The prevalence and implications of depression and anxiety in patients with bronchiectasis: a systematic review and meta-analysis

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Depression and anxiety are common in patients with bronchiectasis. Depression is more common in females and significantly associated with bronchiectasis exacerbation. Depression and anxiety are closely associated with poor health-related quality of life. https://bit.ly/4cwfaWR

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Abstract

Background Comorbidities significantly affect bronchiectasis prognosis. Depression and anxiety are frequently encountered psychological comorbidities that have the greatest impact on bronchiectasis. This systematic review aimed to identify the prevalence of depression and anxiety and describe their implications for bronchiectasis.

Methods Three databases were searched from their inception to October 2023 for studies reporting the prevalence and/or clinical implications of depression and anxiety in patients with bronchiectasis. Two independent reviewers rated the quality of the evidence presented in the studies using the risk of bias tool for prevalence studies.

Results Of the 50 studies identified, 17 studies with 2637 patients were included. The overall risk of bias was classified as low (10 studies) or moderate (seven studies). The pooled prevalence of depression and anxiety was 31% (95% CI 24–38%) and 34% (95% CI 28–40%), respectively. Depression was significantly higher in female compared to male patients (risk difference 10%, 95% CI 0–21%) and associated with bronchiectasis exacerbation (adjusted odds ratio 1.72, 95% CI 1.28–2.15). Depression and anxiety are closely associated with poor health-related quality of life. However, clinical outcomes including dyspnoea symptoms, severity index, computed tomography score, lung function and physical activity were not associated with depression or anxiety.

Conclusion This study revealed a high prevalence of depression and anxiety among patients with bronchiectasis. Depression was more prevalent in females and is significantly associated with bronchiectasis exacerbation. Depression and anxiety were associated with poor health-related quality of life.

Introduction

Bronchiectasis is radiologically defined as an irreversible airway dilatation as observed on chest computed tomography (CT) scans [1]. Most patients with clinically apparent bronchiectasis experience at least one of the following symptoms: cough, sputum production, haemoptysis, exacerbation, and recurrent or chronic bacterial infection. Concurrent comorbidities have a significant impact on mortality and on the prognosis of bronchiectasis, including exacerbation, hospitalisation and quality of life [2, 3]. Depression and anxiety are frequently encountered psychological comorbidities in patients with chronic airway diseases and are considered treatable traits that should be sought because they are independently associated with the exacerbation of underlying airway diseases [4]. Additionally, depression and anxiety can lower adherence to treatment and pulmonary rehabilitation, contributing to the severity of respiratory impairment [5, 6].

International guidelines state that comorbidities should be assessed at the first diagnosis of bronchiectasis and chronic rhinosinusitis (CRS) and that depression and/or anxiety are comorbidities with the greatest

impact on bronchiectasis [7, 8]. In a systematic review, the pooled prevalence of CRS was 62% in patients with bronchiectasis [9]. CRS was associated with heightened bronchiectasis severity, impaired health-related quality of life (HRQOL), increased inflammatory markers, and a greater risk of exacerbation, but not with the degree of airflow obstruction. Only one scoping review has reported the prevalence and impact of overall comorbidities of bronchiectasis, including depression and anxiety [10]. However, the estimated prevalence and detailed clinical implications of concurrent depression and anxiety in patients with bronchiectasis have not yet been reported.

This systematic review aimed to identify the prevalence of depression and anxiety in patients with bronchiectasis. The secondary aim is to describe the clinical implications of depression and anxiety in patients with bronchiectasis.

Methods

Search strategy and selection criteria

We performed a systematic review and meta-analysis according to the Meta-analysis Of Observational Studies in Epidemiology (MOOSE) guidelines [11]. The protocol was registered in the PROSPERO database (CRD42023478475). The MEDLINE, Embase and Cochrane Library databases were searched by investigators from database inception to October 2023. The controlled vocabulary and corresponding text words were included in the search strategy (supplementary table S1 for details). Initial search was conducted without restrictions on language, study design, conference abstracts and publication status.

Endnote software was used to manage the retrieval of results. After filtering out duplicates, the titles and abstracts of all retrieved citations were independently screened by two authors (M-S. Chang and J-H. Lee). This was followed by a full-text review. Studies were eligible for inclusion if they met the following criteria: 1) diagnosis of bronchiectasis was made either by chest high-resolution CT (HRCT) or chest CT; 2) the prevalence of depression and anxiety was acquired from validated screening questionnaires when bronchiectasis was stable for at least 4 weeks from exacerbation or hospitalisation; and 3) association with clinical outcomes of bronchiectasis, including symptoms, HRQOL, severity of bronchiectasis, CT score, lung function, functional exercise capacity and exacerbation. Studies were included if the prevalence and/or clinical implications of depression and anxiety were reported, whereas studies were excluded if all study participants consisted of cystic fibrosis (supplementary table S2). Discrepancies between authors were resolved by consensus.

Data extraction and quality assessment

Two authors (M-S. Chang and J-H. Lee) independently extracted data using a standard MicroSoft Excel template. The extracted data included details of the study design, patient characteristics, definition of bronchiectasis, prevalence of depression and anxiety, and depression and anxiety screening, in addition to clinical parameters such as symptoms, HRQOL, severity of bronchiectasis, CT score, lung function, functional exercise capacity and exacerbation. When published study results did not offer complete data or clear information, such as lack of a cut-off value of the screening questionnaire for depression and anxiety, the corresponding author was contacted by email for further clarification.

Two authors (M-S. Chang and J-H. Lee) independently assessed and appraised the quality of the final included studies after full-text review using the 10-item Risk of Bias Tool developed by Hoy *et al.* [12]. Disagreements were resolved through discussion. The items were individually scored using a dichotomous response and scores of 1 (high) or 0 (low) were assigned to each item. The sum of the assigned scores for the 10 items ranged from 0 to 10, with higher scores indicating a greater risk of bias. The overall risk of bias in the included studies was classified based on the total score as: low (0–3), moderate (4–6) and high (7–10). This classification was established by consensus of two authors (M-S. Chang and J-H. Lee).

