

# Overview of the prevalence, impact, and management of depression and anxiety in chronic obstructive pulmonary disease

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**Abstract:** More than one third of individuals with chronic obstructive pulmonary disease (COPD) experience comorbid symptoms of depression and anxiety. This review aims to provide an overview of the burden of depression and anxiety in those with COPD and to outline the contemporary advances and challenges in the management of depression and anxiety in COPD. Symptoms of depression and anxiety in COPD lead to worse health outcomes, including impaired health-related quality of life and increased mortality risk. Depression and anxiety also increase health care utilization rates and costs. Although the quality of the data varies considerably, the cumulative evidence shows that complex interventions consisting of pulmonary rehabilitation interventions with or without psychological components improve symptoms of depression and anxiety in COPD. Cognitive behavioral therapy is also an effective intervention for managing depression in COPD, but treatment effects are small. Cognitive behavioral therapy could potentially lead to greater benefits in depression and anxiety in people with COPD if embedded in multidisciplinary collaborative care frameworks, but this hypothesis has not yet been empirically assessed. Mindfulness-based treatments are an alternative option for the management of depression and anxiety in people with long-term conditions, but their efficacy is unproven in COPD. Beyond pulmonary rehabilitation, the evidence about optimal approaches for managing depression and anxiety in COPD remains unclear and largely speculative. Future research to evaluate the effectiveness of novel and integrated care approaches for the management of depression and anxiety in COPD is warranted.

**Keywords:** chronic obstructive pulmonary disease, depression and anxiety, health outcomes, pulmonary rehabilitation, cognitive behavioral therapy, multidisciplinary case management

## Introduction

### Prevalence and symptoms of depression and anxiety

Depression is a common mental health problem accompanied by a high degree of emotional distress and functional impairment.<sup>1</sup> The two main symptoms of major depression include depressed mood and loss of interest or pleasure in daily activities. Additional symptoms of depression include fatigue or loss of energy, significant changes in weight, appetite and sleep, guilt/worthlessness, lack of concentration, pessimism about the future, and suicidality. According to the Fifth Edition of the Statistical Manual of Mental Disorders, a diagnosis of major depression is assigned if at least one of two main symptoms and five symptoms in total are present for at least 2 weeks and cause clinically significant impairment in social, occupational, or other important areas of functioning.<sup>2,3</sup> Major depressive disorder accounted for 8.2% of years living with disability in 2010, making it the second leading direct cause of global disease burden.<sup>4</sup>

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Anxiety is also a common mental health problem and is associated with physical and psychological discomfort. All the anxiety disorders share common symptoms, such as fear, anxiety, and avoidance. Other anxiety-related symptoms include fatigue, restlessness, irritability, sleep disturbances, reduced concentration and memory, and muscle tension.<sup>3</sup> Among the anxiety disorders, the most common are specific or social phobias and generalized anxiety disorder.<sup>5</sup>

Depression and anxiety often co-occur; it is estimated that at least half of people with depression also have anxiety. In fact, there is evidence that a mixed state of depression and anxiety is more prevalent than depression alone.<sup>6</sup> The prevalence of depression and anxiety is two to three times higher in people with chronic (long-term) medical conditions.<sup>7</sup> People with a long-term condition and depression/anxiety have worse health status than people with depression/anxiety alone, or people with any combination of long-term conditions without depression.<sup>8</sup>

## Prevalence of depression and anxiety in COPD

A recent meta-analysis that included 39,587 individuals with COPD and 39,431 controls found that one in four COPD patients experienced clinically significant depressive symptoms compared with less than one in eight of the controls (24.6%, 95% confidence interval [CI] 20.0–28.6 versus 11.7%, 95% CI 9.0–15.1).<sup>9</sup> These estimates are consistent with the findings of previous qualitative and quantitative reviews that assessed the prevalence of depressive symptoms in COPD.<sup>10–12</sup> Clinical anxiety has also been recognized as a significant problem in COPD, with an estimated prevalence of up to 40%.<sup>12,13</sup> Additionally, COPD patients are ten times more likely to experience panic disorder or panic attacks compared with general population samples.<sup>14</sup> Of note, the great variability of methods used to assess depression and anxiety in the literature makes it difficult to reach a consensus about the prevalence of depression and anxiety in COPD. Future research should quantify whether prevalence rates for depression and anxiety in COPD are significantly different among samples identified by self-rated or standardized interview methods.

The causes of depression and anxiety in COPD are likely to be multifactorial, but importantly disease severity does not appear to affect the levels of anxiety and depression in COPD patients.<sup>15</sup> Rather, subjective ratings of health-related quality of life (HRQoL), dyspnea, and reduced exercise capacity potentially underlie the development of symptoms of

depression and anxiety in COPD.<sup>16,17</sup> Additionally, depression and anxiety are more often reported in women than in men with COPD, but differences in perceived symptom control and severity of dyspnea symptoms appear to account for this finding.<sup>18,19</sup> The meta-analysis by Zhang et al showed no differences in the prevalence of depression in COPD between studies of Western and non-Western populations.<sup>9</sup> However, there is evidence that certain subgroups of British South Asians have higher rates of depression, but it is not clear what contribution somatic, genetic, or lifestyle factors play in accounting for health differentials between different ethnic groups.<sup>20–22</sup> Further research is needed to examine the effects of ethnicity and nationality on the prevalence rates of depression and anxiety in COPD.

## Impact of depression and anxiety on health-related quality of life

HRQoL is a multifaceted concept that is uniquely linked to health or illness, and includes a number of distinct domains corresponding to the physical, social, and psychological impact of illness.<sup>23</sup> A considerable number of published empirical studies and systematic reviews offer robust evidence that symptoms of depression and anxiety are associated with poorer HRQoL in COPD.<sup>24–26</sup> However, this evidence is mainly derived from cross-sectional studies, which preclude any temporal or causal inferences being made about the association between HRQoL and depression and anxiety in COPD. A recent systematic review by Blakemore et al has examined the longitudinal impact of depression and anxiety on HRQoL. This review found that both depression and anxiety at baseline are significantly associated with worsening levels of HRQoL at 1 year follow-up (pooled  $r=0.48$ , 95% CI 0.37–0.57,  $P<0.001$ ; pooled  $r=0.36$ , 95% CI 0.23–0.48,  $P<0.001$ ; for depression and anxiety, respectively).<sup>27</sup> The findings of this review suggest that HRQoL may be a worthwhile target for interventions aiming to improve the psychological health of people with COPD.<sup>27</sup>

