines respiratory management, psychological screening, self-management education, and family support.

Biological plausibility and prognostic relevance

Although our study did not measure inflammatory or neurobiological markers, existing evidence supports the biological plausibility of COPD-related depression. A Chinese study of severe COPD found that depressive symptoms were associated with lower serum tryptophan and higher kynurenine-to-tryptophan ratio, suggesting involvement of inflammation-related metabolic pathways [23]. Another

Chinese AECOPD study found that depression was associated with lower BDNF and IL-10 and higher PD-1, MMP-9, IL-1 β , and TNF- α , supporting a role for neuroinflammation, immune dysregulation, and reduced neurotrophic support [18]. These findings suggest that depression in COPD should not be viewed only as an emotional reaction to chronic illness, but as a multidimensional condition involving biological, behavioral, and social pathways.

Strengths and limitations

This study has several strengths. It used validated Arabic versions of GAD-7 and PHQ-9, included spirometric assessment at data collection, and evaluated both clinical and patient-reported burden in the same cohort. The study also provides data from Syria, a setting where evidence on mental health among patients with COPD remains limited.

However, several limitations should be acknowledged. First, the cross-sectional design prevents causal inference between COPD-related factors, symptom burden, anxiety, and depression. Second, the single-center hospital-based design and convenience sampling may limit generalizability to all Syrian patients with COPD, especially those without access to specialist care. Third, anxiety and depression were assessed using screening instruments rather than structured psychiatric interviews. Fourth, detailed data on exacerbation history, treatment adherence, medication availability, and long-term outcomes were not collected. Fifth, sparse categories in some variables, such as home oxygen use and COPD duration longer than 5 years, may have affected regression estimates. Finally, the challenge burden score included an anxiety/depression-related challenge item and other components such as sleep difficulty and fatigue, which may overlap conceptually with psychological distress scales. Therefore, its association with GAD-7 and PHQ-9 should be interpreted as reflecting cumulative patient-reported symptom and functional burden rather than as proof of an independent causal predictor.

Conclusion

This study demonstrated a substantial burden of anxiety and, particularly, depressive symptoms among Syrian patients with COPD attending a tertiary outpatient pulmonary clinic. Although spirometric impairment and GOLD category were associated with psychological severity in bivariate analyses, they were not independently associated with anxiety or depression after adjustment. Instead, cumulative patient-reported challenge burden was the most consistent correlate of both anxiety and depressive symptom severity, suggesting that the lived symptom and functional experience of COPD may be more closely related to psychological distress than airflow limitation alone. These findings support integrating brief mental-health screening, symptom-burden assessment, smoking-cessation counseling, sleep and activity interventions, self-management education, and structured follow-up into routine COPD care in Syria. Resource-sensitive, family-supported approaches may be particularly relevant in settings with limited access to specialized pulmonary rehabilitation and mental-health services.

Declarations

All authors reviewed and approved the final manuscript and agreed to be accountable for all aspects of the work, including the accuracy and integrity of the data and analyses.

Ethics approval and consent to participate

The study protocol was approved by the Ethics Committee of the Syrian Private University (SPU), Faculty of Medicine (Approval No. MD-30032026-131). This was a cross-sectional, hospital-based study conducted among patients with established COPD attending the pulmonary outpatient clinic at Damascus Hospital, Syria. Verbal informed consent was obtained from all participants before enrollment. The study was conducted in accordance with the Declaration of Helsinki.

Consent for publication

Not applicable. The manuscript contains no identifiable personal data from any participant.

Competing interests

The authors declare no competing interests.

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Conducted the statistical analysis, performed data curation, contributed to interpretation of the data, and participated substantially in manuscript drafting and writing.

Othman Alawad Almlhem

Contributed to data acquisition, questionnaire administration, literature review, and manuscript drafting.

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Supervised the study, provided academic, clinical, and methodological guidance, contributed to interpretation of the findings, and critically reviewed the manuscript.

Clinical trial number

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Author Contribution

Ibrahim Alkhatib: Conceived and designed the study, contributed to data acquisition, interpreted the findings, and participated substantially in manuscript drafting and writing. Mohammad Alaa Aldakak: Conducted the statistical analysis, performed data curation, contributed to interpretation of the data, and participated substantially in manuscript drafting and writing. Othman Alawad Almlhem: Contributed to data acquisition, questionnaire administration, literature review, and manuscript drafting. Lama Alsaoub: Contributed to data acquisition, data entry, questionnaire administration, coordination of study documentation, discussion writing, and critical review of the manuscript. Hussam Al-Bardan: Supervised the study, provided academic, clinical, and methodological guidance, contributed to interpretation of the findings, and critically reviewed the manuscript. All authors reviewed and approved the final manuscript and agreed to be accountable for all aspects of the work, including the accuracy and integrity of the data and analyses.