Statistical analysis

The selected studies reported the binary variables of depression and anxiety based on a cut-off score for the screening questionnaire. The proportions of depression and anxiety were combined to present a pooled prevalence for all studies. The random-effects model was used because of the expected heterogeneity across studies and to provide a conservative estimate of the prevalence of depression and anxiety. Heterogeneity across studies was assessed using the I^2 statistic, which ranged from 0% to 100%. Heterogeneity was categorised to low level (25–49%), moderate level (50–74%), and high level (⩾75%). A meta-analysis of the clinical outcomes was performed when specific variables in binary or continuous forms were presented in at least two studies. Sensitivity analyses were performed in studies with a low risk of bias and a larger sample size for the outcome of prevalence, whereas each study was omitted for the

outcome of sex differences. Publication bias was examined using Egger's test and funnel plot inspection when at least 10 studies were included. Data analyses were performed using the Stata 18 software.

Results

Study characteristics

A total of 721 articles were retrieved. After removing duplicates, the titles and abstracts of the articles were screened. 50 articles were subjected to full-text review, 17 of which met the inclusion criteria (figure 1 and supplementary table S3). The articles for the systematic review included 16 cross-sectional studies and one prospective cohort study [13–29]. A total of 2637 participants were included in this study. Mean age ranged from 32.2 years to 66.2 years, with forced expiratory volume in 1 s (FEV_1) ranging from 32.9% to 78.5%. 15 studies reported prevalence and clinical implications of both depression and anxiety, whereas two studies reported only one or the other (table 1). The Hospital Anxiety and Depression Scale-Depression (HADS-D) and HADS-Anxiety (HADS-A) were the most frequently used instruments: 76.5% (13/17) for depression and 81.2% (13/16) for anxiety. Definitions and prevalence using the instrument and the clinical implications for depression and anxiety are described in detail in supplementary tables S4 and S5.

Quality assessment

The overall quality of the 17 studies ranged from low to moderate risk of bias (table 2). The high risk of bias items were mostly related to sampling biases because almost all the studies were conducted in a single centre and the sampling method was not specified.

Prevalence

The prevalence of depression was reported in 15 studies [13–20, 22–28], while that of anxiety was reported in 14 studies [13–15, 17–20, 22–28]. The pooled prevalence of depression was 31% (95% CI 24–38%; I^2=93%) (figure 2a) and pooled prevalence of anxiety was 34% (95% CI 28–40%; I^2=87%) (figure 2b). Funnel plot asymmetry was identified in the prevalence of depression (Egger's test, p<0.001) and anxiety (p=0.003). Subgroup analysis showed significant differences in the prevalence of depression and anxiety according to the screening questionnaire (supplementary figure 1). The prevalence of depression

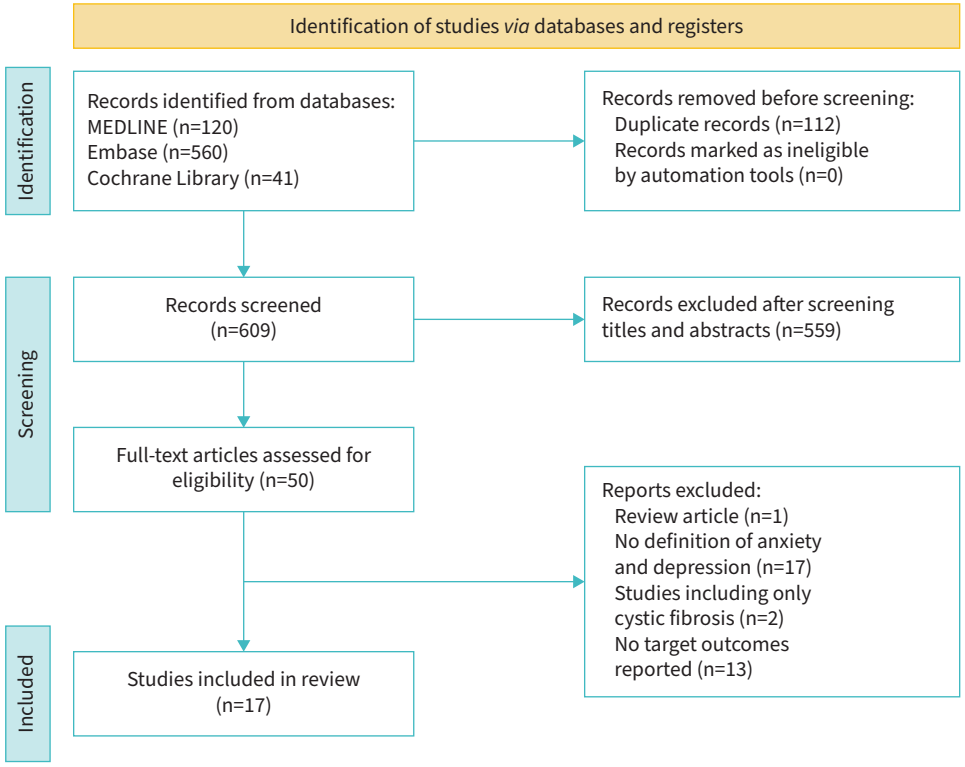

FIGURE 1 Flow diagram of included studies based on Preferred Reporting Items for Systematic Reviews and Meta-Analyses protocols.

