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What conservative interventions can improve the long-term quality of life, depression, and anxiety of individuals with stable COPD? A systematic review and meta-analysis

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Abstract

Purpose Many conservative interventions are used in the management of stable chronic obstructive pulmonary disease (COPD). It could be helpful for the prescribers to know what the evidence suggests about the effects of these interventions on the long-term quality of life (QoL), depression, and anxiety. This study aimed to summarize the rationale for the use of conservative interventions to improve the long-term QoL, depression, and anxiety in patients with stable COPD.

Methods The MEDLINE, Embase, Cochrane Library, and Web of Science databases were searched from database inception to December 2019. Randomized clinical trials (RCTs) investigating the long-term effects of conservative interventions on three parameters, including QoL, depression, and anxiety in patients with COPD were eligible for further analysis. To improve methodological rigor, only RCTs examining these parameters as primary outcomes were included. The standardized mean differences (SMD) with 95% confidence intervals (CIs) were calculated using random effects models. Quality of evidence was rated using the updated version of Van Tulder's criteria.

Results Thirty-eight RCTs were identified. Regarding long-term depression, there was moderate evidence supporting cognitive behavioral therapy compared with usual care in patients with COPD; regarding the long-term QoL of patients with COPD, there was limited evidence supporting walking programs, supplementary sugarcane bagasse dietary fiber, roflumilast, and tiotropium.

Conclusions Cognitive behavioral therapy is effective in alleviating the long-term depression of patients with COPD. Evidence for other interventions was insufficient, making it difficult to draw conclusions in terms of their effectiveness on the long-term QoL, depression, and anxiety.

Keywords Chronic obstructive pulmonary disease · Quality of life · Depression · Anxiety · Cognitive behavioral therapy · Systematic review and meta-analysis

Introduction

Chronic obstructive pulmonary disease (COPD) is a common, preventable, and treatable disease that is characterized by persistent respiratory symptoms and airflow limitation [1]. COPD is a leading cause of morbidity and mortality worldwide that induces a substantial economic and social burden [1]. Extrapulmonary comorbidities in COPD are common and can be very detrimental, including cardiovascular disease, osteoporosis, sarcopenia, and diabetes [1]. Interestingly, extrapulmonary brain-related comorbidities of COPD, such as depression and anxiety, are also common. The prevalence of depression and anxiety is higher among patients with COPD than the prevalence among non-COPD

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individuals [2]. Despite the increased prevalence, mental issues among COPD individuals are somewhat neglected by the medical community compared to the physical problems.

Associations between adverse psychological factors and COPD are well established. A previous systematic review and meta-analysis revealed a bidirectional relationship between depression or anxiety and COPD, that depression and anxiety adversely affected prognosis of COPD, and conversely, COPD increased the risk of developing depression [3]. The overall health status of an individual with COPD is the result of interplay between psychological and physical factors, as COPD is nowadays considered as a multicomponent disease, despite being defined by the presence of persistent airflow limitation [4]. Mental health complications are associated with worsening of disease progression, as evidenced by increased mortality and frequency of exacerbations, and decreased exercise capacity in depressed and anxious COPD patients [5–8].

Quality of life (QoL) is decreased in COPD patients due to physical and psychological impairments [9], of which depression and anxiety have a stronger association with the reduced QoL in COPD, compared with the widely used spirometric value [10]. Since QoL is considered a major goal in managing the disease, therapies should be focused on improving it.

QoL, depression, and anxiety are important indicators of psychological well-being in patients with COPD. A summary of evidence regarding the efficacy of different interventions on psychological well-being may support clinical treatment decision-making. Therefore, we conducted a systematic review (SR) and meta-analysis to synthesize evidence of different conservative interventions in improving long-term QoL, depression, and anxiety in patients with stable COPD.

Materials and methods

This systematic review and meta-analysis was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines [11]. The study was registered in PROSPERO (Registration Number: CRD42020216443).

Search strategy

We searched the MEDLINE (via PubMed), Embase (via Ovid), Cochrane Library, and Web of Science databases for relevant articles from database inception to December 2019. Reference list of the included studies were also reviewed for potential eligible trials. The search strategy is presented in Supplementary Table S1.