## Impact of depression and anxiety on health care utilization

Comorbid depression and anxiety in COPD is associated with a disproportionate increase in health care utilization rates and costs. A population-based study among people with six chronic conditions (including COPD) showed that comorbid depression doubled the likelihood of health care utilization, functional disability, and work absence.<sup>28</sup> Similarly, a US study among a managed care population showed that COPD patients with comorbid depression were 77% more likely

to have a COPD-related hospitalization, 48% more likely to have an emergency room visit, and 60% more likely to have a hospitalization/emergency room visit compared with COPD patients without comorbid depression.<sup>29</sup> Other studies in this area suggest that depression in COPD leads to excessive health care utilization rates and costs, including longer hospital stay after acute exacerbation,<sup>30</sup> increased risk of exacerbation and hospital admission,<sup>31,32</sup> and hospital readmission.<sup>33</sup> Comorbid anxiety and panic disorder in COPD is also associated with increased risk of exacerbations, relapse within 1 month of receiving emergency treatment,<sup>34</sup> and hospital readmission.<sup>35</sup>

Evidence from systematic reviews and empirical studies suggests that the presence of mental health problems (including depression and anxiety) inflates the costs of care for long-term conditions by at least 45% after controlling for severity of physical illness.<sup>36-41</sup> In COPD in particular, a recent study showed that comorbid depression and anxiety significantly inflated average annual all-cause health care costs (\$23,759 versus \$17,765 per patient,  $P < 0.001$ ) and COPD total health care costs (\$3,185 versus \$2,680 per patient;  $P < 0.001$ ).<sup>29</sup> Moreover, Howard et al found that the addition of a psychological component in a breathlessness clinic for COPD led to savings of £837 per patient 6 months after the intervention (which were mainly attributed to lower emergency room visits and fewer hospital bed days).<sup>42</sup>

## Impact of depression and anxiety on mortality in COPD

COPD is the fourth leading cause of morbidity worldwide and is expected to be the third leading cause of mortality by 2020.<sup>43</sup> The bulk of studies exploring mortality in patients with COPD have mainly focused on physiologic prognostic factors.<sup>44</sup> In the past decade, an increasing number of prognostic studies have indicated that mental health problems also contribute significantly to mortality risk in COPD. Depression is a particularly strong predictor for mortality in COPD (odds ratios ranging from 1.9 to 2.7)<sup>30,45,46</sup> and its predictive ability persists over and above the effects of other prognostic factors, including physiological factors, demographic factors, and disease severity.<sup>47,48</sup> Moreover, preliminary evidence suggests that depression and anxiety interact with other risk factors (eg, physiological factors and smoking) to produce stronger combined effects on mortality risk in COPD.<sup>49</sup> On these grounds, the risk for death in COPD might be better ascertained by the simultaneous consideration of physiological and psychological prognostic factors and the awareness that the impact of these factors on mortality could be cumulative.

## Managing depression and anxiety in COPD

There is a growing consensus in respiratory medicine that the therapeutic focus in COPD should move beyond disease modification and survival alone, and include assessment and improvement of patient-centered outcomes, including health status and psychological health.<sup>50,51</sup> Likewise, in recognition of the increased health and economic burden associated with aging populations with long-term conditions, governments and policymakers are equally keen to promote approaches that integrate physical and mental health care, leading to improved patient outcomes, reduced unscheduled care, and reduced health care costs.<sup>52</sup> In the UK, for example, the National Institute for Health and Care Excellence has published clinical guidelines that recommend the use of stepped approaches to psychological and/or pharmacological treatment of depression in adults in primary care;<sup>53</sup> similar guidelines have been published to underpin comparable approaches for managing depression in people with long-term conditions.<sup>54</sup> Treatments include psychological therapies based on a cognitive and behavioral framework with or without antidepressant medication.<sup>55</sup> But while there is good evidence that psychological therapies are as effective as antidepressants,<sup>56</sup> and that patients prefer psychological therapies,<sup>57</sup> treatment of depression and anxiety in people with long-term conditions is not as optimal as it could be. This is especially true in primary care where the majority of COPD patients are managed. Time-limited consultations that prioritize physical health mean that depression and anxiety remain underdetected and undertreated in people with COPD.<sup>58</sup>

Outside of general practice-led primary care, the most promising intervention to meet the challenges of managing depression in people with COPD is pulmonary rehabilitation. There is growing evidence that pulmonary rehabilitation can not only improve HRQoL and exercise capacity,<sup>59,60</sup> but depression and anxiety too.<sup>61</sup> The next section of this overview offers a detailed summary of the comparative effectiveness of pulmonary rehabilitation and other non-pharmacological interventions for managing depression in people with COPD.

## Multidisciplinary pulmonary rehabilitation

Coventry et al recently conducted a systematic review with meta-analysis that examined the comparative effects of a broad range of psychological and/or lifestyle interventions on depression and anxiety in COPD.<sup>62</sup> Interventions were divided into four subgroups: cognitive behavioral therapy (CBT) interventions, multicomponent interventions