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TABLE 1 Characteristics of included studies

Study	Study design	Country	Participants (n)	Age (years)	Sex (% female)	FEV_1 (% pred)	Clinical outcomes
Gao *et al.* [13] (2023)	Prospective cohort	China	434	59.3±11.9	60.8	71.2	Exacerbation, hospitalisation, time to first exacerbation
Umoh *et al.* [14] (2022)	Cross-sectional	Nigeria	103	49.1±14.4	47.6	NR	HRQOL (WHOQOL-BREF)
Ceyhan *et al.* [15] (2022)	Cross-sectional	Turkey	90	45.0±17.0	58.9	66.1±29.2	Exacerbation, BSI, FACED, CT score, HRQOL (SF-36 and QoL-B)
Lee *et al.* [16] (2021)	Cross-sectional	Korea	810	64.3±9.3	55.8	64.7±20.9	Exacerbation, hospitalisation, BSI, FACED, CT score, FEV_1%, mMRC, HRQOL (BHQ)
Bekir *et al.* [17] (2020)	Cross-sectional	Turkey	90	45.1±16.8	58.9	66.1±29.4	Exacerbation, BSI, FACED, FEV_1%, mMRC
Yildiz *et al.* [18] (2018)	Cross-sectional	Turkey	41	43.8±13.9	65.9	70.6±18.3	Physical activity (ISWT)
Gao *et al.* [19] (2018)	Cross-sectional	China	163	45.8±13.8	62.6	67.1±22.9	Exacerbation, BSI, FACED, CT score, FEV_1%, mMRC, sleep disturbance, HRQOL (SGRQ)
Özgün *et al.* [20] (2016)	Cross-sectional	Turkey	133	49.5±14.5	60.9	62.2±23.8	ER visit, hospitalisation, FEV_1%
Bulcun *et al.* [21] (2015)	Cross-sectional	Turkey	78	48.1±13.5	59.0	78.5±18.4	HRQOL (SOLQ)
Olveira *et al.* [22] (2014)	Cross-sectional	Spain	205	57.2±18.1	62.4	68.3±22.2	Exacerbation, FEV_1%, mMRC, HRQOL (SGRQ)
Boussoffara *et al.* [23] (2014)	Cross-sectional	Tunisia	53	54.2±17.8	64.2	NR	Hospitalisation, mMRC
Morsi *et al.* [24] (2014)	Cross-sectional	Egypt	33	42.9±11.5	54.5	32.9±16.6	FEV_1%, mMRC, physical activity (6MWD), HRQOL (SGRQ)
Olveira *et al.* [25] (2013)	Cross-sectional	Spain	93	32.2±14.3	55.9	67.0±24.2	Exacerbation, hospitalisation, CT score, FEV_1%, HRQOL (SGRQ)
Girón *et al.* [26] (2013)	Cross-sectional	Spain	74	66.2±14.2	68.9	74.0±23.0	Exacerbation, FEV_1%, mMRC, HRQOL (SGRQ)
Ryu *et al.* [27] (2010)	Cross-sectional	Korea	33	63.3±28.1	54.5	55.0±19.0	Not reported
O'Leary *et al.* [28] (2002)	Cross-sectional	UK	111	52.0±13.0	60.4	66.4±28.8	CT score, FEV_1%, mMRC, physical activity (ISWT), HRQOL (SGRQ)
Chan *et al.* [29] (2002)	Cross-sectional	China	93	59.0±14.2	65.6	73.5±29.2	HRQOL (SGRQ)

Data are presented as mean±SD unless otherwise indicated. HRQOL: health-related quality of life; WHOQOL-BREF: World Health Organization quality of life brief; BSI: Bronchiectasis Severity Index; CT: computed tomography; SF-36: Short Form-36; QoL-B: Quality of Life-Bronchiectasis; FEV_1: forced expiratory volume in 1 s; mMRC: modified Medical Research Council; BHQ: Bronchiectasis Health Questionnaire; ISWT: incremental shuttle walk test; SGRQ: St George's Respiratory Questionnaire; ER: emergency room; SOLQ: Seattle Obstructive Lung Disease Questionnaire; 6MWD: 6-min walk distance.

TABLE 2 Quality assessment of included studies

Study	Risk of bias for individual items										
	1	2	3	4	5	6	7	8	9	10	Summary
Gao *et al.* [13] (2023)	Low	High	Low	Low	Low	Low	Low	Low	Low	Low	Low
Umoh *et al.* [14] (2022)	High	High	High	Low	Low	Low	Low	Low	Low	Low	Low
Ceyhan *et al.* [15] (2022)	High	High	High	Low	Low	Low	Low	Low	Low	Low	Low
Lee *et al.* [16] (2021)	Low	High	Low	Low	Low	Low	Low	Low	Low	Low	Low
Bekir *et al.* [17] (2020)	High	High	High	Low	Low	Low	Low	Low	Low	Low	Low
Yildiz *et al.* [18] (2018)	High	High	High	High	Low	Low	Low	Low	Low	Low	Moderate
Gao *et al.* [19] (2018)	High	High	High	Low	Low	Low	Low	Low	Low	Low	Low
Özgün *et al.* [20] (2016)	High	High	High	Low	Low	Low	Low	Low	Low	Low	Low
Bulcun *et al.* [21] (2015)	High	High	High	High	Low	Low	Low	Low	Low	Low	Moderate
Oliveira *et al.* [22] (2014)	Low	High	Low	Low	Low	Low	Low	Low	Low	Low	Low
Boussoffara *et al.* [23] (2014)	High	High	High	High	Low	Low	High	Low	Low	High	Moderate
Morsi *et al.* [24] (2014)	High	High	High	High	Low	Low	Low	Low	High	Low	Moderate
Oliveira *et al.* [25] (2013)	High	High	High	Low	Low	Low	Low	Low	Low	Low	Low
Girón *et al.* [26] (2013)	High	High	High	Low	Low	High	High	Low	Low	High	Moderate
Ryu *et al.* [27] (2010)	High	High	High	High	Low	Low	High	Low	Low	Low	Moderate
O'Leary *et al.* [28] (2002)	High	High	High	Low	Low	Low	Low	Low	Low	Low	Low
Chan *et al.* [29] (2002)	High	High	High	Low	Low	High	Low	Low	Low	High	Moderate