Selection criteria

Two reviewers independently screened the titles and abstracts for eligibility. Full-text reviews were then performed. Disagreements were resolved by consensus or by consulting a third reviewer when needed. Randomized controlled trials (RCTs) that investigate the effectiveness of any conservative interventions on QoL, depression, and anxiety in patients with stable COPD were included. Specifically, studies were included if they met the following criteria:

1. Participants: Participants were patients with stable COPD of any disease severity. We excluded studies whose participants had acute exacerbations of COPD at enrollment. There was no restriction on age, sex, race, or comorbidities of the participants.
2. Interventions: No restrictions were placed on the intervention, except that the intervention should be "conservative." Surgery or other invasive procedures, such as lung volume reduction surgery or lung transplantation, were considered non-conservative.
3. Outcomes: Studies were eligible whose primary outcomes were QoL and/or depression and/or anxiety. Studies that only provided scores of the QoL subscale instead of the total score were excluded. Focusing on primary outcomes is a useful strategy for improving methodological rigor [12]. The primary outcome of RCT is the basis for the estimation of sample size, which therefore increases the power of the study to find differences in this specific outcome, and the intervention is more likely to be targeted to the primary outcome [12]. Therefore, only studies that considered QoL, depression, and anxiety as their primary outcomes were included in this SR. We considered the outcome as primary if it was directly described by the study as "primary," "main," or "key" outcomes. When no outcome was specified as the primary outcome, the outcome that was used in the power analysis was considered the primary outcome. If an RCT did not specify the primary outcome or did not use a certain outcome to perform power analysis, the RCT was excluded. Since we only focused on the long-term benefits of interventions, we only included studies with a follow-up $\geq$ 6 months (or 24 weeks).
4. Study design: The study design was limited to RCTs.

The language was limited to English. In case the relevant data could not be obtained through the published manuscript, the corresponding author was contacted to request the data. If we could not obtain the data after the contact, the study was excluded.

Data extraction

Two reviewers independently extracted the data from the included studies. A third reviewer was involved in case of discrepancies.

Assessment of methodological quality and risk of bias

Methodological quality assessment of each study was performed using the Physiotherapy Evidence Database (PEDro) scale [13]. Scores on the PEDro scale range from 0 (very low methodological quality) to 10 (high methodological quality). Besides, the risk of bias was assessed using the Cochrane risk of bias tool [14]. All assessments were performed by two independent reviewers. Discrepancies were resolved through discussion or by consulting a third reviewer when needed.

Data management and statistical analysis

Pooling of data was conducted where studies investigated similar interventions using comparable outcome measures. When data could not be pooled due to the limited number the studies (i.e., fewer than two studies), they were summarized in a forest plot (without an overall pooled estimate of effect) to give easy visualization of the results. We calculated the standardized mean differences (SMD) with 95% CIs using random effects models for continuous data. Heterogeneity was quantified by the I^2 statistic. Data analysis was performed using Review Manager 5.4 [15]. For each finding, we rated the level of evidence as "strong," "moderate," "limited," "very limited," and "conflicting," using the updated version of Van Tulder's criteria [16]. According to the criteria, the level of evidence was determined based on the number and the quality of studies, and the degree of statistical homogeneity among the studies. Detailed information of this criteria is available in Supplementary Table S2.

Results

Study characteristics

The flowchart of the study selection is provided in Fig. 1. Thirty-eight studies were eligible for inclusion in the current SR. Most of the included studies ($N = 34$) evaluated QoL, four studies evaluated depression, and four studies evaluated anxiety in patients with COPD as the primary outcome.

Methodological quality assessment and assessment of bias risk

The PEDro quality assessment for each study is listed in Supplementary Table S3. Fourteen studies were rated as high quality [17–30], and 24 studies as low quality [31–54].

