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## **EFFECTIVENESS OF COGNITIVE BEHAVIORAL THERAPY ON HEALTH OUTCOMES IN PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE: A SYSTEMATIC REVIEW AND META-ANALYSIS**

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### **Abstract**

The incidence of psychological distress (such as anxiety and depression) is high in COPD patients. CBT has been proved to reduce depression and anxiety and enhance quality of life. This meta-analysis evaluated the effectiveness of cognitive behavioral therapy(CBT) on patients with chronic obstructive pulmonary disease(COPD).

The following electronic databases were searched from inception to March 2020: PubMed, EMBase, Cochrane Library, Web of Science, Medline, OVID, CINAHL, Chinese Biomedical Literature Database (CBM), China National Knowledge Infrastructure (CNKI), Wangfang Database (WF), PsycARTICLES, VIP database. The Scopus and Google scholar database that we did not use. Randomized controlled trials (RCTs) that compared CBT with routine methods of care in COPD were retrieved in electronic databases. The Cochrane Risk of Bias Tool and Review Manager version 5.3 were used for risk of bias assessment and meta-analysis, respectively. Both data synthesis and descriptive analysis were used for outcome assessment. A total of 10 RCTs involving 1173 patients were included.

Data synthesis showed that CBT was statistically significant in improving short- and medium-term depression and treatment compliance. Medium-term anxiety and quality of life were improved among COPD patients

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receiving CBT, although no significant effect was found for short-term quality of life and anxiety. Descriptive analysis showed that CBT could reduce dyspnea. No clear evidence supports the effectiveness on improving self-efficacy in COPD patients with the use of CBT ( $P > 0.05$ ).

CBT can be a useful strategy to improve the symptoms of depression, dyspnea and treatment compliance in patients with COPD. It can also improve patients' quality of life and anxiety to some extent, but there is still lack of strong evidence in improving patients' self-efficacy.

**Keywords:** Chronic obstructive pulmonary disease, Cognitive behavioral therapy, Systematic review

### **Introduction**

Chronic obstructive pulmonary disease (COPD) represents a common, preventable and treatable multi-factorial chronic disease characterized by airflow limitation and persistent respiratory symptoms. With COPD, the limitation of airflow is not completely reversible and might progressively deteriorate (Singh et al., 2019). COPD currently ranks the fourth among the top 10 leading causes of death worldwide and in China, it is the number-one health burden posed by chronic diseases (Rycroft, Heyes, Lanza, & Becker, 2012). Globally, the burden of COPD is projected to mount in coming decades due to continued exposure to COPD risk factors and overall aging of the population (Kim et al., 2015). According to an epidemiological study conducted in China, the overall prevalence of COPD stood at 8.2% in people over 40 years old, indicating that approximately 40 million people had COPD patients in China, and, on average, 2.5 patients died of COPD per minute (Tian, & Zhang, 2015). COPD has become a global public health problem that imposes enormous financial, health-care and emotional burdens on its victims, their families and the society at large (Singh et al., 2019; vos et al., 2010). Studies have shown that, the incidence of psychological distress (such as anxiety and depression) is higher in COPD patients than their counterparts suffering from other chronic diseases. COPD could reportedly double the likelihood of comorbid depression and about 40% of COPD patients had depressive symptoms, and 10%~30% had anxiety symptoms (Pirraglia, Casserly, Velasco, Borgia & Nici, 2016). When COPD patients have accompanying anxiety and depression, their physical conditions, treatment compliance and quality of life will suffer substantially. Therefore, it is of great

importance to help COPD patients to lower the possibility of complications and improve their quality of life by identifying the negative emotions early and managing them effectively.

Cognitive behavioral therapy (CBT) is a structured method of psychological intervention designed to change dysfunctional thoughts, beliefs and behaviors of patients by identifying and evaluating negative emotions, and helping patients reconstruct cognitive structure. It is a short-term psychotherapy aimed to eliminate negative emotions and behaviors (McMain, Newman, Segal, & DeRubeis, 2015). An early systematic review showed a significant relationship existed between COPD and cognitive impairment, and the cognitive domains memory and attention were significantly impaired in COPD patients (Torres-Sánchez et al., 2015). Given that the barriers to the COPD management mainly lie in the treatment of cognitive and behavioral problems, an intervention consisting of cognitive and behavioral treatments may improve the outcomes of the patients.

In recent years, CBT has been proved to be effective in various diseases, such as diabetic mellitus (Uchendu & Blake, 2017) and breast cancer (Ye et al., 2018), and mounting evidence showed that CBT could improve patients' health outcomes to some extent, including reducing depression and anxiety and enhancing quality of life. At present, some researchers used CBT in COPD patients, but the results were conflicting. And the application of CBT in COPD remains at early stage in China. Currently no review has been available on the effect of CBT on the health outcomes of COPD patients. The aim of this review was to critically and systematically review the RCT studies about the effect of CBT on COPD patients.