1: Was the study's target population a close representation of the national population in relation to relevant variables? 2: Was the sampling frame a true or close representation of the target population? 3: Was some form of random selection used to select the sample, or was a census undertaken? 4: Was the likelihood of nonresponse bias minimal? 5: Were data collected directly from the subjects? 6: Was an acceptable case definition used in the study? 7: Was the study instrument that measured the parameter of interest shown to have reliability and validity? 8: Was the same mode of data collection used for all subjects? 9: Was the length of the shortest prevalence period for the parameter of interest appropriate? 10: Were the numerators and denominators for the parameter of interest appropriate? Summary: Overall risk of study bias.

was significantly higher in female patients compared to male patients (risk difference 10%, 95% CI 0–21%; I^2=81%), whereas prevalence of anxiety did not differ (supplementary figure 2).

In sensitivity analyses, the prevalence of depression decreased to 26% (95% CI 20–32%; I^2=90%) in studies with low risk of bias and 23% (95% CI 17–28%; I^2=87%) in studies with sample size ⩾100. However, the predominance of females with depression was not affected (supplementary table S6). Moreover, the prevalence of anxiety decreased to 30% (95% CI 24–35%; I^2=80%) in studies with low risk of bias and 29% (95% CI 21–36%; I^2=87%) in studies with sample size ⩾100. No sex differences in anxiety levels were identified (supplementary table S7).

Exacerbation

Patients with depression had a higher number of exacerbations compared to those without depression (mean difference (MD) 0.66, 95% CI 0.20–1.11; I^2=71%) (figure 3a). Depression was associated with the risk of having exacerbation (adjusted OR 1.72, 95% CI 1.28–2.15; I^2=0%) (supplementary figure 3a). However, two studies reported no association between depression and risk of exacerbation (unadjusted OR 0.94, 95% CI 0.53–1.35; I^2=48%) (supplementary figure 3b). A prospective study reported that depression was associated with hospitalisation (rate ratio 2.06, 95% CI 1.21–3.51; p=0.008) [13]. However, other cross-sectional studies have not identified a relationship with hospitalisation [16, 20, 23, 25].

Patients with anxiety had a higher number of exacerbations than those without anxiety (MD 0.69, 95% CI 0.16–1.22; I^2=66%) (figure 3b). Two studies showed a positive correlation between HADS-A scores and the frequency of exacerbations [15, 25]. However, no significant association between anxiety and risk of exacerbation was noted in a meta-analysis (unadjusted OR 1.28, 95% CI 0.94–1.63; I^2=9%) (supplementary figure 3c) and prospective observational study [13]. Hospitalisation did not correlate with anxiety scores and was not associated with anxiety [13, 20, 23, 25].

Bronchiectasis severity

Bronchiectasis Severity Index (BSI) was significantly higher for patients with depression than in those without depression in one study [16], whereas other studies did not find a significant relationship [15, 17, 19].