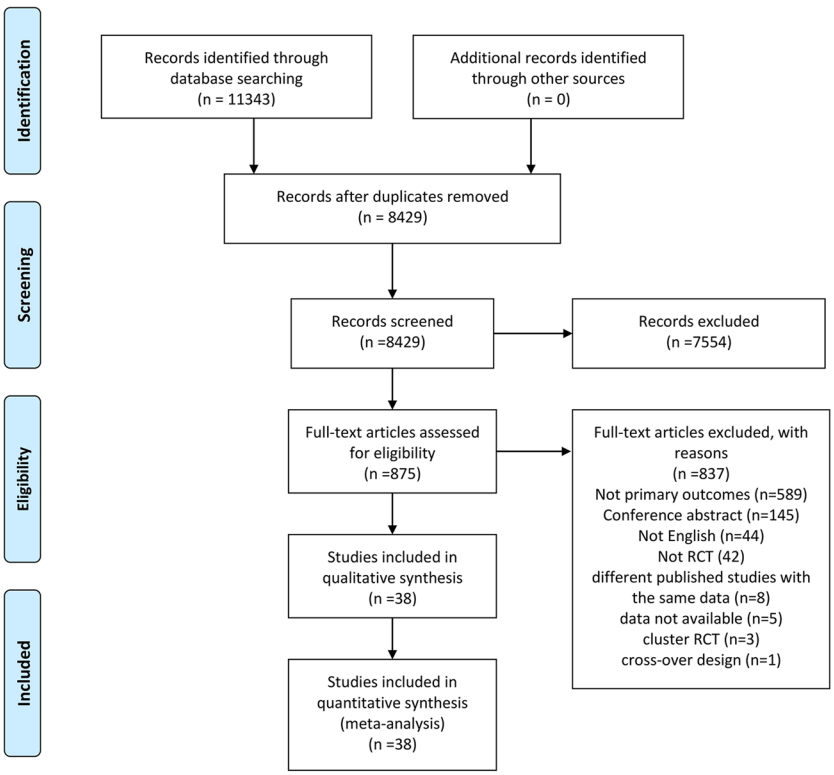

Fig. 1 Flowchart of the study selection

Lack of blinding to the subjects and therapist was the most common methodological limitation of the studies, which could be explained by the difficulty in blinding due to the design of the interventions.

The assessment of the bias risk of each included study is presented in Supplementary Figs. S1 and S2. Similarly, the most common risk of bias was the lack of blinding to the patients, personnel, and assessors.

Meta-analyses

A summary of the findings of the meta-analyses is presented in Table 1.

Effects of interventions on QoL

The results that could be pooled are presented in Figs. 2, 3, 4; the results that could not be pooled are presented in Fig. 5.

Effects of an integrated pulmonary rehabilitation (PR) program on long-term QoL

Overall, three studies [28, 39, 46] (414 participants) provided with limited level of evidence that an integrated PR program was not superior to control interventions in improving long-term QoL in patients with COPD (SMD = − 0.37, CI − 1.14 to 0.40, $p = 0.34$, $I^2 = 93\%$). Specifically, pooled data from two studies (304 participants) showed that an integrated PR program was not effective compared to usual care to improve long-term QoL (SMD = − 0.69, CI − 1.56 to 0.19, $p = 0.12$, $I^2 = 93\%$). One study (110 participants) showed that an integrated PR program was as effective as Tai Chi in improving long-term QoL (SMD = 0.27, CI − 0.11 to 0.64, $p = 0.16$) (Fig. 2A).

Effects of exercise on long-term QoL

Three studies investigated the effects of exercise [32, 43, 51] (302 participants). Pooled data demonstrated that exercise was not superior to control in improving the long-term QoL of patients with COPD. The level of evidence was considered limited according to the Van Tulder's criteria. Specifically, in the comparison of exercise VS usual care, or exercise + PR VS PR alone, the difference was not statistically significant (SMD = − 0.50, CI − 1.21 to 0.21, $p = 0.17$) (SMD = 0.36, CI − 0.44 to 0.76, $p = 0.08$) (Fig. 2B).