## **Methods**

### *Eligibility criteria*

Inclusion criteria in this review were as follows. 1) Types of studies: RCTs with or without blinding design of research participants and practitioners. 2) Language of studies: English language and Chinese language. 3) Types of participants: patients (men and women aged 18 years and above) with a confirmed diagnosis of COPD according to Global Initiative for Chronic Obstructive Lung Disease (GOLD) standard (version 2019) (Singh et al., 2019): patients with

dyspnea, chronic cough or sputum production, and a history of exposure to risk factors for the disease;  $FEV_1/FVC < 0.70$  after inhalation of bronchodilators confirms the presence of persistent airflow limitation. Stable patients (patients with cough, sputum, shortness of breath and other symptoms stable or lighter). Patients with normal verbal communication skills. 4) The group of intervention: CBT and standard methods of care as the major part of the intervention. The content of CBT intervention in this review is defined as follows: First, the researchers elicit irrational beliefs and behaviors related to participants' own symptoms by using the method of questions, demonstrations, etc. And help participants learn to identify automated thinking processes of the connection between thinking activities and behavior; Then, the researchers reassess the participants' cognition and beliefs when the target symptoms are induced; Next, using dialectical thinking to help participants recognize unreasonable beliefs through psychological interventions such as reasonable emotional therapy; Finally, to eliminate unhealthy motion and improve health behavior by reconstructing new rational thinking belief. 5) The control group: standard methods of care provided in the study settings, such as quitting smoking, preventing and controlling respiratory infection, nutrition guidance, pulmonary rehabilitation and self-management. 6) Outcomes: the outcomes measures of this interview included depression (measured by BDI, HADS, PHQ-9 and HAMD), quality of life (measured by SGRQ, CAT and CRQ), anxiety (measured by BAI and HADS), treatment compliance, self-efficacy (measured by GSES and CSES) and dyspnea symptoms (measured by CRQ, IBPQ and Borg scale). Studies that had active education components in the comparison as the group of intervention were excluded. The patients with stroke, myocardial infarction or malignant tumor were excluded. The patients who combines with arthritis or pulmonary hypertension may lead to severe adverse reactions in exercise were excluded.

### *Search strategy and steps*

The following electronic databases were searched from inception to March 2020: PubMed, EMBase, Cochrane Library, Web of Science, Medline, OVID, CINAHL, Chinese Biomedical Literature Database (CBM), China National Knowledge Infrastructure (CNKI), Wangfang Database (WF), PsycARTICLES, VIP database. The Scopus and Google scholar database that we did not use. A comprehensive literature research of databases was conducted to identify RCTs on effectiveness of CBT on health outcomes with COPD patients. At the same time, the two review authors also screened the latest journals and conference papers in chronic

disease, pulmonary disease and health education. Relevant English and Chinese Mesh terms, key words and free words were incorporated into the search strategies as shown in Figure 1. Taking PubMed as a representative, the specific search strategy was shown in Figure 1.

Mesh Terms	
1	Pulmonary Disease, Chronic Obstructive; Lung Disease, Obstructive
2	Cognitive Therapy; Cognitive Psychotherapy; Behavior Therapy, Cognitive;
Key Words and Free Words	
1	Chronic obstructive pulmonary diseas*; Chronic obstructive lung diseas*; Chronic obstructive airway diseas*; COPD; 慢性阻塞性肺疾病 ; 慢性阻塞性气道疾病 ; 慢阻肺
2	Cogniti* therap*; Cogniti* psychotherap*; Behavio* therap*, Cogniti*; Therapy*, cogniti* behavior*; Cogniti* behavio* therap*; CBT ; 认知疗法 ; 认知心理疗法 ; 认知行为疗法 ;
#1	Search (Pulmonary Disease, Chronic Obstructive[MeSH Terms]) OR Lung Oisease, Obstructive [MeSH Terms]
#2	Search (((Chronic obstructive pulmonary diseas*[Title/Abstract]) OR Chronic obstructive lung diseas*[Title/Abstract]) OR Chronic obstructive airway diseas*[Title/Abstract]) OR COPD[Title/Abstract]) OR COAD[Title/Abstract]
#3	#1 OR #2
#4	Search ((Cognitive Therapy[MeSH Terms]) OR Cognitive Psychotherapy[MeSH Terms]) OR Behavior Therapy, Cognitive[MeSH Terms]
#5	Search (((((Cogniti* therap*[Title/Abstract]) OR Cogniti* psychotherapy*[Title/Abstract]) OR Behavio* therap*, Cogniti*[Title/Abstract]) OR Therapy*, cogniti* behavior*[Title/Abstract]) OR Cogniti* behavior* therap* [Title/Abstract]) OR CBT[Title/Abstract])
#6	#4 OR #5
#7	#3 AND #6
#8	Search (((Randomized controlled trial [Publication Type]) OR Controlled clinical trial [Publication Type]) OR randomized [Title/Abstract]) OR randomly [Title/Abstract]) OR trial[Title/Abstract]
#9	Search (Animals[Mesh Terms])
#10	#8 NOT #9
#11	#7 AND #10

**Figure 1.** The specific search strategy of PubMed

The search of literature includes 4 steps: 1) Search the relevant systematic review or meta-analysis in Cochrane Library, JBI and CNKI, etc. 2) The literature retrieval is carried out with the combination of subject words and free words in the above database. Two reviewers eliminated the literature unrelated after assessing the abstracts of literatures identified from search independently. 3) According to

## *Articles Section*

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inclusion and exclusion criteria, screening the literatures further after reading the full text. 4) A "snowball" search based on the references to the included literature and the articles cited.

### *Methodological quality assessment*

The quality of included studies was assessed by two reviewers (all of whom participated in the course of evidence-based Nursing) independently by using the assessment criteria for sources of risk of bias, which was recommended by the Cochrane Handbook of Reviews of Interventions (version 5.1.0) (Higgins, & Green, 2011). The risk of bias assessment criteria as follows: 1) Random sequence generation (selection bias); 2) Allocation concealment (selection bias); 3) Blinding of participants and researchers (performance bias); 4) Blinding of outcome assessment (detection bias); 5) Incomplete outcome data (attrition bias); 6) Selective reporting (reporting bias); 7) Other bias. Group discuss among the reviewers was considered when different opinions were presented on the risk of bias judgment for some items, where consensus could not be reached, a third reviewer was consulted to make the final decision.