**Table 1** Characteristics of the study populations

Reference	Sample size	Mean age, years	Males (%)	COPD severity (GOLD stage)	Where recruited
Blumenthal et al <sup>86</sup>	158	50	44	Severe (stage 3)	Secondary care
Bucknall et al <sup>87</sup>	464	69.1	37	I, severe (stage 3) C, severe (stage 3)	Secondary care
de Blok et al <sup>88</sup>	21	64.1	43	I, moderate (stage 2) C, severe (stage 3)	Tertiary care
de Godoy and de Godoy <sup>89</sup>	30	60.5	73	Severe (stage 3)	Secondary care
Donesky-Cuenco et al <sup>90</sup>	41	70	28	I, moderate (stage 2) C, severe (stage 3)	Primary care
Effing et al <sup>91</sup>	142	63.4	59	I, moderate (stage 2) C, severe (stage 3)	Secondary care
Elçi et al <sup>92</sup>	78	58.9	85	Severe (stage 3)	Tertiary care
Emery et al <sup>93</sup>	79	66.6	47	Severe (stage 3)	Primary care
Gift et al <sup>94</sup>	26	68.5	31	Moderate (stage 2)	Primary care
Griffiths et al <sup>95</sup>	200	68.3	60	Severe (stage 3)	Primary care and secondary care
Güell et al <sup>96</sup>	40	67	94	Severe (stage 3)	Tertiary care
Hospes et al <sup>97</sup>	39	62.2	60	Moderate (stage 2)	Secondary care
Hynninen et al <sup>98</sup>	51	61	49	Moderate (stage 2)	Secondary care
Kapella et al <sup>99</sup>	23	63	83	I, moderate (stage 2) C, moderate (stage 2)	Community
Kayahan et al <sup>100</sup>	45	66	87	Moderate (stage 2)	Tertiary care
Kunik et al <sup>101</sup>	53	71.3	83	Severe (stage 3)	Secondary care
Kunik et al <sup>102</sup>	238	66.3	97	Severe (stage 3)	Primary care
Lamers et al <sup>103</sup>	187	71	60	Mild to moderate (stage 1 to 2)	Primary care
Livermore et al <sup>104</sup>	41	73.4	44	Moderate (stage 2)	Secondary care
Lolak et al <sup>105</sup>	83	67.7	37	Severe (stage 3)	Secondary care
Lord et al <sup>106</sup>	28	67.4	Not stated	Severe (stage 3)	Secondary care
McGeoch et al <sup>107</sup>	159	71	59.5	Moderate (stage 2)	Primary care
Özdemir et al <sup>108</sup>	50	62.5	100	Moderate (stage 2)	Tertiary care
Paz-Díaz et al <sup>109</sup>	24	64.5	73	Severe (stage 3)	Secondary care
Ries et al <sup>114</sup>	119	62.6	73	Severe (stage 3)	Primary care
Sassi-Dambrosi et al <sup>110</sup>	89	67.4	55	Moderate (stage 2)	Secondary care
Spencer et al <sup>111</sup>	59	66	46	Moderate (stage 2)	Secondary care

Depressed at baseline	Anxious at baseline	Depression assessment	Anxiety assessment	Baseline mean (SD) depression score	Baseline mean (SD) anxiety score
No	No	BDI	STAI	I, 13.4 (8.3) C, 10.9 (7.4)	I, 40.3 (12.6) C, 35.6 (11.3)
Yes	Yes	HADS	HADS	I, 8.5 (3.9) C, 8.3 (4.1)	I, 10 (4.5) C, 9.3 (4.6)
No	No	BDI	N/A	I, 12.6 (95% CI 7.5–17.7) C, 12.9 (95% CI 8.5–17.2)	N/A
Yes	Yes	BDI	BAI	I, 13.7 (8.9) C, 14.9 (11.5)	I, 12.9 (6.9) C, 10.9 (9.8)
No	No	CES-D	STAI	I, 9.5 (4.5) C, 12.6 (9.4)	I, 30.2 (8) C, 33.8 (9)
No	No	HADS	HADS	I, 4.4 (3.5) C, 4.6 (4)	I, 4.6 (3.3) C, 4.8 (4)
No	No	HADS	HADS	Not reported	Not reported
No	No	SCL-depression	SCL-anxiety	I, 59.2 (7.6) <sup>a</sup> I, 55.5 (5.3) <sup>b</sup> C, 60 (7.7)	I, 54.3 (7.2) <sup>a</sup> I, 54.0 (5.3) <sup>b</sup> C, 53.4 (4.5)
No	No	N/A	STAI	N/A	I, 45 (9) C, 37 (6)
No	No	HADS	HADS	I, 7.3 (3.2) C, 7.5 (4.3)	I, 8.6 (4.7) C, 8.9 (4.3)
No	No	SCL-90-R	SCL-90-R	I, 1.3 (0.8) C, 0.6 (0.6)	I, 1.0 (0.5) C, 0.6 (0.7)
No	No	BDI	N/A	I, 8.4 (5.2) C, 9.1 (8.3)	N/A
Yes	Yes	BDI-II	BAI	I, 20.7 (8.6) C, 20.5 (9.7)	I, 17.5 (7.3) C, 17.5 (9.5)
Unknown	Unknown	POMS-D	POMS-A	I, 9.9 (10.3) C, 10.4 (8.2)	I, 9.4 (8.2) C, 8.6 (3.7)
No	No	HAM-D	HAM-A	I, 5.43 (4.8) C, 7.18 (6.5)	I, 8.91 (6.9) C, 7.91 (6.6)
No	No	GDS	BAI	I, 11.5 (0.3) C, 7.7 (5.4)	I, 15.3 (9.2) C, 10 (6.8)
Yes	Yes	BDI-II	BAI	I, 23.4 (12.5) C, 21.1 (12)	I, 22.67 (14.2) C, 23 (13.9)
Yes	No	BDI-II	SCL	I, 17.1 (6.5) C, 18.3 (7.2)	I, 20.6 (6.2) C, 20.4 (7.3)
No	No	HADS	HADS	I, 3.9 (2.1) C, 4.1 (2.8)	I, 5.2 (2.9) C, 5.9 (2.7)
No	No	HADS	HADS	I, 6.6 (4) C, 4.9 (3)	T, 6 (4.3) C, 6.35 (3.8)
No	No	HADS	HADS	I, 5.7 (2.8) C, 5.8 (3.6)	I, 6.3 (3.1) C, 5.3 (2.6)
No	No	HADS	HADS	I, 4.6 (3.7) C, 4.1 (2.9)	I, 6.2 (4.2) C, 5.3 (3.6)
No	No	HADS	HADS	I, 6 (3) C, 7.0 (4.6)	I, 6.8 (3.2) C, 7.1 (4.9)
No	No	BDI	STAI	I, 14 (8) C, 18 (8)	I, 35 (26) C, 33 (25)
No	No	CES-D	N/A	I, 14.0 (8.7) C, 15.3 (10)	N/A
No	No	CES-D	STAI	I, 14.2 (10.2) C, 11.9 (7.6)	I, 33.8 (9.7) C, 34.1 (9.5)
No	No	HADS	HADS	I, 4 (2) C, 5 (3)	I, 6 (3) C, 6 (3)

(Continued)

Table 1 (Continued)

Reference	Sample size	Mean age, years	Males (%)	COPD severity (GOLD stage)	Where recruited
Taylor et al <sup>112</sup>	116	69.5	46	Moderate (stage 2)	Primary care
Yeh et al <sup>113</sup>	10	65.5	60	Moderate (stage 2)	Secondary care
Alexopoulos et al <sup>68</sup>	138	68.5	Not stated	Severe (stage 3)	Tertiary care
Gurgun et al <sup>65</sup>	46	64.7	95.6	Severe (stage 3)	Tertiary care
Jiang et al <sup>69</sup>	100	64.95	69.75	Control: moderate (stage 2) 63.8%; severe (stage 3) 36.2% Intervention: moderate (stage 2) 59.2%; severe (stage 3) 40.8%	Tertiary care
Wadell et al <sup>66</sup>	48	55.8	56	Severe (stage 3)	Tertiary care
Walters et al <sup>67</sup>	182	67	52.5	Moderate (stage 2)	Primary care

**Notes:** <sup>a</sup>Comparison 1, exercise, education, and stress management. <sup>b</sup>Comparison 2, education and stress management.