Effects of self-management and education on long-term QoL

Eleven studies [25, 33, 34, 42, 44, 45, 48–50, 52, 54] (1737 participants) evaluated the effectiveness of self-management and education in the long-term QoL of patients compared with control interventions. The evidence derived from these studies was conflicting according to the Van Tulder's criteria. Specifically, there was moderate evidence from three studies (714 participants) that self-management and education (meeting or coaching) was not superior to educational booklets in improving long-term QoL in COPD patients (SMD = − 0.15, CI − 0.30 to 0.00, $p = 0.05$, $I^2 = 0\%$). There was conflicting evidence from eight studies (1023 participants) as to the effectiveness of self-management and education compared with usual care in long-term QoL (SMD = − 0.17, CI − 0.85 to 0.50, $p = 0.62$, $I^2 = 96\%$) (Fig. 3A).

Effects of physical activity on long-term QoL

Limited evidence from one study [21] (125 participants) suggested that the walking program was superior to usual care in improving long-term QoL (SMD = − 0.40, CI − 0.77 to − 0.04, $p = 0.03$) (Fig. 3B). There was limited evidence from two studies [22, 37] (309 participants) that the walking program with active feedback demonstrated no superiority over walking without active feedback (SMD = − 0.19, CI − 0.47 to 0.10, $p = 0.21$, $I^2 = 25\%$) (Fig. 3B).

Effects of telemonitoring on long-term QoL

Pool data from two studies [29, 53] (591 participants) suggested that telemonitoring was not effective compared to usual care in long-term QoL (SMD = 0.15, CI − 0.12 to 0.42, $p = 0.28$, $I^2 = 64\%$) (Fig. 3C). Level of evidence was limited.

Effects of other interventions on long-term QoL

Limited evidence suggested that supplementary sugarcane bagasse dietary fiber [20] (SMD = − 0.56, CI − 0.87 to − 0.25, $p = 0.0004$), roflumilast [17] (SMD = − 2.51, CI − 2.70 to − 2.31, $p < 0.00001$), and tiotropium [27] (SMD = − 0.30, CI − 0.47 to − 0.12, $p = 0.001$) were superior to control interventions (e.g., conventional treatment or placebo) in improving long-term QoL in patients with COPD (Fig. 5).

Limited evidence suggested that two-year home-based nocturnal non-invasive ventilation added to PR was not superior to PR alone [23], and that 24 weeks of once-daily triple therapy (fluticasone furoate/umeclidinium/vilanterol 100 µg/62.5 µg/25 µg; ELLIPTA ® inhaler) were as effective as 24 weeks of twice-daily ICS/LABA therapy (budesonide/formoterol 400 µg/12 µg; Turbuhaler ®) [19]. Additionally, limited evidence showed that Bushen Fangchuan tablet [26], Bushen Yiqi granule [26], and ginseng extract [18] were not effective compared to placebo in improving long-term QoL (Fig. 5).