### *Data extraction*

Data were captured by the two authors independently with a pre-defined form of data extraction, including name of first author, year of publication, sample size, mean age of participants in each group, CBT intervention (sessions of CBT and components), control group, outcome measures and outcome assessment.

### *Data analysis*

Statistical synthesis and descriptive analysis were adopted. Data synthesis was performed with Review Manager software (RevMan v. 5.3 Cochrane Collaboration, Oxford, UK). For dichotomous data, such as the data on treatment compliance, risk ratio (RR) with 95% confidence interval (CI) was calculated for synthesis. For continuous data, such as the data on depression, quality of life, anxiety and self-efficacy, if the same outcome was measured by same assessment scales, the Weighted Mean Difference (WMD) and corresponding 95% CI were calculated. Otherwise the Standardized Mean Difference (SMD) and corresponding 95% CI were calculated. In each meta-analysis  $I^2$  statistic was used for heterogeneity of outcomes, and a fixed effect

model was applied if  $I^2 < 50\%$ . According to the guidance in Cochrane Handbook,  $I^2 \geq 50\%$  may be considered as indicator of substantial heterogeneity, and random effect model might be applied. Random effects model was considered as a priori for different population characteristics, intervention formats and measurements in the studies included. In studies where there were several post-treatment follow-ups, if do not state the specific assessment time, the measurements of the last follow-up were integrated as effect values. Within each subgroup of different outcome assessment time points, further subgroup syntheses based on different types of assessment tools if sufficient trials were available for analysis. Negative MDs indicate an improvement in depression, anxiety and quality of life, favoring the intervention. Positive SMD indicate an improvement in self-efficacy, favoring the intervention. Typically, according to Cohen's parameters (Cohen, 1988), effect sizes of 0.20-0.30 are considered small, 0.50 medium and  $\geq 0.80$  large. For studies without available data for synthesis, descriptive analysis was adopted.

## **Results**

### *Characteristics of included studies*

A total of 624 articles were detected after removal of duplications, including 286 in Chinese and 338 in English. Removing the articles that failed to meet the predetermined criteria after the initial title and abstract screenings, 37 relevant articles were identified, including 27 in English and 10 in Chinese. And 2 articles were included by the way of citation searches. 39 publications were retrieved in full text for further assessment. There were four literatures, of which two published from the same author (Livermore, Sharpe, & McKenzie, 2010; Livermore et al., 2015), two published from another author (Kunik et al., 2001; 2008), and the review included two of them updated to avoid bias. Finally, 10 RCTs totaled 1173 COPD patients were included, of which seven studies were published in English, whereas the other three were in Chinese, and the sample size in each study ranged from 31 to 238. The ten studies were published from 2008 to 2018, and the countries of origin differed. The studies selection is shown in Fig. 2 and the characteristics of the included studies are shown in table 1.

**Table 1.** Characteristics of the analyzed randomized controlled trials

First author Year Reference	Country	Participants		CBT intervention	Control Group	Outcome measures	Outcome assessment
		Sample size	Age (mean±SD)				
Livermore et al. 2015	Spain	IG (n=18) CG (n=13)	Total (72 ± 6)	<b>Sessions of CBT:</b> three 60 min sessions, once per week over 8 weeks <b>Components:</b> psychoeducation, training in cognitive challenging of negative thoughts, instructions on pursed lip breathing and activity planning, etc.	Routine methods of care	- Depression: HADS - QoL: SGRQ - Anxiety: HADS - Dyspnea: IBPQ, Borg scale	at baseline and 6 months follow-up
Kunik et al. 2008	USA	IG (n=118) CG (n=120)	IG (66.1±10.1) CG (66.5±10.4)	<b>Sessions of CBT:</b> eight 1h sessions over 8 weeks <b>Components:</b> psychoeducation, advice on relaxation training, cognitive and behavioral symptoms of anxiety and depression, instructions on sleep management skills and practice exercises, etc.	COPD education: breathing strategies and airway management, et al.	- Depression: BDI - QoL: CRQ - Anxiety: BAI - Dyspnea: CRQ	at baseline, end of treatment, 8 weeks follow-up and 52 weeks follow-up
Lamers et al. 2010	Netherlands	IG (n=96) CG (n=91)	IG (70.5±6.3) CG (71.5±7.1)	<b>Sessions of CBT:</b> five sessions for two to ten visits over 3 months <b>Components:</b> psychoeducation, keeping a diary, instructions on self-management, and awareness of mood relation to behavior, etc.	Routine methods of care	- Depression: BDI - QoL: SGRQ - Anxiety: SCL	1week follow-up, 3months follow-up and 9 months follow-up
Hynninen et al. 2010	Norway	IG (n=25) CG (n=26)	IG (59.3±7.6) CG (62.6±9.9)	<b>Sessions of CBT:</b> Seven 2h group sessions, once per week over 7 weeks <b>Components:</b> psychoeducation, advice on relaxation exercise, cognitive and behavioral activation, fear-based exposure and sleep management skills, et al.	Routine methods of care	- Depression: BDI - QoL: SGRQ - Anxiety: BAI	pre-treatment, post-treatment, and 6 months follow-up
Howard et al. 2014	UK	IG (n=112) CG (n=110)	IG (71.2±10.4) CG (73.2±11.4)	<b>Sessions of CBT:</b> 1 h per day over a 5-week period and each week divided into six sections <b>Components:</b> reading a section, writing in a question response, practice a physical exercise and listening to a track from the relaxation CD.	Routine methods of care: COPD booklets	- Depression: HADS - Anxiety: HADS - Dyspnea: CRQ	at baseline, 6weeks follow-up and 6 months follow-up
Doyle et al. 2017	Australia	IG (n=54) CG (n=56)	IG (68.5±9.4) CG (67±9.1)	<b>Sessions of CBT:</b> not reported <b>Components:</b> behavioral strategies such as behavioral activation, activity scheduling, relaxation training, exposure hierarchies, and social skills training and cognitive strategies such as cognitive restructuring, structured problem-solving, and behavioral experiments.	Routine methods of care: sessions on neutral, not involve discussion of symptoms or difficulties in client's lives, problem-solving strategies, or exploration of emotions.	- Depression: PHQ-9 - QoL: CAT - Anxiety: BAI - Self-efficacy: GSES	pre-treatment, post-treatment, and 8 weeks follow-up