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None

Data Availability

De-identified data and analysis outputs are available from the corresponding author on reasonable request.

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Figures

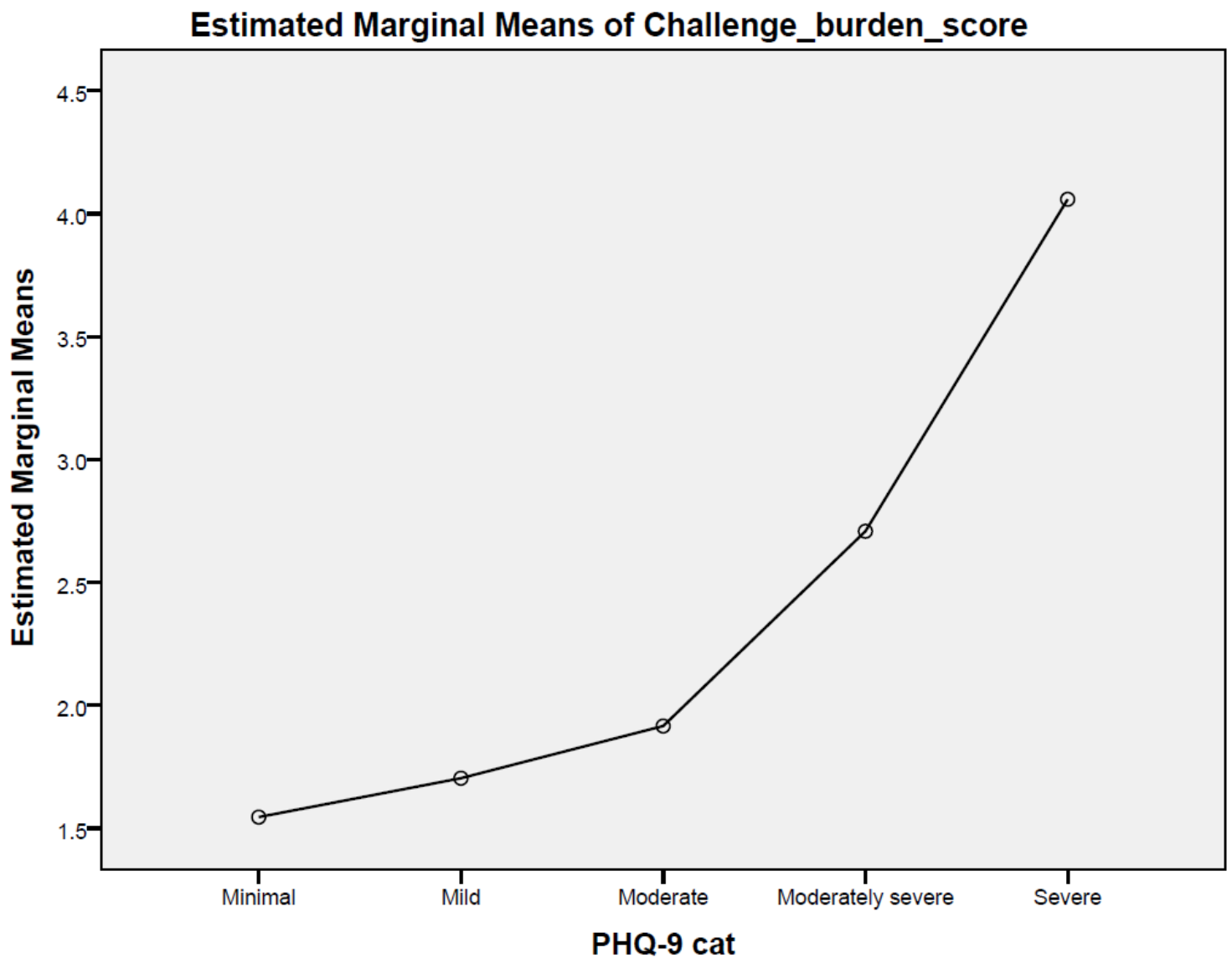


Figure 1

Estimated marginal means of challenge burden score across PHQ-9 depression severity categories.

The figure shows a stepwise increase in the estimated marginal mean challenge burden score from minimal/no depression to severe depression, indicating that greater cumulative patient-reported symptom and functional burden was associated with higher depressive symptom severity. PHQ-9, Patient Health Questionnaire-9.

Supplementary Files

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