Table 1 Summary of findings

Interventions or comparisons Subgroup analysis	Number of RCTs (*N*) and participants (*n*)	SMD, 95% CI	*p*	Level of evidence	Plain language summary
Outcome: long-term QoL					
PR program	$N=3, n=414$	−0.37 [−1.14, 0.40]	0.34	Limited	PR program may not be superior to control interventions in improving long-term QoL
PR VS usual care	$N=2, n=304$	−0.69 [−1.56, 0.19]	0.12		
PR VS Tai Chi	$N=1, n=110$	0.27 [−0.11, 0.64]	0.16		
Exercise	$N=3, n=302$	−0.21 [−0.85, 0.42]	0.51	Limited	Exercise may not be superior to control interventions in improving long-term QoL
Exercise VS usual care	$N=2, n=204$	−0.5 [−1.21, 0.21]	0.17		
Exercise + PR VS PR alone	$N=1, n=98$	0.36 [−0.04, 0.76]	0.08		
Self-management and education	$N=11, n=1737$	−0.16 [−0.60, 0.28]	0.47	Conflicting	The effect of self-management and education on long-term QoL is uncertain
Self-management and education (meeting or coaching) VS educational booklet	$N=3, n=714$	−0.15 [−0.30, 0.00]	0.05		
Self-management and education (meeting or coaching) VS usual care	$N=8, n=1023$	−0.17 [−0.85, 0.50]	0.62		
Physical activity	Data not suitable for pooling due to vast difference among comparisons			Limited	Walking program may improve long-term QoL; Walking program with active feedback may not be superior to walking without feedback in improving long-term QoL
Walking program VS usual care	$N=1, n=125$	−0.40 [−0.77, −0.04]	0.03		
Walking program with active feedback VS walking without feedback	$N=2, n=309$	−0.19 [−0.47, 0.10]	0.21		
Telemonitoring	$N=2, n=591$	0.15 [−0.12, 0.42]	0.28	Limited	Telemonitoring may not be superior to usual care in improving long-term QoL
Supplementary sugarcane bagasse dietary fiber	$N=1, n=166$	−0.56 [−0.87, −0.25]	0.0004	Limited	supplementary sugarcane bagasse dietary fiber may improve long-term QoL
Roflumilast	$N=1, n=763$	−2.51 [−2.70, −2.31]	<0.00001	Limited	Roflumilast may improve long-term QoL
Tiotropium	$N=1, n=492$	−0.30 [−0.47, −0.12]	0.001	Limited	Tiotropium may improve long-term QoL
Home-based nocturnal non-invasive ventilation added to PR	$N=1, n=35$	−0.11 [−0.78, 0.56]	0.75	Limited	home-based nocturnal non-invasive ventilation added to PR may not superior to PR alone in improving long-term QoL
Triple therapy (fluticasone furoate/umeclidinium/vilanterol) and ICS/LABA therapy (budesonide/formoterol)	$N=1, n=356$	−0.20 [−0.41, 0.01]	0.06	Limited	Triple therapy may be as effective as ICS/LABA therapy in improving long-term QoL
Bushen Fangchuan tablet	$N=1, n=180$	−0.01 [−0.31, 0.28]	0.93	Limited	Bushen Fangchuan tablet may not improve long-term QoL
Bushen Yiqi granule	$N=1, n=173$	−0.00 [−0.30, 0.30]	0.99	Limited	Bushen Yiqi granule may not improve long-term QoL
Ginseng extract	$N=1, n=144$	−0.13 [−0.45, −0.20]	0.44	Limited	Ginseng extract may not improve long-term QoL
Honey supplementation	$N=1, n=34$	−1.05 [−1.80, −0.30]	0.006	Very limited	The effects of honey supplementation in improving the long-term QoL is uncertain

Table 1 (continued)

Interventions or comparisons Subgroup analysis	Number of RCTs (*N*) and participants (*n*)	SMD, 95% CI	*p*	Level of evidence	Plain language summary
Supervised, outpatient-based exercise plus unsupervised home exercise following PR VS only unsupervised home exercise training following PR	$N=1, n=48$	0.64 [0.06, 1.22]	0.03	Very limited	It is uncertain whether supervised, outpatient-based exercise plus unsupervised home exercise is superior to only unsupervised home exercise training following PR in improving long-term QoL
Once-daily indacaterol plus glycopyrronium VS once-daily tiotropium plus twice-daily formoterol	$N=1, n=821$	−0.06 [−0.19 to 0.08]	0.42	Very limited	It is uncertain whether Once-daily indacaterol plus glycopyrronium is superior to once-daily tiotropium plus twice-daily formoterol in improving long-term QoL
Rehabilitation in a warm climate VS that in a colder climate	$N=1, n=96$	−0.26 [−0.67, 0.16]	0.23	Very limited	It is uncertain whether rehabilitation in a warm climate and that in a colder climate have different effects in long-term QoL
Outcome: long-term depression					
CBT	$N=3, n=209$	−0.50 [−0.78, −0.22]	0.0005	Moderate	CBT can improve long-term depression
Guided self-change plus NRT VS NRT alone	$N=1, n=38$	0.06 [−0.57, 0.70]	0.85	Limited	A guided self-change plus NRT may be as effective as NRT alone in improving long-term depression
Outcome: long-term anxiety					
CBT	$N=3, n=264$	−0.42 [−0.86, −0.02]	0.06	Limited	CBT may not improve long-term anxiety
Guided self-change plus NRT VS NRT alone	$N=1, n=38$	0.11 [−0.53, 0.74]	0.75	Limited	A guided self-change plus NRT may be as effective as NRT alone in improving long-term anxiety