First author Year Reference	Country	Participants		CBT intervention	Control Group	Outcome measures	Outcome assessment
		Sample size	Age (mean±SD)				
Farver- Vestergaard et al. 2018	Denmark	IG (n=39) CG (n=45)	IG (66.67±8.03) CG (67.67±7.54)	<b>Sessions of CBT:</b> one 30 to 60 min individual telephone interview followed by eight weekly 105-min group sessions <b>Component:</b> instructions on thoughts and feelings exercise, gathering the scattered mind, meditation education, cognitive exercises, instruction on physical exercise, disease- and lifestyle-oriented education, etc.	Routine methods of care: two weekly sessions over an 8-week period and one weekly session lasted 90 min, with physical exercise only. The other weekly session lasted 150 min and included physical Exercise, disease- and lifestyle-oriented education.	- Depression: HADS - QoL: CAT - Anxiety: HADS - Self-efficacy: CSES	at baseline, mid-intervention, post-intervention, 3 months follow-up, 6 months follow-up
Zhang et al. 2014	China	IG (n=40) CG (n=40)	IG (58.4±5.1) CG (61.7±5.2)	<b>Sessions of CBT:</b> not reported <b>Component:</b> COPD-related knowledge, quit smoking, psychoeducation, group discussion, video learning, cognitive therapy and structured problem-solving, etc.	Routine methods of care: diet, functional exercise, oxygen therapy, etc.	Treatment compliance	12 months follow-up
Guo et al. 2015	China	IG (n=45) CG (n=45)	Not reported, but no difference between groups	<b>Sessions of CBT:</b> first, second, and fourth week of the first month after discharge from the hospital, followed by once per month, eight times in total, each duration not exceeding 60 min <b>Component:</b> psychoeducation, instructions on relaxation exercise, behavioral management strategies, knowledge of COPD and peer education, etc.	Routine methods of care: instructions for pharmacological treatment, smoking cessation, psychological support, oxygen therapy, pulmonary rehabilitation training, etc.	- Depression: HAMD	at discharge, 3 months follow-up and 6 months follow-up
Xu et al. 2017	China	IG (n=40) CG (n=40)	IG (49.1±4.0) CG (49.9±4.5)	<b>Sessions of CBT:</b> twice times per week, two hours each, for a total of ten hours <b>Component:</b> education of COPD, emotion management strategy to alter behavior, mental meditative intervention, repeating knowledge points, etc.	Routine methods of care: rational drug use, oxygen therapy, etc.	- QoL: SGQR - Treatment compliance	2 weeks follow-up and 8 weeks follow-up

CBT: Cognitive behavioral therapy; IG: Intervention group; CG: Control group; SD: Standard Deviation; QoL: Quality of life; HADS: The Hospital Anxiety and Depression scale; BDI: Beck Depression Inventory; PHQ-9: Patient Health Question-9; HAMD: Hamilton Depression Scale; SGQR: St. George Respiratory Question; CAT: Chronic Obstructive Pulmonary Disease Assessment Test; CRQ: Chronic Respiratory Disease Questionnaire; BAI: Beck Anxiety Inventory; SCL: Anxiety Subscale of the Symptom Checklist-90; IBPQ: The Interpretation of Breathing Problems Questionnaire.

### *Characteristics of participants*

In all included studies with the exception of one study that did not report sex and age of participants (Guo et al., 2015), 56.8% of participants were men, and the age ranged from 46 to 85 years. Participants in the included studies were recruited from inpatient department (Farver-Vestergaard et al., 2018; Livermore et al., 2015; Xu et al., 2017; Zhang et al., 2017), outpatient pulmonary clinics (Livermore et al., 2015; Hynninen et al., 2010), community (Doyle et al., 2017) and family (Guo et al., 2015; Howard, & Dupont, 2014). One study recruited patients from general practices (Lamers et al., 2010), another from a medical center, flyers and advertisements methods (Kunik et al., 2008).