**Abbreviations:** BAI, Beck Anxiety Inventory; BDI, Beck Depression Inventory; CES-D, Centre for Epidemiologic Studies Depression Scale; C, Control group; CI, confidence interval; COPD, chronic obstructive pulmonary disease; GDS, Geriatric Depression Scale; GOLD, Global Initiative for Chronic Obstructive Lung Disease; HADS, Hospital Anxiety and Depression Scale; HAM-A, Hamilton Anxiety Rating Scale; HAM-D, Hamilton Depression Rating Scale; I, intervention group; N/A, not applicable; POMS-A, Profile of Mood States Anxiety scale; POMS-D, Profile of Mood States Depression scale; SCL, Symptom Checklist; SCL-90-R, Symptom Checklist-90-Revised; SD, standard deviation; STAI, State Trait Anxiety Inventory.

with an exercise component, relaxation techniques, and self-management education. This meta-analysis included 29 randomized controlled trials and 2,063 participants, and demonstrated that the pooled effects of psychological and/or lifestyle interventions led to small but significant reductions in symptoms of depression (standardized mean difference [SMD] 0.28, 95% CI -0.41, -0.14) and anxiety (SMD -0.23, 95% CI -0.38, -0.09). When grouped according to intervention components, the only intervention associated with significant improvements in symptoms of depression (SMD -0.47, 95% CI -0.66, -0.28) and anxiety (SMD -0.45, 95% CI -0.71, -0.18) was multicomponent pulmonary rehabilitation. Cognitive and behavioral treatment approaches and relaxation techniques were associated with small but not significant reductions in depression and anxiety. Self-management interventions that included disease education did not have an effect on depression or anxiety symptoms.

When the analysis was restricted to the five trials that included both psychological and exercise components, the effect size increased to 0.64 for depression and to 0.59 for anxiety, suggesting that complex interventions containing a combination of psychological techniques and

exercise training have the greatest effects on depression and anxiety.<sup>62</sup>

This meta-analysis observed a great variability in the methods used to assess depression and anxiety across the studies included in the meta-analysis; some of the studies included patients with a diagnosis of depression and anxiety, while others measured symptoms of depression and anxiety (some of which did not report above threshold levels of depression). Coventry et al showed that the effectiveness of psychological and/or lifestyle interventions for reducing symptoms of depression and anxiety is equivalent across studies with confirmed depressed or above threshold samples (SMD -0.29 and -0.21 for depression and anxiety, respectively) and studies with unknown levels of depression and anxiety at baseline (SMD -0.24 and -0.27 for depression and anxiety, respectively).<sup>62</sup> Better reporting of severity of depression at baseline in clinical trials will aid more informed assessment of the impact of symptom severity on treatment outcomes.

## Updated systematic review

In recognition of the expanding evidence base and the clinical importance of this area, we updated the systematic review completed by Coventry et al in 2013.<sup>62</sup>

Depressed at baseline	Anxious at baseline	Depression assessment	Anxiety assessment	Baseline mean (SD) depression score	Baseline mean (SD) anxiety score
No	No	HADS	HADS	I, 5.4 C, 4.8	I, 6.1 C, 6.7
No	No	CES-D	N/A	I, 14 (11–46) C, 12 (2–17) (median, range)	N/A
Yes	N/A	HAM-D	N/A	I, 24.72 (3.86) C, 24.80 (3.46)	N/A
No	No	HADS	HADS	I, 8.4 (3.1) <sup>a</sup> I, 6.8 (3.6) <sup>b</sup> C, 8.8 (4.5)	I, 9.1 (5.6) <sup>a</sup> I, 6.8 (4.9) <sup>b</sup> C, 8.8 (4.5)
No	No	HADS	STAI	I, 7.16 (3.02) C, 7.08 (2.92)	Trait anxiety: I, 42.91 (6.78) C, 42.46 (7.04)
No	No	HADS	HADS	I, 5.1 (3.3) C, 4.2 (2.9)	I, 5.8 (3.5) C, 4.5 (2.8)
No	No	HADS, CES-D	HADS	HADS: I, 4.6 (3.1) C, 5.1 (3.6) CES-D: I, 4.6 (3.1) C, 5.1 (3.6)	I, 6.7 (4.1) C, 7 (4.1)

## Methods

The methods used to search, select, extract, and analyze data resembled that reported in the original systematic review.<sup>62</sup> To avoid repetition, we will only briefly present some key methodological aspects of this updated systematic review.

## Data sources and search strategy

All searches were initially carried out from inception to April 2012<sup>62</sup> and were updated in April 2014. The following electronic databases were searched: Medline, Embase, PsycINFO, Cinahl, Web of Science, and Scopus. The above searches were complemented by hand searches of the reference lists of the included studies.

## Eligibility criteria

Studies had to fulfill the following criteria to be included in the review (see Coventry et al<sup>62</sup> for more details):

- Study design – cluster or individual randomized controlled trials
- Population – individuals with COPD confirmed by post-bronchodilator spirometry of forced expiratory volume in 1 second/forced vital capacity ratio of 70%, and a forced expiratory volume in 1 second of 80%

- Intervention – single or multiple component interventions that include psychological and/or lifestyle components
- Comparators – any control (eg, waiting list, usual care, attention or active control)
- Outcomes – standardized measure of depression and/or anxiety.