PR pulmonary rehabilitation, *SMD* standard mean difference, *CI* confidence interval, *QoL* quality of life, *ICS/LABA* Inhaled corticosteroid/long-acting beta-2 agonist; *CBT* cognitive behavioral therapy, *NRT* nicotine replacement therapy

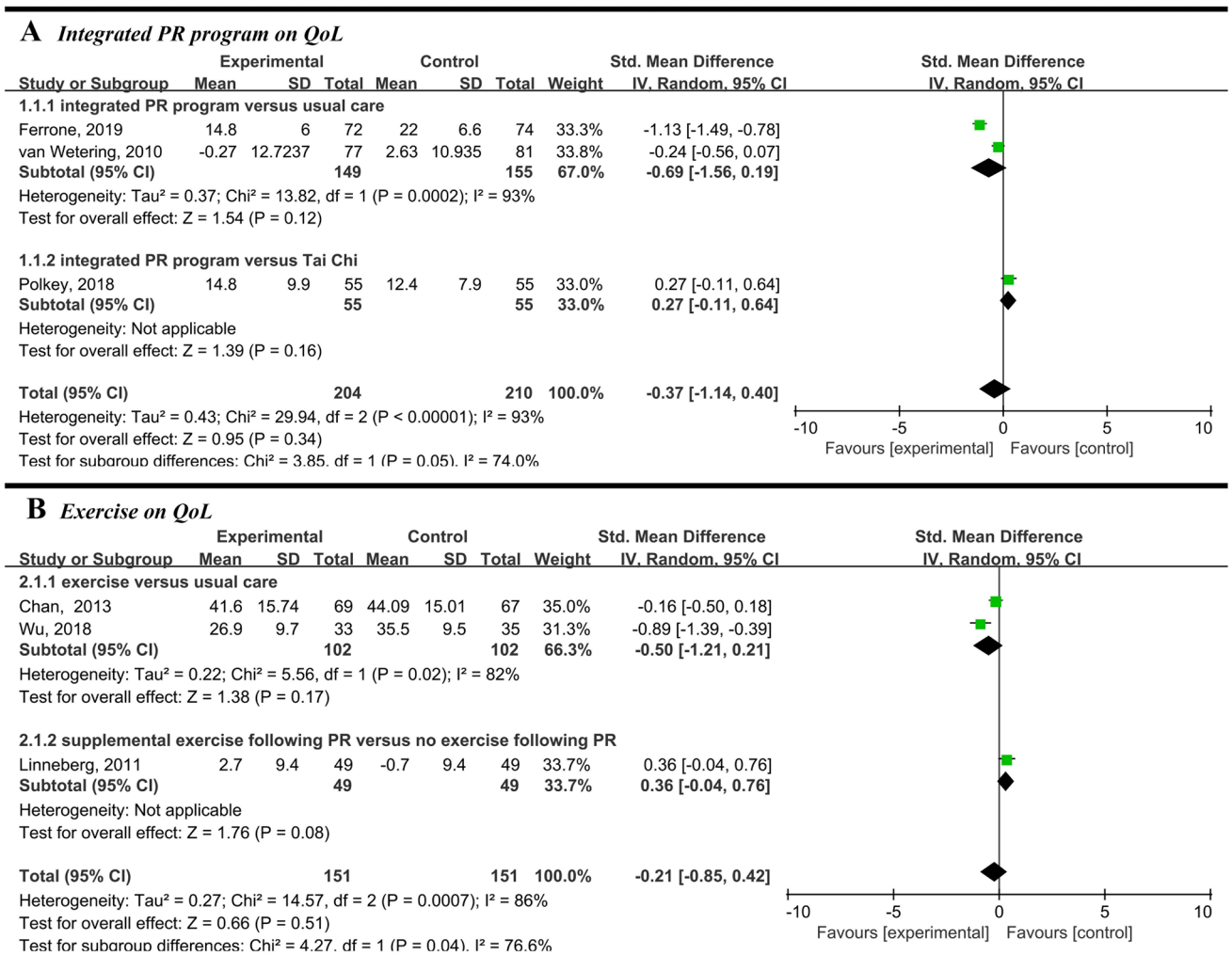

Fig. 2 Forest plot comparing the effects of interventions on the long-term QoL (Part I). **A** Integrated pulmonary rehabilitation program VS control; B Exercise VS control

There was very limited evidence that a 6-month regime of honey supplementation was superior to standard care in improving the long-term QoL of patients with COPD [38] (SMD = − 1.05, CI − 1.80 to − 0.30, $p = 0.006$). There was also very limited evidence that supervised, outpatient-based exercise plus unsupervised home exercise following PR was superior to unsupervised home exercise training alone in improving long-term QoL [41] (SMD = 0.64, CI 0.06 to 1.22, $p = 0.03$) (Fig. 5).