### *Methodological quality assessment*

The assessment for risk of bias and grading were completed for all included studies based on Cochrane Handbook of Reviews of Interventions. The quality of the included 10 RCTs were mostly medium, and the results were shown in table 2. Due to the need to obtain informed consent of patients, and the nature of CBT intervention made it difficult to conduct the blinding design among patients and practitioners, therefore it only included the blinding design for outcome assessment in this review. The 10 RCTs were included in this review, all of which clearly defined the inclusion and exclusion criteria for participants. The baseline data and the outcome assessment time points were similar between study groups. Most of the studies (Doyle et al., 2017; Farver-Vestergaard et al., 2018; Hynninen et al., 2010; Howard, & Dupont, 2015; Kunik et al., 2008; Lamers et al., 2010; Xu et al., 2017) described the methods of randomization. Six studies (Doyle et al., 2017; Farver-Vestergaard et al., 2018; Howard, 2015; Hynninen et al., 2010; Kunik et al., 2008; Lamers et al., 2010) reported the allocation concealment methods. Three studies (Doyle et al., 2017; Howard, & Dupont, 2014; Hynninen et al., 2010) reported that it was difficult to conduct the blinding design among participants and researchers. Blinding design of outcome assessment were reported in three studies (Doyle et al., 2017; Kunik et al., 2008; Lamers et al., 2010) and the participant dropouts were reported in the majority of included studies with acceptable attrition rate (Doyle et al., 2017; Farver-Vestergaard et al., 2018; Howard & Dupont, 2014; Kunik et al., 2008; Lamers et al., 2010; Livermore et al., 2015;). One of which reported a 36% dropout (Lamers et al., 2010), slightly higher than the expected 30%, and the comparison for baseline data showed the control group of patients with a slightly older than the intervention group, but the difference is not statistically significant.

**Table 2.** Quality assessment of the included randomized controlled trials

First author, year, reference	Random sequence generation	Allocation concealment	Blinding of participants and researchers	Blinding of outcome assessment	Incomplete outcome data	Selective reporting	Other bias
Livermore et al. 2015	Unclear	Unclear	Unclear	Unclear	Low	Low	Low
Kunik et al. 2008	Using the SAS Institute, to create the randomization list	Flipping a coin.	Unclear	Low	Low	Low	Low
Lamers et al. 2010	A computerized random number generator	A block randomization scheme numbered containers that	Unclear	Low	Unclear	Low	Low
Hynninen et al. 2010	Randomized pairing	were identical in appearance for the two groups.	High	Unclear	Low	Low	Low
Howard et al. 2014	Computerized random blocks of six	Randomly assigned	High	Unclear	Low	Low	Low
Doyle et al. 2017	A computer-generated random sequence	Computer-generated randomized permuted blocks with varied block sizes	High	Low	Low	Low	Low
Farver-Vestergaard et al. 2018	An independent researcher used PASS to generate allocation sequence of 12	Researchers and clinicians were blind to the allocation sequence	Unclear	Unclear	Low	Low	Low
Zhang et al. 2014	Unclear	Unclear	Unclear	Unclear	Low	Low	Unclear
Guo et al. 2015	Unclear	Unclear	Unclear	Unclear	Low	Low	Low
Xu et al. 2017	Random number table	Unclear	Unclear	Unclear	Low	Low	Low

“Low”- low risk of bias; “Unclear”- Unclear risk; “High”- high risk of bias.

*Effectiveness of CBT on health outcomes in COPD patients*

*Depression*

Eight of 10 included RCTs assessed the effects of CBT on depression in COPD patients (Doyle et al., 2017; Farver-Vestergaard, 2018; Guo, Yang, Chen, Gong, Lu & Li, 2015; Howard, & Dupont, 2014; Hynninen, Bjerke, Pallesen, Bakke, & Nordhus, 2010; Kunik et al., 2008; Lamers et al., 2010; Livermore, 2015). All eight studies provided sufficient data for meta-analysis. Owing to the difference of time points of outcome assessment and psychometric scales, the interventions’ summary effect for depression was assessed at the assessment time point of last

follow-up in this review, and the effect values were standardized by using the standardized mean difference. Data synthesis was performed, with a heterogeneity level of 58%, excluding clinical heterogeneity, a random effect model was adopted. The pooled effects favored the direction of the intervention group, showing significant improvements in depression [SMD = -0.39, 95% CI = -0.63 to -0.15,  $P=0.002$ ] (Fig. 3). When sensitivity analyses were conducted by the systematic removal of each study, the treatment direction showed no change. Subgroup analysis was performed based on the time points of assessment and psychometric scales.

Six studies were analysed for the short-term effect (up to 3 months) of CBT on depression (Doyle et al., 2017; Farver-Vestergaard et al., 2018; Guo et al., 2015; Howard, & Dupont, 2014; Kunik et al., 2008; Lamers et al., 2010), with no significant heterogeneity between studies ( $P=0.31$ ,  $I^2=17\%$ ). A fixed effect model meta-analysis and standardized mean difference were performed. The pooled effects favored the intervention group with better improvement in depression in short term [SMD = -0.25, 95% CI = -0.41 to -0.10,  $P=0.001$ ]. Five studies were analysed for the medium-term effect (up to 6 months) (Farver-Vestergaard et al., 2018; Guo et al., 2015; Hynninen et al., 2010; Howard, & Dupont, 2014; Livermore et al., 2015), and the heterogeneity test showed there was no significant heterogeneity between studies ( $P=0.57$ ,  $I^2=0\%$ ). The pooled effects favored the intervention group, showing significant improvements in depression for medium-term effect of CBT [SMD = -0.62, 95% CI = -0.83 to -0.40,  $P<0.00001$ ]. (Shown in Fig. 4)