## Study selection and data extraction

The titles/abstracts and the full texts of potentially relevant studies were screened by four reviewers independently. Data were extracted using a standardized data extraction form. Extracted data included characteristics of patients, interventions, outcomes, and quality appraisal of the studies. Study authors were contacted to retrieve data not available in published reports. Any disagreements during the process of study selection and data extraction were resolved by consensus in group meetings with all review authors.

## Data analysis

Meta-analyses using random effects models were undertaken to assess the effectiveness of different types of complex interventions on reducing symptoms of depression and anxiety in those with COPD. Effect sizes were expressed

**Table 2** Characteristics of the interventions

Reference	Intervention	Control group	Lifestyle components	Psychological components
Alexopoulos et al <sup>68</sup>	Problem-solving techniques	Usual care	Education	Problem-solving techniques
Blumenthal et al <sup>86</sup>	Telephone-based coping skills training	Usual medical care including clinic visits with pulmonologists and regular contact with nurse coordinators	General education Relapse prevention	Problem-solving techniques CBT relaxation
Bucknall et al <sup>87</sup>	Supported self-management	Usual medical care from GP and hospital based specialists (including out of hours care)	General education, skills training	Miscellaneous (empowerment and increased self-efficacy)
de Blok et al <sup>88</sup>	PR plus physical activity counseling	Regular PR containing exercise training, dietary intervention and educational modules	General education Exercise skills training, behavior therapy	Biofeedback miscellaneous (physical activity counselling, motivational interviewing)
de Godoy and de Godoy <sup>89</sup>	CBT, physiotherapy, exercise and education	Physiotherapy, exercise, and education	General education Exercise Skills training	CBT relaxation Miscellaneous (logotherapy)
Donesky-Cuenco et al 2009 <sup>90</sup>	Yoga training	Usual care (also received educational pamphlet, offered yoga at the end as waiting list control)	Exercise Skills training	Miscellaneous (relaxation)
Effing et al <sup>91</sup>	Psychotherapeutic exercise; self-management education	Self-management education	General education Skills training Exercise	Problem-solving techniques
Elçi et al <sup>92</sup>	PR	Standard medical care (including instructions on use of respiratory medicines)	General education Exercise Skills training	Miscellaneous (psychological counseling)
Emery et al <sup>93</sup>	Treatment a. Exercise, education and stress management Treatment b. Education and stress management	Waiting list control	General education Group discussion Exercise	CBT relaxation Miscellaneous (stress management)
Gift et al <sup>94</sup>	Progressive muscle relaxation with prerecorded tapes	Participants instructed to sit quietly for 20 minutes	N/A	Relaxation (Bernstein and Borkovec method)
Griffiths et al <sup>95</sup>	Multidisciplinary PR	Standard medical management	General education Exercise Skills training	Relaxation miscellaneous (stress management to promote mastery and control over illness)
Güell et al <sup>96</sup>	PR including breathing training and exercise	Usual care	General education Exercise Skills training	Relaxation
Gurgun et al <sup>65</sup>	PR with exercise, education and nutritional supplementation	Usual care	Exercise, education	Relaxation
Hospes et al <sup>97</sup>	Pedometer-based exercise counseling program	Usual care	Exercise	Biofeedback problem-solving techniques Exercise counseling Motivational interviewing
Hynninen et al <sup>98</sup>	CBT	Enhanced standard care for COPD	N/A	CBT
Jiang et al <sup>69</sup>	Uncertainty management with CBT	Usual care	Skills training	CBT, relaxation
Kapella et al <sup>99</sup>	CBT	COPD education	N/A	CBT
Kayahan et al <sup>100</sup>	PR	Usual care	General education Exercise Skills training	Relaxation



Sessions (n)	Session length (minutes)	Delivered by	Delivery method	Follow-up
9	30 (for discharge session)	Social workers	Not reported (first session was at discharge and remainder in their own homes)	28 weeks
12	30	Clinical psychologists, social workers	Individual, face-to-face, and remote	12 weeks
22	40	Respiratory nurses	Individual, face-to-face	52 weeks
4	30	Physical therapists	Group and individual, face-to-face	9 weeks
24 exercise sessions 24 physiotherapy sessions 12 psychotherapy sessions	Not reported	Respiratory physicians	Group, face-to-face	12 weeks
24	60	Expert yoga instructors	Group, face-to-face	12 weeks
Four education sessions First phase: 72 exercise sessions Second phase: 40 voluntary exercise sessions	120 education sessions	Respiratory nurse and physiotherapist	Group, face-to-face, and remote	28 weeks
24	90	Nurse	Individual, face-to-face, and remote	4 weeks
37 exercise classes 16 lectures 10 stress management sessions	240 (all modules)	Respiratory specialists and clinical psychologist	Group, face-to-face	10 weeks
4	20	Primary care practitioners	Individual, face-to-face	4 weeks
18	120	Occupational therapist, physiotherapist, dietetic staff, specialist respiratory nurse, and a smoking cessation counselor	Group, face-to-face	6 weeks
Phase 1, 16 sessions Phase 2, 40 sessions	30	Not reported	Group, face-to-face	16 weeks
16	60–80	Not stated	Not stated	8 weeks
5	30	Trained exercise counselor	Individual, face-to-face	12 weeks
7	60	Masters level psychology student	Group, face-to-face	4 weeks
4	35	Intervention nurses	Telephone	40 weeks
6	Not reported	Nurse behavioral sleep medicine specialist	Group, face-to-face	6 weeks
24	150	Not reported	Individual and group, face-to-face	8 weeks

(Continued)