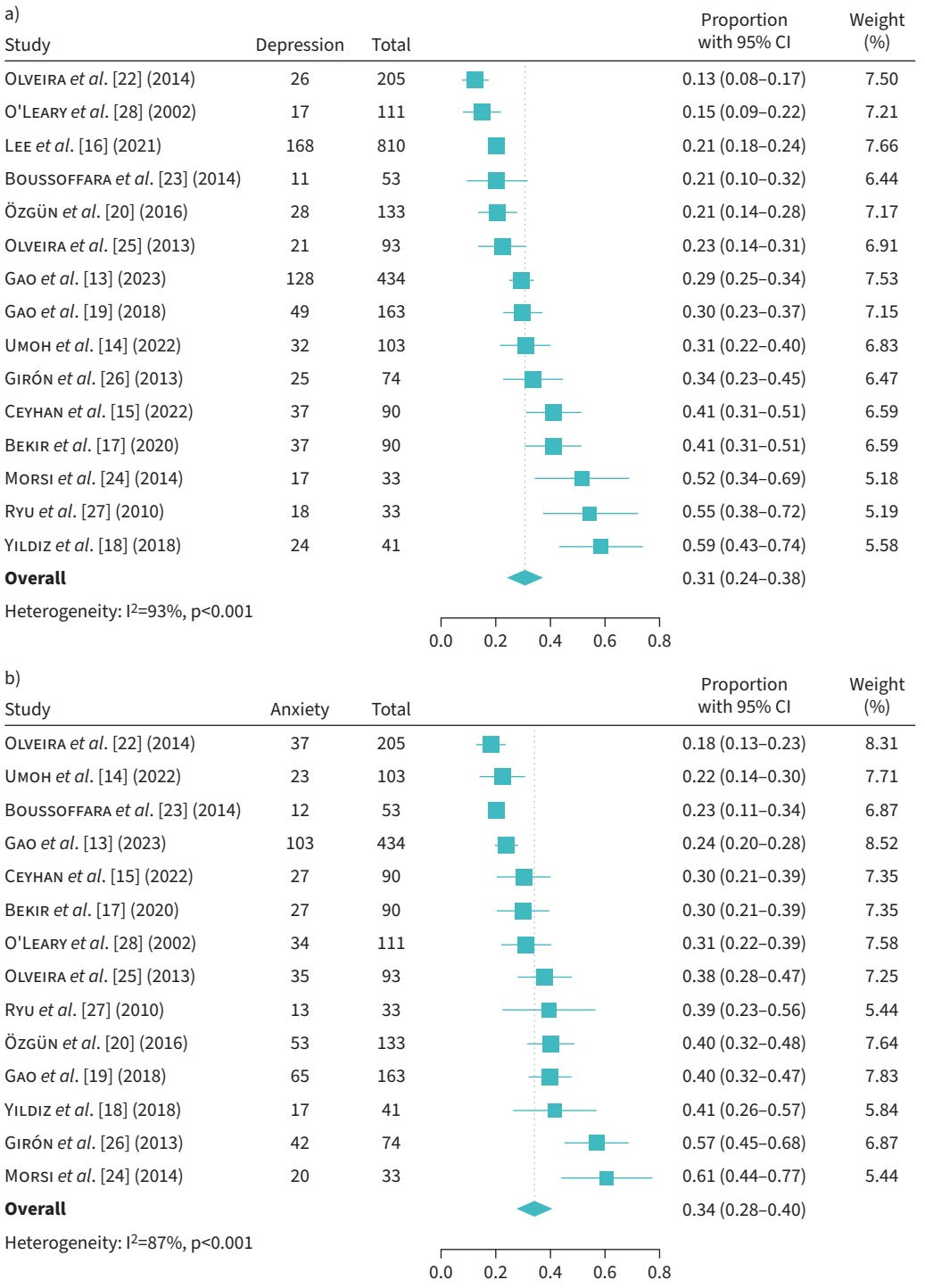

FIGURE 2 Pooled prevalence of the depression (a) and anxiety (b) in patients with bronchiectasis.

FACED score was not associated with depression in any of the reported studies [15–17, 19], and neither BSI nor FACED were related to anxiety [15, 17, 19].

HRCT scores did not correlate with depressive symptoms in any of the reported studies [15, 16, 19, 25, 28]. One study showed an association between HRCT scores and anxiety in the univariate analysis; however, an association was not found in the multivariate analysis [19]. Three additional studies did not show a significant relationship between HRCT scores and anxiety [15, 25, 28].

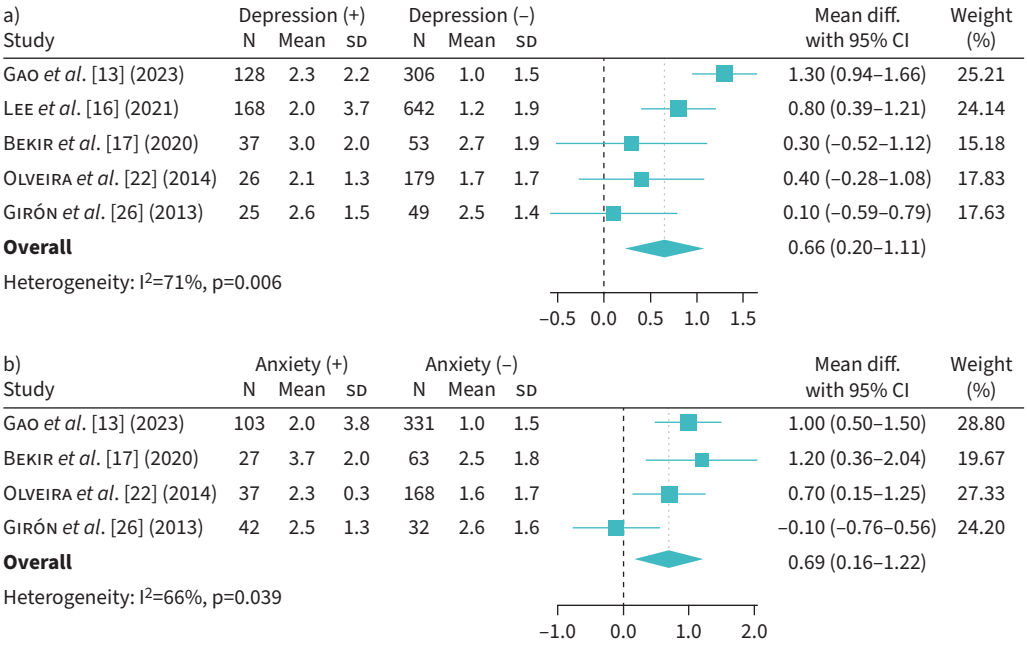

FIGURE 3 Mean differences in the number of exacerbations during a previous year in depression (a) and anxiety (b).

The mean difference of FEV_1% was −3.78% (95% CI −7.47–−0.10; I^2=20%) between patients with and without depression (figure 4a). Depressive symptoms did not correlate with FEV_1% (r 0.029, 95% CI −0.100–0.158; I^2=0%) (figure 4b). FEV_1% did not significantly differ between patients with and without anxiety (MD 0.05, 95% CI −4.48–4.59; I^2=0%) (figure 4c). Anxiety symptoms did not correlate with FEV_1% (r −0.062, 95% CI −0.190–0.068; I^2=0%) (figure 4d).

The mean modified Medical Research Council (mMRC) score was significantly higher in patients with depression compared to those without depression (MD 0.38, 95% CI 0.16–0.60; I^2=54%) (figure 5a). The correlation between mMRC scores and depressive symptoms displayed contradicting results [24, 28]. The mean mMRC score was not significantly different between patients with and without anxiety (MD −0.18, 95% CI −0.62–0.27; I^2=77%) (figure 5b). Additionally, the mMRC score did not correlate with anxiety