Short-term assessment (up to 3 months) of BDI scores were reported in two studies (Kunik et al., 2008; Lamers et al., 2010), with no significant heterogeneity between studies ( $P=0.81$ ,  $I^2=0\%$ ). The pooled effects supported the intervention group, showing small improvement in depression, but the between-group did not reach statistical significance [MD = -1.86, 95% CI = -3.97 to 0.26,  $P=0.08$ ]. Short-term assessment of HADS scores were reported in another two studies (Howard, & Dupont, 2014; Farver-Vestergaard et al., 2018), with no significant heterogeneity between studies ( $P=0.90$ ,  $I^2=0\%$ ). The pooled effects favored the intervention group with better improvement in depression [MD = -1.87, 95% CI = -2.58 to 0.88,  $P=0.0002$ ]. Medium-term assessment (up to 6 months) of HADS scores were reported in three studies (Farver-Vestergaard, 2018; Howard, & Dupont, 2014; Livermore et al., 2015) with no significant heterogeneity between studies ( $P=0.74$ ,  $I^2=0\%$ ). The pooled effects favored the intervention group with significant improvement in depression [MD = -1.63, 95% CI = -2.51 to -0.75,  $P=0.0003$ ]. (Shown in Fig. 5)

### *Quality of life*

Eight of 10 included RCTs assessed the effects of CBT on quality of life in COPD patients (Doyle et al., 2017; Farver-Vestergaard et al., 2018; Howard et al., 2014; Hynninen et al., 2010; Kunik et al., 2008; Lamers et al., 2010; Livermore et al., 2015; Xu et al., 2017). Only domains scores were counted in two studies without

total scores which measured quality of life in patients by CRQ (Howard, & Dupont, 2014; Kunik et al., 2008), therefore, they were excluded from meta-analysis. The interventions' summary effect for quality of life was assessed at the assessment time point of last follow-up in this review, and the effect values were standardized by using the standardized mean difference. There was a significant heterogeneity between studies ( $P < 0.00001$ ,  $I^2 = 91\%$ ), excluding clinical heterogeneity, the random effect method was used for data synthesis. The pooled effects was a moderate effect size in favor of the intervention group [SMD = - 0.78, 95% CI = - 1.48 to - 0.07,  $P = 0.03$ ]. The treatment direction showed no change when sensitivity analysis was conducted by excluding the study (Xu et al., 2017) rated there was a significant difference on assessment time points with other studies [SMD = - 0.39, 95% CI = - 0.73 to - 0.06,  $P = 0.02$ ], and the  $I^2$  value decreased to 54%. The follow-up outcome assessment of the study (Xu et al., 2017) was at 2 weeks, which was significantly shorter than other studies (assessment time was at 2 months for follow-up at least). Descriptive analysis in two studies (Howard et al., 2014; Kunik et al., 2008) showed conflicting findings. One (Kunik et al., 2008) reported that the CBT significantly improved QoL, but there were no significant differences between groups, and the other reported better CRQ domains scores in the intervention group compared to the control group. The subgroup analysis was conducted based on the time points of outcome assessment, including short-term (up to 3 months) and medium-term (up to 6 months), and assessment scales.

Four of six studies were analysed for short-term effect of CBT on quality of life (Doyle et al., 2017; Farver-Vestergaard et al., 2018; Lamers et al., 2010; Xu et al., 2017). With a heterogeneity level of 94%, the pooled effects supported the intervention group with better quality of life, but the between-group difference did not reach statistical significance [SMD = - 0.86, 95% CI = - 1.87 to - 0.14,  $P = 0.09$ ]. Following sensitivity analysis, the treatment direction showed no change by excluding the study (Xu et al., 2017) rated there was a significant difference on assessment time points with other studies [SMD = - 0.30, 95% CI = - 0.71 to - 0.12,  $P = 0.16$ ], and the  $I^2$  value decreased to 62%. Three studies were analysed for medium-term effect of CBT on quality of life (Farver-Vestergaard et al., 2018; Hynninen et al., 2010; Livermore et al., 2015). With no significant heterogeneity between studies ( $P = 0.32$ ,  $I^2 = 11\%$ ), the pooled effects favored the intervention group, showing significant improvements in quality of life for medium-term effect of CBT [SMD = - 0.48, 95% CI = - 0.82 to - 0.14,  $P = 0.005$ ].

Data synthesis was performed for two studies reporting short-term assessment of quality of life on SGRQ scores (Lamers et al., 2010; Xu et al., 2017), with no significant heterogeneity between studies ( $P = 0.74$ ,  $I^2 = 0\%$ ), and the pooled effects favored the intervention group with significant improvement in quality of life [MD = - 7.74, 95% CI = - 9.01 to - 6.47,  $P < 0.00001$ ]. Data synthesis was performed for another two studies reporting short-term assessment of quality of life

on CAT scores (Doyle et al., 2017; Farver-Vestergaard et al., 2018), with no significant heterogeneity between studies ( $P = 0.21$ ,  $I^2 = 36\%$ ), and the pooled effects favored the intervention group with better quality of life, but the between-group difference did not reach statistical significance [MD = - 0.63, 95% CI = - 2.53 to 1.27,  $P = 0.52$ ]. Data synthesis was performed for two studies reporting mid-term assessment in quality of life on SGRQ scores (Hynninen et al., 2010; Livermore et al., 2015), with no significant heterogeneity between studies ( $P = 0.83$ ,  $I^2 = 0\%$ ), and the pooled effects favored the intervention group with significant improvement in quality of life [MD = - 9.37, 95% CI = - 15.15 to - 3.58,  $P = 0.002$ ]. This indicated a significant medium-term improvement in quality of life in favor of CBT. (Shown in Fig. 6)

### *Anxiety*

Seven of 10 included RCTs assessed the effects of CBT on anxiety in COPD patients (Doyle et al., 2017; Farver-Vestergaard et al., 2018; Howard, & Dupont, 2014; Hynninen et al., 2010; Kunik et al., 2008; Lamers et al., 2010; Livermore et al., 2015). All seven studies provided sufficient data for meta-analysis. The interventions' summary effect for anxiety was assessed at the assessment time point of last follow-up in this review, and the standardized mean difference was adopted. Data synthesis was performed, with a heterogeneity level of 52%, excluding clinical heterogeneity, a random effect model was adopted. The pooled effects favored the direction of the intervention group, showing significant improvements in anxiety [SMD = - 0.31, 95% CI = - 0.48 to - 0.15,  $P = 0.0002$ ]. When sensitivity analyses were conducted by the systematic removal of each study, the treatment direction showed no change. Subgroup analysis was performed based on the time points of assessment and psychometric scales.