**Table 2** (Continued)

Reference	Intervention	Control group	Lifestyle components	Psychological components
Kunik et al <sup>101</sup>	CBT	COPD education	N/A	CBT
Kunik et al <sup>102</sup>	CBT group treatment intervention	COPD education	N/A	CBT
Lamers et al <sup>103</sup>	Minimal psychological intervention	Usual care	Skills training	Problem-solving techniques CBT
Livermore et al <sup>104</sup>	CBT	Routine care (including PR)	N/A	CBT
Lolak et al <sup>105</sup>	Progressive muscle relaxation and PR	Exercise training	General education Exercise Skills training	Relaxation (Bernstein and Borkovec method)
Lord et al <sup>106</sup>	Singing teaching	Usual care	Skills training	Relaxation
McGeoch et al <sup>107</sup>	Usual care and education on the use of a written self-management plan	Usual GP care	General education Skills training	N/A
Özdemir et al <sup>108</sup>	Water-based PR	Usual care	Exercise	N/A
Paz-Díaz et al <sup>109</sup>	Exercise rehabilitation program	Usual care	Exercise Skills training	Miscellaneous (relaxation techniques)
Ries <sup>114</sup>	Pulmonary rehabilitation	Education (videotapes, lectures, and discussions but no individual instruction or exercise training)	General education Exercise Skills training	Relaxation miscellaneous (psychological support)
Sassi-Dambrom et al <sup>110</sup>	Dyspnea self-management training	General health education	General education Group discussion Skills training	Relaxation (progressive muscle relaxation) Miscellaneous (self-talk and panic control)
Spencer et al <sup>111</sup>	Supervised outpatient-based exercise plus unsupervised home exercise	Unsupervised exercise	Exercise	N/A
Taylor et al <sup>112</sup>	Disease-specific self-management program	Usual care	Skills training	Miscellaneous (self-management using social cognitive self-efficacy theory)
Wadell et al <sup>166</sup>	PR	Usual care	Exercise, education	Miscellaneous (managing emotions and stress)
Walters et al <sup>67</sup>	Health mentoring using negotiated goal setting	Usual care	Education, skills training	CBT, problem-solving techniques
Yeh et al <sup>113</sup>	Tai Chi classes	Usual care	Exercise	Relaxation miscellaneous (meditation and mindfulness)

**Abbreviations:** CBT, cognitive and behavioral therapy; COPD, chronic obstructive pulmonary disease; GP, general practitioner; N/A, not applicable; PR, pulmonary rehabilitation.

as the SMD; an SMD of 0.56–1.2 is large, SMD 0.33–0.55 is moderate, and SMD of <0.32 is small.<sup>63</sup> Heterogeneity was evaluated using the  $I^2$ , which provides a quantitative measure of the degree of between-study differences caused by factors other than sampling error; higher  $I^2$  rates indicate higher heterogeneity.<sup>64</sup>

## Results

The updated searches yielded 736 citations excluding duplicates. Of these, 714 citations were excluded at the title and abstract screening stage. The full texts for 22 citations were retrieved and checked against the eligibility criteria of the review. Following full-text screening, we identified five

additional studies (providing six relevant comparisons) as eligible for inclusion in the review.

## Characteristics of included studies

A total of 34 studies that provided 36 relevant comparisons ( $n=2,577$ ) were included in the updated meta-analysis. The COPD patients had a median age of 66 years with an equal sex distribution. The severity of COPD ranged from moderate to severe across the majority of the studies (see Table 1 for patient characteristics).

The majority of studies (80%) evaluated complex interventions that included both psychological and lifestyle components, while six included only psychological components,

Sessions (n)	Session length (minutes)	Delivered by	Delivery method	Follow-up
1 (+6 phone calls)	120	Board-certified gero-psychiatrist	Group, face-to-face and individual, remote	6 weeks
8	60	Psychology interns and postdoctoral fellows	Group, face-to-face	4 weeks
Average of 4 contacts	60	Primary care nurses	Individual, face-to-face	12 week
4	60	Clinical psychologist	Individual, face-to-face	6 weeks
12	60	Multidisciplinary PR team	Group, face-to-face	8 weeks
12	60	Singing teacher	Group, face-to-face	7 weeks
1	60	Practice nurse or respiratory educator in association with GP	Individual, face-to-face	24 weeks
12	35	Physiotherapist and chest physician	Group, face-to-face	4 weeks
24	85	Not reported	Group, face-to-face	8 weeks
12	240	Not reported	Group, face-to-face	8 weeks
6	Not reported	Graduate student in psychology and a clinical nurse	Group, face-to-face	6 weeks
52	50	Physiotherapist	Group, face-to-face	12 weeks
7	150	Lay trainer and respiratory physician	Group, face-to-face	8 weeks
24	210	COPD nurse	Face-to-face	8 weeks
16	30	Community health nurses	Telephone	24 weeks
24	60	Tai Chi instructors	Group, face-to-face	12 weeks

and four lifestyle interventions alone. Among the five trials identified from the new searches, two studies (including three comparisons) comprised multicomponent exercise interventions<sup>65,66</sup> and three studies comprised CBT interventions.<sup>67-69</sup> None of the new trials evaluated relaxation techniques or self-management interventions (see Table 2 for intervention characteristics).

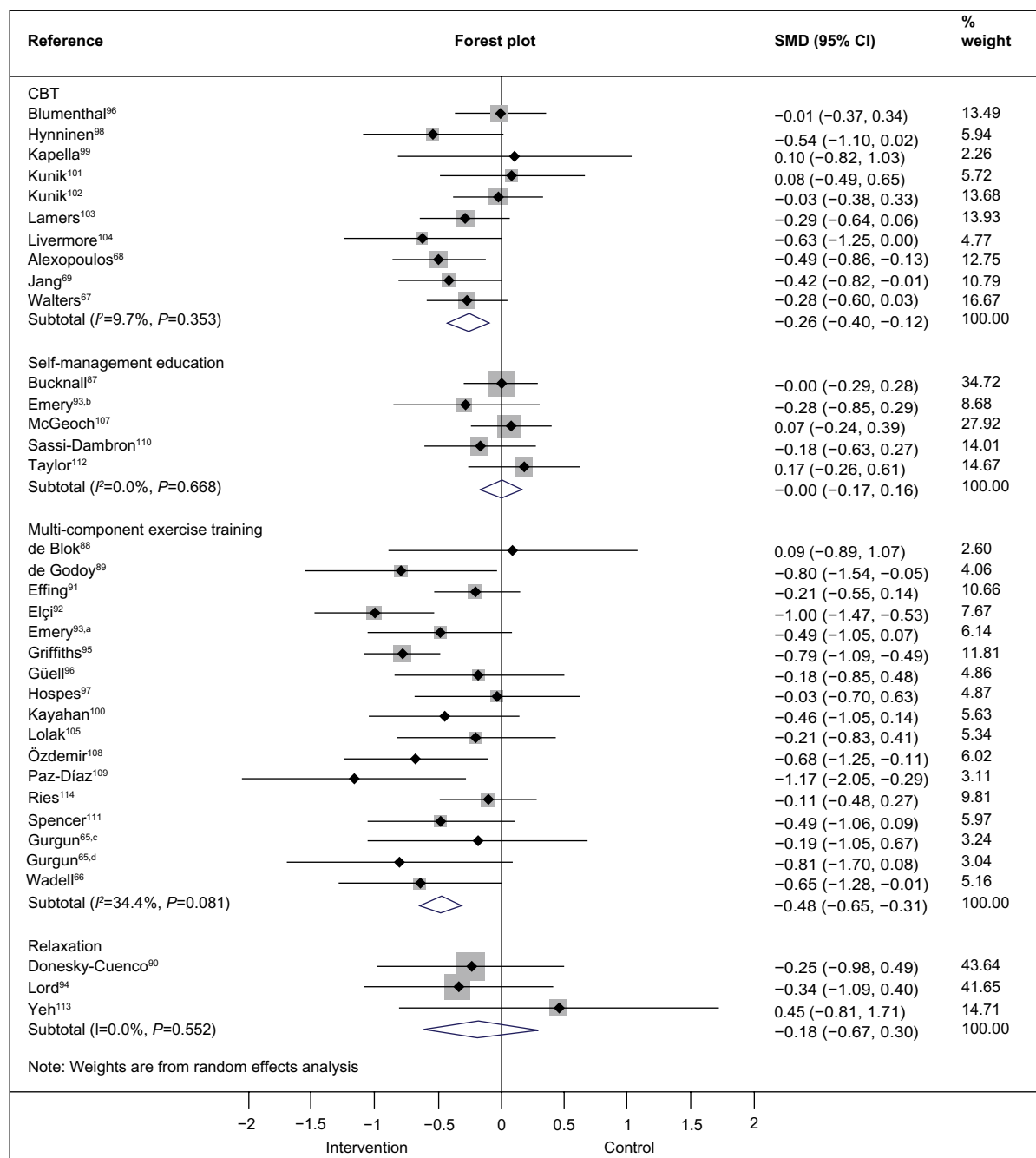
### Effects of different types of complex interventions on depression and anxiety