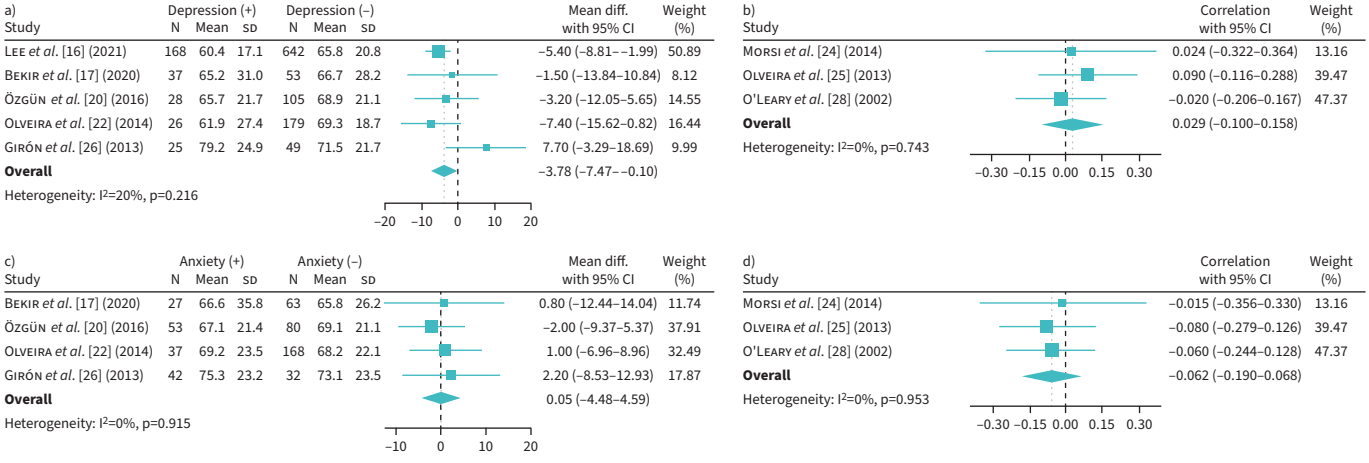

FIGURE 4 Pooled (a) mean differences of forced expiratory volume in 1 s (FEV_1)% between patients with and without depression (a) and correlation of FEV_1% with depressive symptom (b). Pooled mean differences of FEV_1% between patients with and without anxiety (c) and correlation of FEV_1% with anxiety symptom (d).

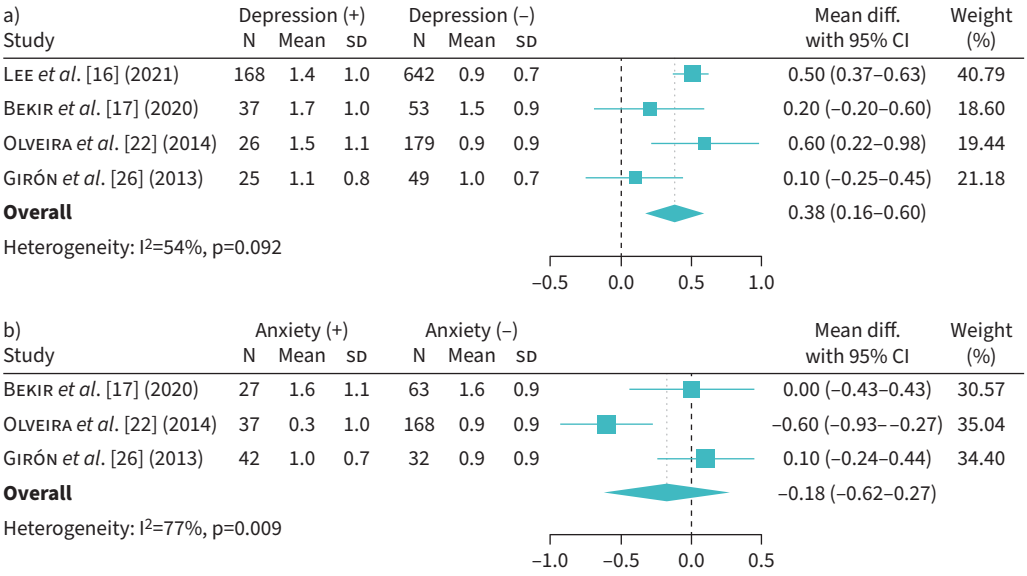

FIGURE 5 Mean difference of modified Medical Research Council dyspnoea scales in depression (a) and anxiety (b).

symptoms [28]. There was no association between depression or anxiety and mMRC scores (supplementary figure 4).

Physical activity was measured using the shuttle walk test and 6-min walk test. Physical activity did not correlate with depressive symptoms (r −0.113, 95% CI −0.425–0.199; I^2=73%) (figure 6a) and anxiety symptom (r 0.021, 95% CI −0.126–0.168; I^2=0%) (figure 6b).

HRQOL

HRQOL ranges from 0 to 100, with higher scores indicating a poorer quality of life. The mean HRQOL score was significantly higher in patients with depression compared to those without depression (MD 13.28, 95% CI 12.01–14.55; I^2=0%) (figure 7a). The three subdomains of the St George's Respiratory Questionnaire (SGRQ) were consistently higher in patients with depression than in those without