Five of seven studies were analysed for short-term effect of CBT on anxiety (Doyle et al., 2017; Farver-Vestergaard et al., 2018; Howard, & Dupont, 2014; Kunik et al., 2008; Lamers et al., 2010). The fixed effect model was used for data synthesis because there was no significant heterogeneity between studies ( $P = 0.57$ ,  $I^2 = 0\%$ ). The pooled effects favored the intervention group, but no significant difference was identified between groups [SMD = - 0.11, 95% CI = - 0.28 to - 0.06,  $P = 0.21$ ]. Four studies were analysed for medium-term effect of CBT on anxiety (Farver-Vestergaard et al., 2018; Howard, & Dupont, 2014; Hynninen et al., 2010; Livermore et al., 2015). With no significant heterogeneity between studies ( $P = 0.20$ ,  $I^2 = 36\%$ ), the pooled effects favored the intervention group, showing significant improvements in anxiety for medium-term effect of CBT [SMD = - 0.45, 95% CI = - 0.70 to - 0.20,  $P = 0.0004$ ]. (Shown in Fig. 7)

Data synthesis was performed for two studies reporting short-term assessment of anxiety measured by BAI (Doyle et al., 2017; Kunik et al., 2008), and the pooled effects favored the intervention group with better improvement in anxiety,

but the between-group difference did not reach statistical significance [MD = - 0.82, 95% CI = - 4.82 to 2.63,  $P = 0.64$ ]. Data synthesis was performed for another two studies reporting short-term assessment of anxiety measured by HADS (Farver-Vestergaard et al., 2018; Howard, & Dupont, 2014), with a heterogeneity level of 50%, and the pooled effects favored the intervention group with better improvement in anxiety, but the comparison did not show any significant difference [MD = - 0.64, 95% CI = - 2.10 to 0.81,  $P = 0.39$ ]. Data synthesis was performed for three studies reporting mid-term assessment in anxiety measured by HADS (Farver-Vestergaard et al., 2018; Howard, & Dupont, 2014 ; Livermore et al., 2015), and the fixed effect model analysis found a large effect size showing significant improvement in anxiety in favor of CBT [MD = - 1.33, 95% CI = - 2.36 to - 0.30,  $P = 0.01$ ]. (Shown in Fig. 8)

#### *Treatment compliance*

The treatment compliance of COPD patients was assessed in two studies (Xu & OU, 2017; Zhang et al., 2017). With no significant heterogeneity between studies ( $P = 0.76$ ,  $I^2 = 0\%$ ), the fixed effect model meta-analysis was used to synthesize the findings. Data synthesis favored the intervention group, which had significant higher treatment compliance [RR = 0.26, 95% CI = 0.10 to 0.66,  $P = 0.004$ ].

#### *Self-efficacy*

The self-efficacy of COPD patients was reported in two studies (Doyle et al., 2017; Farver-Vestergaard et al., 2018), Which was assessed by GSES and CSES. With no significant heterogeneity between studies ( $P = 0.56$ ,  $I^2 = 0\%$ ), the fixed effect method was used for data synthesis. The pooled results indicated that the self-efficacy was relatively higher in the intervention group compared to the control group, but the difference showed no statistical significance [SMD = 0.11, 95% CI = - 0.20 to 0.41,  $P = 0.5$ ].

#### *Dyspnea symptoms*

The assessment of the symptoms of dyspnea in patients was reported in three studies. In two studies (Howard, & Dupont, 2014; Kunik et al., 2008), dyspnea was measured by Chronic Respiratory Disease Questionnaires (CRQ) as one domain. In one study (Livermore et al., 2015), dyspnea was measured by Borg Scale and the Interpretation of Breathing Problems Questionnaire (IBPQ). Given the varying scales used and the difference of time points on assessment, their results were presented in dissimilar patterns and unsuitable for synthesis in a meta-analysis. The descriptive analysis was performed. Kunik et al. (2008) reported that there was an improvement in mean CRQ subcategory scores including dyspnea scores, however, the difference did not reach statistical significance between groups at either 8 or 44 weeks. Livermore et al. (2015) reported full participants' dyspnea intensity were rated when breathing through resistive loads, and the CBT group showed a

significantly larger decrease in their ratings between baseline assessment and 6-month follow-up assessment compared to the routine care group ( $P=0.008$ ). The IBPQ scores at 6-month follow-up showed the CBT group had significantly improved compared to the control group, and the significant difference was identified for within-group and between-group. Howard et al. (2014) showed the symptoms of dyspnea were significantly improved in CBT group.

### **Discussion and conclusion**

#### *Discussion*

The National Institute for Health and Care Excellence (NICE) recommends CBT as a treatment choice for mental health problems in chronically ill patients and as an adjunct to other therapies (2009). This review of CBT intervention for COPD patients identified a number of RTCs. The outcomes from these studies suggest that CBT understudy resulted in positive outcomes for participants in most cases. This systematic review supported positive impacts of CBT on the reduction of depression, anxiety in COPD patients, and on the improvement of QoL and treatment compliance. CBT may also show some beneficial effects on the improvement of the symptoms of dyspnea in COPD patients.