Thirty-four trials reported data on depression and 30 trials reported data on anxiety. As with the results of the original review,<sup>62</sup> the pooled effects of the interventions indicated small

but significant improvements in depression (SMD  $-0.30$ , 95% CI  $-0.41$ ,  $-0.19$ ) and in anxiety (SMD  $-0.31$ , 95% CI  $-0.49$ ,  $-0.10$ ). Subgroup analysis showed that CBT interventions were associated with small and significant improvements in depression. The results for the subgroup of multicomponent exercise training interventions were unchanged; multicomponent exercise training interventions were associated with the largest treatment effects in favor of a reduction in depression and anxiety (forest plot, Figures 1 and 2).

### Implications for practice and research

Multicomponent exercise training with or without psychological support is associated with the greatest improvements



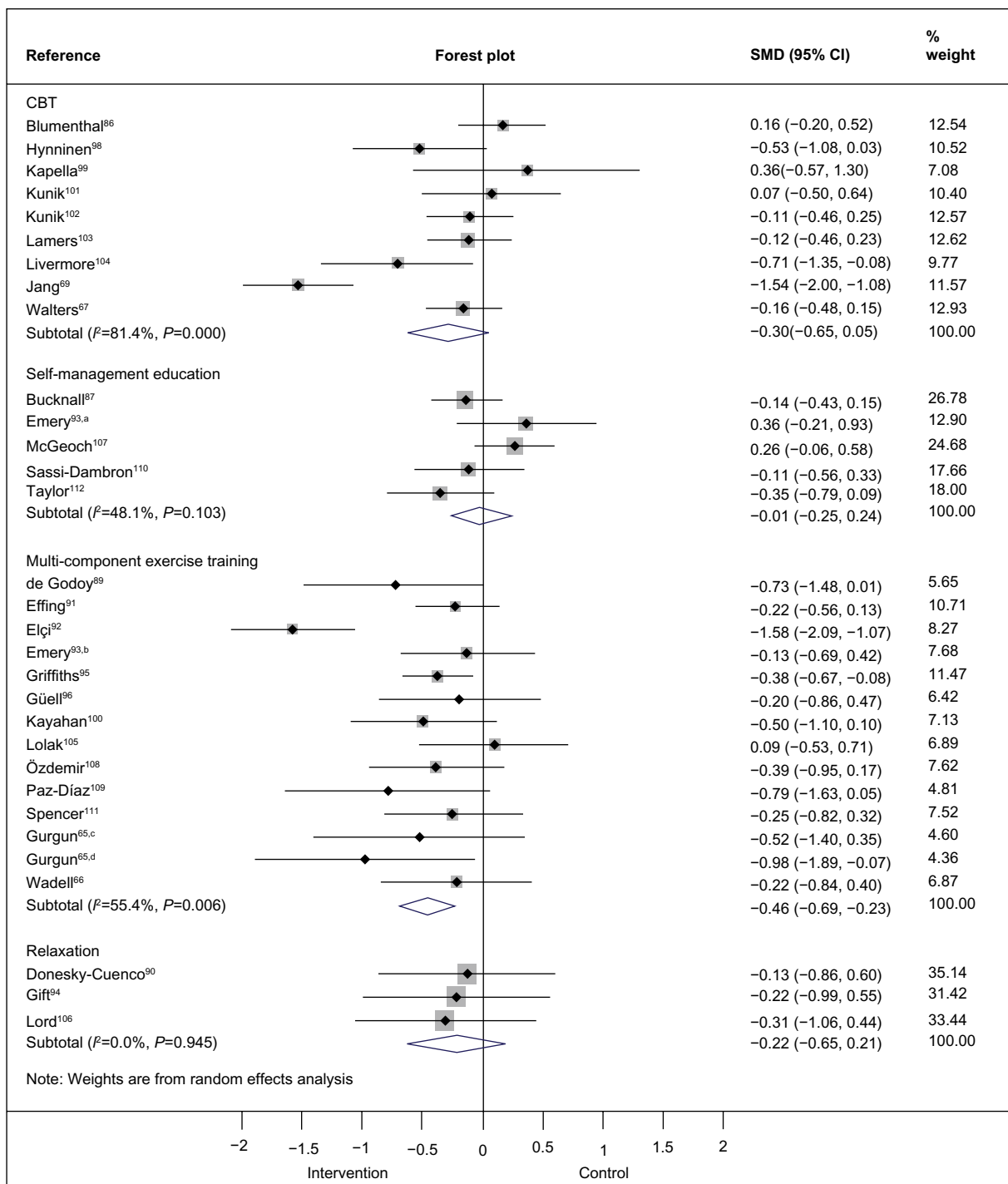
**Figure 1** Effects of subgroups of complex interventions on self-reported depression at post-treatment.