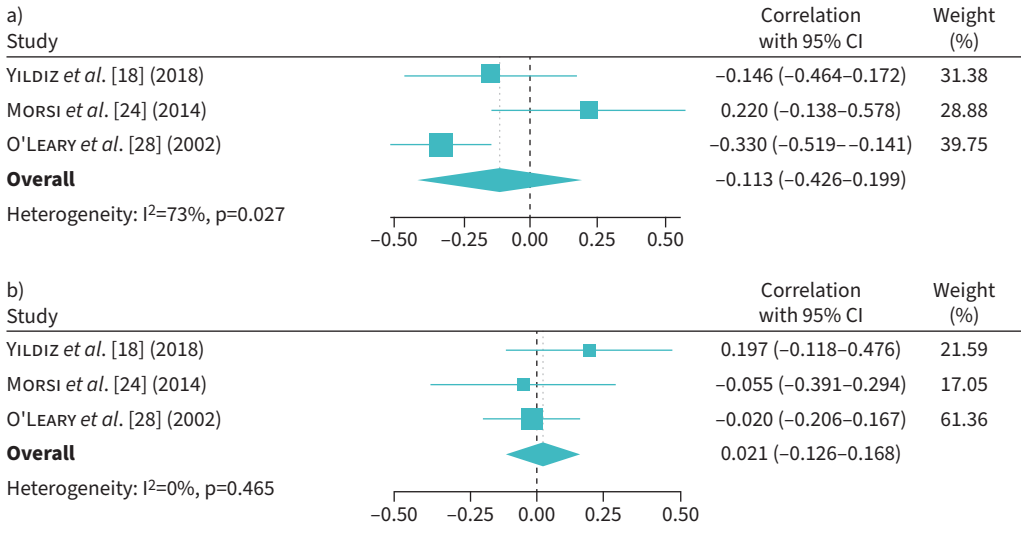

FIGURE 6 Correlation analyses between degree of physical activity and depressive symptoms (a) and anxiety symptoms (b).

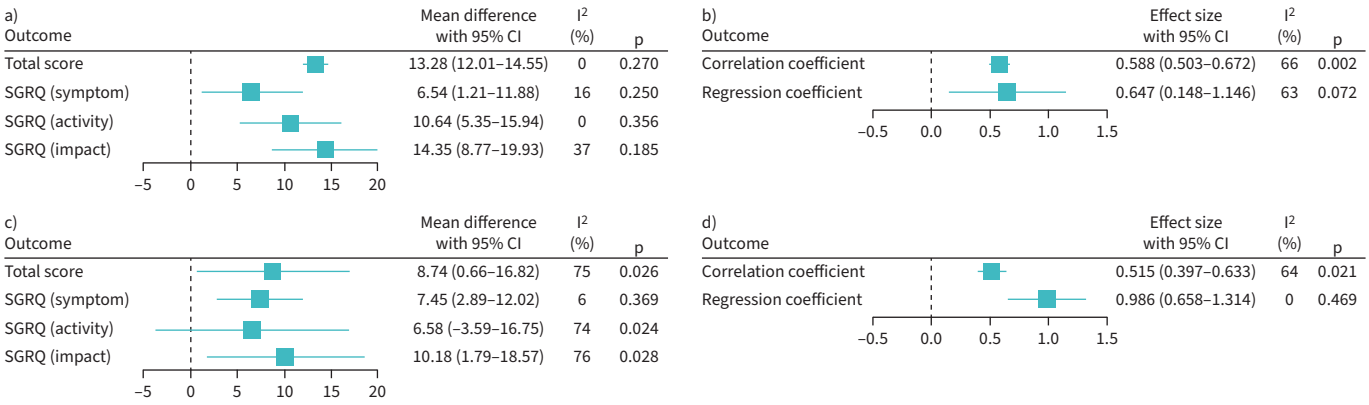

FIGURE 7 Summary of meta-analysis in studies regarding health-related quality of life. Mean difference between patients with and without depression (a) and coefficient outcomes in depression (b). Mean difference between patients with and without anxiety (c) and coefficient outcomes in anxiety (d). SGRQ: St George's Respiratory Questionnaire.

depression (supplementary figure 5). HRQOL significantly correlated with depressive symptoms (r 0.588, 95% CI 0.503–0.672; I^2=66%) and had significant association with depression (regression coefficient: 0.647; 95% CI: 0.148–1.146; I^2=63%) (figure 7b). The mean score of HRQOL was significantly higher in patients with anxiety compared to those without anxiety (MD: 8.74, 95% CI: 0.66–16.82; I^2=75%) (figure 7c). Subdomains of SGRQ such as symptom and impact, except for activity, were significantly higher in patients with anxiety (supplementary figure 6). HRQOL significantly correlated with anxiety symptoms (r: 0.515; 95% CI: 0.397–0.633; I^2=64%) and had significant association with anxiety (regression coefficient 0.986, 95% CI 0.658–1.314; I^2=0%) (figure 7d). Meta-analyses of the correlation coefficient for SGRQ and regression coefficient for depression and anxiety are presented in detail in supplementary figures 7–9.

Discussion

This systematic review and meta-analysis included 17 studies reporting the prevalence and implications of depression and anxiety in individuals with bronchiectasis. The overall risk of bias ranged from low to moderate. The prevalence of depression and anxiety was 31% and 34%, respectively. Female patients had a higher prevalence of depression than male patients. Depression was associated with a higher number of exacerbations. Depression and anxiety were strongly associated with poor HRQOL. However, the clinical outcomes reflecting the severity of bronchiectasis were not associated with depression and anxiety.

The studies included in this review reported a high but wide-ranging prevalence of depression and anxiety. The International Committee on Mental Health in Cystic Fibrosis recommends annual screening for depression and anxiety using the Patient Health Questionnaire-9 and Generalised Anxiety Disorder-7 for individuals aged 12 years and older [30]. This guideline facilitated the implementation of mental health screening in cystic fibrosis clinics [31]. However, the importance of mental health and the need for intervention are rarely addressed in clinical guidelines for bronchiectasis [32]. Given the high rate of depression and anxiety, regular screening and proper intervention should be considered in bronchiectasis clinics.

The variation in prevalence may be due to the use of diverse questionnaires; although the Hospital Anxiety and Depression Scale (HADS) was used in approximately three-quarters of the studies, depression and anxiety were screened using four and three questionnaires, respectively. HADS is a simple and widely adopted screening instrument. However, it measures only limited domains of depressive disorders [33]. HADS excludes somatic symptoms of fatigue and sleep disturbance that are important in diagnosing depression [34]. HADS has not been validated for certain populations, such as individuals with cystic fibrosis [35]. Its diagnostic accuracy is relatively low for COPD and malignancies compared to that of the Patient Health Questionnaire-9 [36–38]. Moreover, varying HADS cut-off values were used to define depression and anxiety. Setting a higher cut-off value generated less sensitivity and more specificity in the screening accuracy of psychological disorders [39]. The study sample size may be another reason for the variation in prevalence. Prevalence of depression and anxiety substantially decreased in studies of larger sample size (⩾100) and publication bias was identified through funnel plot asymmetry, indicating that small-study effect may overestimate the prevalence of depression and anxiety.