In this review, depression, quality of life and anxiety were analyzed by subgroups based on the assessment time points of follow-up and assessment scales for sufficient data. Since the duration of follow-up less than six months in most studies, only short-term (up to 3 months) and mid-term (up to 6 months) effects were assessed. The findings showed significant improvement in short- and mid-term depression after intervention, and medium-term quality of life and anxiety were improved after intervention, although no significant effect was found for mid-term quality of life and anxiety. There is controversy in subgroup analyzing short-term quality of life in COPD patients by different assessment tools, so there is a need for well-designed studies to confirm it. The findings showed CBT resulted in positive effects on treatment compliance and dyspnea, so the wrong cognitive concept, beliefs regarding COPD could be changed and the negative emotions of patients (such as negative pessimism and low self-esteem, etc.) could be eliminated through the CBT, but there was no obvious effect on improving the patients' self-efficacy, pending further verification in more studies. The content of CBT in this review included identifying cognitive impairment, assessing behavioral status, recognizing cognitive impairment, intervention for psychological (emotional and stress management, interpersonal communication, etc.) and behavioral (recording notes and individualized breathing exercise programs, etc.). Sleep management (Hynninen et al., 2010) and mental meditation methods (Xu & Ou, 2017; Farver-Vestergaard et al., 2018) were adopted in three studies. The mode of intervention mainly was the



combination of individual session and group session. With the development of interdisciplinary cooperation, the nurses, clinical psychologists and physiotherapists were involved in the CBT intervention for COPD patients, and the interventions based on face-to-face or telephone-delivered follow-up (Doyle et al., 2017; Howard, & Dupont, 2014; Farver-Vestergaard et al., 2018) was performed in some studies proved to be effective in improving depression, anxiety and quality of life of patients in both forms. However, one study (Doyle et al., 2017) revealed conflicting results with the meta-analysis showed that the CBT delivered by telephone was not more effective than the control group in improving depression, anxiety and QoL, but there was a significant change in general self-efficacy in both groups. This might be due to other psychological or psychiatric services as part of usual care were received by 19% of participants, so there is a need for well-designed studies powered to confirm the effectiveness of CBT on psychological outcomes and to identify the most suitable methods for the delivery of the CBT. Major study findings of this review were little difference with early published systematic review (Smith, Sonogo, Ketcheson & Larson, 2014), which assessed the effectiveness of psychological intervention used for anxiety and depression in COPD. That review including four RCTs about the effect of CBT on anxiety and depression in COPD patients showed there were small improvement in patients' anxiety and depression, but the between-group difference did not reach statistical significance.

Decreased ratings of dyspnea was shown in the CBT group. The CBT could change the patient's perception of dyspnea and help to improve the symptom of dyspnea. A previous evidence suggested there was an association between respiratory sensation ratings and the outcomes of psychological interventions (Norweg & Collins, 2013). Livermore et al. (2010a; 2010b) showed an association between catastrophic interpretations of dyspnea and panic-related anxiety in COPD. Applying the CBT to COPD patients with negative emotions, which can reduce the patients' breathless belief and relieve the fear and anxiety (Livermore et al., 2010a; 2010b). Chenivresse et al. (2014) showed respiratory sensory gating was decreased by negative emotions in healthy humans, and psychological therapies have been proposed as a means to increase gating and reduce emotion-related dyspnea. The preventative CBT interventions that encourages the early recognition of dyspnea provide beneficial cognitive education and behavioral management strategies for COPD patients based on a non-catastrophic interpretation of the symptoms.

### *Limitations*

The Scopus and Google scholar database that we did not use, which could not avoid the omission of literatures. This study included only RCTs that are the gold standard of research on the effectiveness of interventions, which yield the highest quality of evidence. But some limitations were identified in the included RCTs. Only the published Chinese and English literatures were retrieved, and there was a possibility that bias of publication existed. The time points of assessment follow-up,

assessment tools, frequency and duration of delivery were different in some of the trials, which might yield a potential possibility for an overestimation of effect. And the compliance to CBT intervention between groups was not assessed in most of the included studies, which might underestimate the study power. According to the outcome assessment time points in the included studies, the insufficient number of trials with long-term (up to 12 months) follow-up made it impossible for us to conduct further analysis for long-term effect of the CBT, so this review only assessed the short-term and medium-term effect of the CBT on the main outcomes (depression, QoL and anxiety). In order to evaluate the effects of the CBT on COPD patients more scientifically and comprehensively, there is a need for further research to address the above limitations.

### Conclusion

This review and meta-analysis showed that CBT can be an effective strategy to reduce depression, anxiety and dyspnea, and improve quality of life and compliance in patients with COPD, but the evidence is insufficient to confirm the improvement on the patients' self-efficacy, and there are limited studies measuring long-term effect on health outcomes. The CBT may play a significant role in improving health outcomes in patients with COPD. With the insufficient studies, the smoking states, cost-economic, accident and emergency (A&E) visit rate and COPD-related hospitalizations were not assessed, requiring further improvement later. There is a need for further multicenter and large sample sizes RCTs to determine the long-term effect of the CBT and the most appropriate methods for the delivery of the CBT to ensure maximum benefit to patients with COPD.

In the future, multi-center, large-sample, high-quality RCT studies should be carried out. Follow-up was conducted to understand the long-term efficacy of CBT in COPD patients. And the difference of CBT's effect on improving anxiety and depression in COPD patients with different cultural backgrounds.

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