**Note:** Random-effects model was used. <sup>a</sup>Independent comparison 1, exercise, education, and stress management; <sup>b</sup>independent comparison 2, education and stress management; <sup>c</sup>independent comparison 1, pulmonary rehabilitation and nutritional support; <sup>d</sup>independent comparison 2, pulmonary rehabilitation.

**Abbreviations:** CBT, cognitive and behavioral therapy; CI, confidence interval; SMD, standardized mean difference.

in symptoms of depression and anxiety in COPD compared with other nonpharmacological approaches. Components of pulmonary rehabilitation vary, but typically include prescribed supervised exercise training and self-management advice as well as multidisciplinary education about COPD and nutrition for a minimum of 6 weeks. Psychological and behavioral interventions may also be provided in the context

of self-management advice, with an emphasis on promoting adaptive behaviors such as self-efficacy.<sup>51</sup> However, psychological interventions are rarely provided alongside or integrated within pulmonary rehabilitation.<sup>70</sup> Future research could address whether mental health professionals, in collaboration with multidisciplinary pulmonary rehabilitation teams, could play important roles in the delivery of psychological



**Figure 2** Effects of subgroups of complex interventions on self-reported anxiety at post-treatment.

**Note:** Random-effects model was used. <sup>a</sup>Education and stress management; <sup>b</sup>exercise, education, and stress management; <sup>c</sup>independent comparison 1, pulmonary rehabilitation and nutritional support; <sup>d</sup>independent comparison 2, pulmonary rehabilitation.

**Abbreviations:** CBT, cognitive and behavioral therapy; CI, confidence interval; SMD, standardized mean difference.

interventions for common mental health problems in COPD patients attending pulmonary rehabilitation.

Interventions based on a CBT format are also potentially effective for managing depression in COPD. These results are consistent with other meta-analyses showing that

psychological interventions that include CBT significantly reduce symptoms of depression in people with long-term conditions.<sup>71,72</sup> However, the size of the treatment effects associated with CBT in populations with long-term conditions are small and possibly of trivial importance for patients.

Existing evidence about the beneficial effects of CBT in anxiety disorders<sup>73</sup> and in other long-term conditions<sup>74</sup> implies that unique features of COPD might account for the relatively small treatment effects for CBT in this patient group. For instance, the use of CBT techniques to counter ruminative thinking and avoidance behaviors might not be acceptable to COPD patients when these behaviors are triggered as a response to real and meaningful COPD symptoms such as dyspnea.<sup>62</sup> Alternative or “third wave” psychological therapies that target the process of thoughts (rather than their content, as in CBT) and help people to become aware of their thoughts and accept them in a nonjudgmental way are equally effective for depression as CBT.<sup>75</sup> Mindfulness meditation is associated with longer-term mental health benefits when compared with relaxation alone<sup>76</sup> and is acceptable among people with long-term conditions,<sup>77</sup> but its effectiveness among COPD patients has not yet been confirmed.<sup>78</sup>

Other explanations for why stand-alone interventions such as CBT may only confer modest benefits in people with COPD point to the need to embed psychological interventions within collaborative and multidisciplinary frameworks that promote proactive case management of patients and supervision of psychological therapists. Collaborative care is a complex intervention that typically involves a case manager working in conjunction with the patient’s physician (usually their primary care physician), often with the support and supervision of a mental health specialist (a psychiatrist or psychologist). When compared with usual care, collaborative care is associated with significant improvement in depression and anxiety outcomes over the short-, medium-, and long-term.<sup>75</sup> There is also evidence that collaborative care can improve both physical and mental health in people with long-term conditions.<sup>79</sup> However, there is less evidence that collaborative interventions are effective in COPD, and trials to date have focused on self-management interventions to reduce exacerbations and improve medication adherence in acute illness, not on reducing depression or anxiety.<sup>80,81</sup>

In this overview, we have focused on the benefits of non-pharmacological interventions for the management of depression and anxiety in COPD. Psychological interventions are as effective as drug therapies for improving the psychological ill health of patients with COPD and are rated as preferable to drug therapies by patients.<sup>57,82</sup> Additionally, psychological interventions with or without medication have been recommended for managing depression and anxiety in COPD.<sup>55</sup> To date, the levels of evidence for the efficacy of pharmacological interventions in reducing depression and anxiety in COPD are limited. Two recent reviews suggested that no firm conclusions

can be drawn about the effectiveness of antidepressants (selective serotonin reuptake inhibitors and tricyclic antidepressants) in reducing depression in COPD because there are only a small number of published trials in this area, many of which have important methodological limitations, such as small sample sizes, and high dropout rates.<sup>83,84</sup>

## Conclusion and future directions

There is ample research evidence that depression and anxiety are important determinants of health outcomes and health care utilization in COPD. Health care policy has highlighted the need to manage depression and anxiety in long-term conditions, including COPD, but finding effective and innovative ways of implementing existing treatments remains a major challenge. Contemporary research suggests that complex psychological and/or lifestyle interventions which include a pulmonary rehabilitation component have the greatest effects on depression and anxiety in patients with COPD. However, further work is needed to understand how exercise improves anxious and depressed moods in COPD. Additionally, CBT appears to be effective in improving depression in COPD, but its benefits could be enhanced if embedded within collaborative care models that integrate physical and mental health care. Collaborative care models that focus on building partnerships between mental health and other professionals to foster integration of care for people with complex morbidities present a fruitful framework for the management of mental health in COPD. In particular, the integration of pulmonary rehabilitation and psychological therapies such as CBT has the potential to lead to significant patient benefits. Moreover, further research into ways to target markers of psychological health such as HRQoL could advance the clinical management of mental health in COPD.

In conclusion, finding ways to strengthen the delivery of effective mental health care within the context of innovative chronic disease management programs such as pulmonary rehabilitation in primary care offer opportunities to meet the challenge set out by the World Health Organization that there can be “no health without mental health”.<sup>85</sup>

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## Disclosure

The authors report no conflicts of interest in this work.

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