A meta-analysis of sex differences in the prevalence of psychological disorders showed that depression was more common in females than in males, which is in line with the general population and those with chronic diseases [40, 41]. However, the prevalence of anxiety did not differ between the male and female patients. Generally, female patients with bronchiectasis have a greater prevalence and severity of bronchiectasis than male patients [42]. In our study, the exacerbation and severity outcomes were not associated with anxiety. Therefore, it is postulated that the greater severity of bronchiectasis in female patients did not increase symptoms of anxiety. Meanwhile, female predominance of anxiety does not always appear in chronic diseases [43].

Depression was significantly associated with exacerbations, whereas anxiety was not. Two studies with the largest sample size demonstrated the association between depression and the risk of having exacerbations with a significant adjusted odds ratio [13, 16]. However, no significant adjusted or unadjusted odds ratios were identified for anxiety. A prospective observational study showed contrasting results between depression and anxiety, in which exacerbation, hospitalisation, and time to first exacerbation were significantly associated with depression. However, anxiety was not associated with exacerbation-related outcomes [13]. These results indicate that depression is a stronger risk factor for exacerbation than anxiety. However, HADS may not effectively capture anxiety symptoms. HADS could not discriminate between depression and anxiety and has not been validated to identify anxiety in bronchiectasis [35, 44]. The implication of anxiety in bronchiectasis exacerbation needs to be re-evaluated with validated screening measures. Immune system activation is closely linked to the development of depression, and a high prevalence of depression has been observed in a range of chronic conditions with elevated inflammation [45]. It is hypothesised that inflammation in peripheral tissue increases the permeability of the blood brain barrier and leads to the entry of inflammatory molecules, which results in structural and functional changes in the brain. Patients with bronchiectasis often experience episodes of exacerbations, which are characterised by the deterioration of respiratory or systemic symptoms that require changes in bronchiectasis treatment [46]. The exacerbations of bronchiectasis are driven by increased airway inflammation [47]. However, screening questionnaires were administered when bronchiectasis was stable: persistent airway inflammation following exacerbation of bronchiectasis may have led to an increase in depression.

Measurements of bronchiectasis severity, such as composite scores (BSI and FACED), HRCT score, lung function, mMRC and physical activity, were not related to depression and anxiety, whereas depression and anxiety were strongly associated with poor HRQOL. Patients with depression showed lower FEV_1 (−3.78%) and higher mMRC scores (0.38) than those without depression. However, these mean differences were within the minimal clinically important differences suggested for COPD, which are 5% (100 mL) in FEV_1 and 0.5 in mMRC [48, 49]. Our results indicate that the measurement of severity outcomes did not reflect the burden of psychological distress in bronchiectasis. In patients with CRS and bronchiectasis, C-reactive protein levels were elevated compared to those in patients without CRS. Levels of inflammatory markers were significantly higher in patients with bronchiectasis, COPD and CRS [9]. In a meta-analysis of inflammatory bowel disease, the active state of the disease compared to the inactive state showed a significantly higher odds ratio for depression and anxiety [43]. Therefore, disease activity rather than disease severity may be linked to psychological distress. Neutrophil elastase activity is associated with a risk of exacerbation and decline in lung function in bronchiectasis [50]. Neutrophil extracellular traps have been associated with quality of life, hospital admissions and mortality [51]. Future studies are warranted to determine whether bronchiectasis activity is related to the risk of developing psychological comorbidities.

This study had several limitations. First, we could not adjust for various confounding factors that could affect the prevalence of psychological disorders. A high level of heterogeneity existed; the kind of screening questionnaires and cut-off values for defining psychological disorders varied in each study. Furthermore, we found publication bias in the included studies, possibly overestimating the prevalence of psychological disorders. For our analysis, we collected data from eight countries. The baseline characteristics of the study participants, cultural behaviour, ethnic characteristics, vulnerability and social status of women may have influenced the response rate to questionnaires on depressive and anxiety symptoms.

Second, only a small number of studies were included in the meta-analysis for the implication outcomes of psychological disorders, which may have limited the provision of strong clinical evidence. Each study collected different variables, and the results of the adjusted analyses were provided in a few studies.

Third, the Bronchiectasis Health Questionnaire [52], a disease-specific measure of HRQOL, was adopted in only one study [16], whereas most studies used the SGRQ. HRQOL measures tailored to specific diseases are more responsive and clinically relevant compared to generic HRQOL measures. Additionally,

the SGRQ and HADS generally have a strong correlation across various conditions [53, 54], making it difficult to distinguish whether this correlation is specific to bronchiectasis or due to the general correlation between the two questionnaires.

In conclusion, this study revealed high prevalence of depression and anxiety in patients with bronchiectasis. Depression was more prevalent in females than in males. Bronchiectasis exacerbation was a risk factor for depression, whereas bronchiectasis severity outcomes, including extent of bronchiectasis in HRCT, lung function, dyspnoea scale and physical activity, were not related to depression. Female predominance and risk factors for anxiety were not identified. Depression and anxiety were closely associated with poor HRQOL. However, clinical evidence regarding the implication of psychological disorders in bronchiectasis is weak due to the small number of studies. A prospective study with a larger sample size should be conducted to optimise the appropriate instrument for screening depression and anxiety with the best cut-off value and to evaluate the precise prevalence of psychological disorders after adjusting for confounding factors. Paramount risk factors that impact the prevalence and severity of psychological disorders, such as bronchiectasis activity rather than severity, need to be evaluated.

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