There was also very limited evidence that once-daily indacaterol plus glycopyrronium was as effective as once-daily tiotropium plus twice-daily formoterol [31], and that rehabilitation in a warm climate compared with that in a colder climate [35] were as effective in improving long-term QoL in individuals with COPD (Fig. 5).

Effect of interventions on long-term depression and anxiety

Only the data from studies investigating cognitive behavioral therapy (CBT) could be pooled (Fig. 4). Data that could not be pooled are presented in Fig. 5.

Effects of CBT on long-term depression

There was moderate evidence from three studies (209 participants) that CBT was superior to usual care in improving long-term depression in patients with COPD [36, 40, 47] (SMD = − 0.50, CI − 0.78 to − 0.22, $p = 0.0005$, $I^2 = 0\%$) (Fig. 4A).

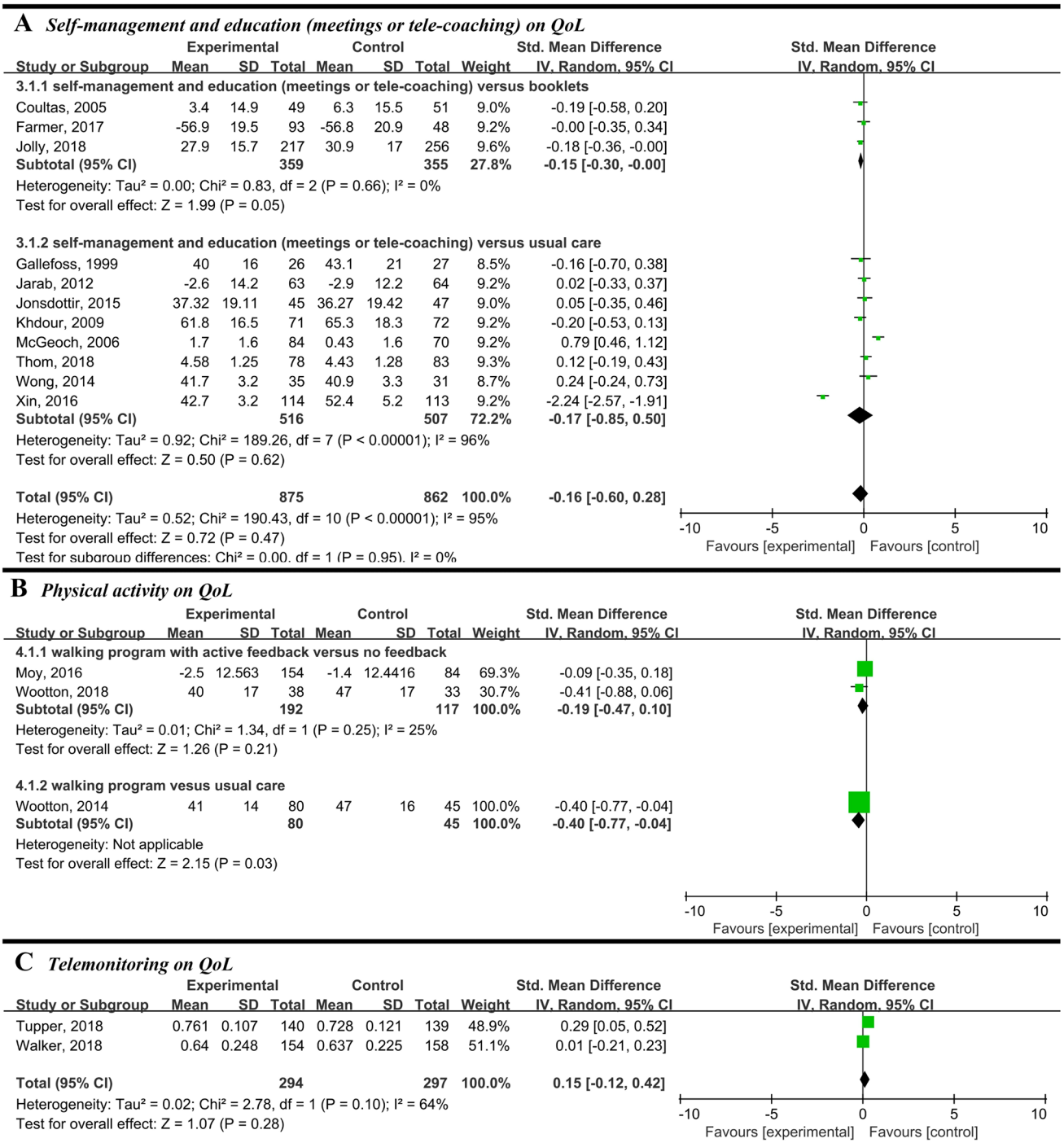

Fig. 3 Forest plot comparing the effects of interventions on the long-term QoL (Part II). **A** Self-management or education program (via meetings or tele-coaching) VS control; **B** Active feedback VS no feedback in a walking program, and walking program VS usual care; **C** Telemonitoring VS control

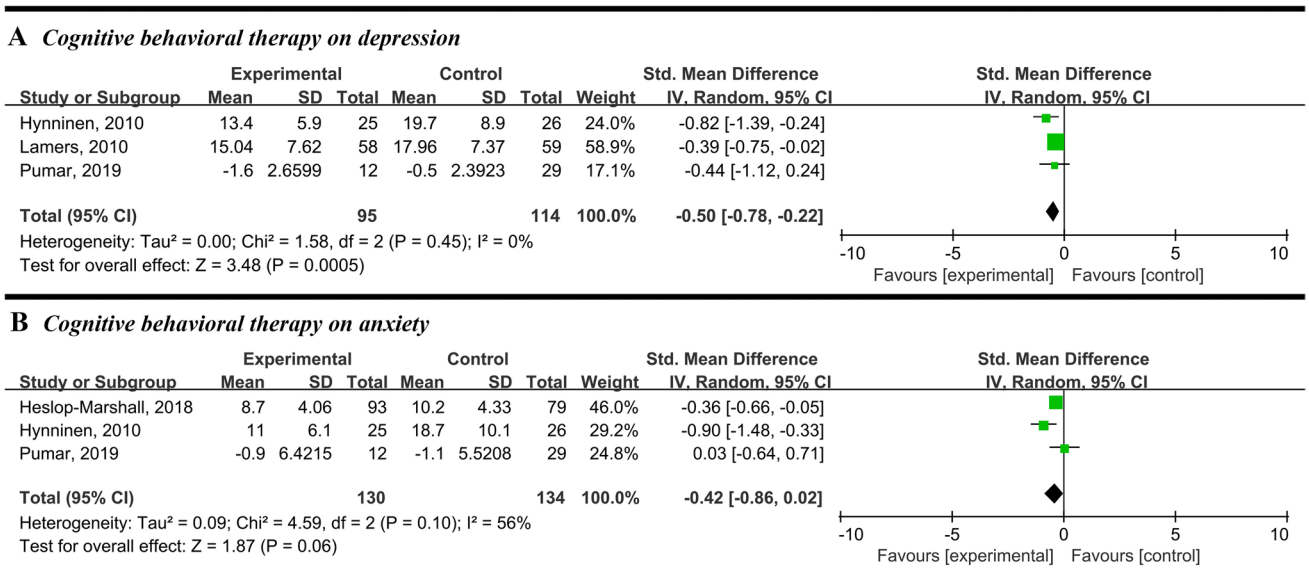

Fig. 4 Forest plot comparing CBT with control on long-term depression and anxiety. A, CBT VS control on long-term depression; B, CBT VS control on long-term anxiety. CBT: cognitive behavioral therapy

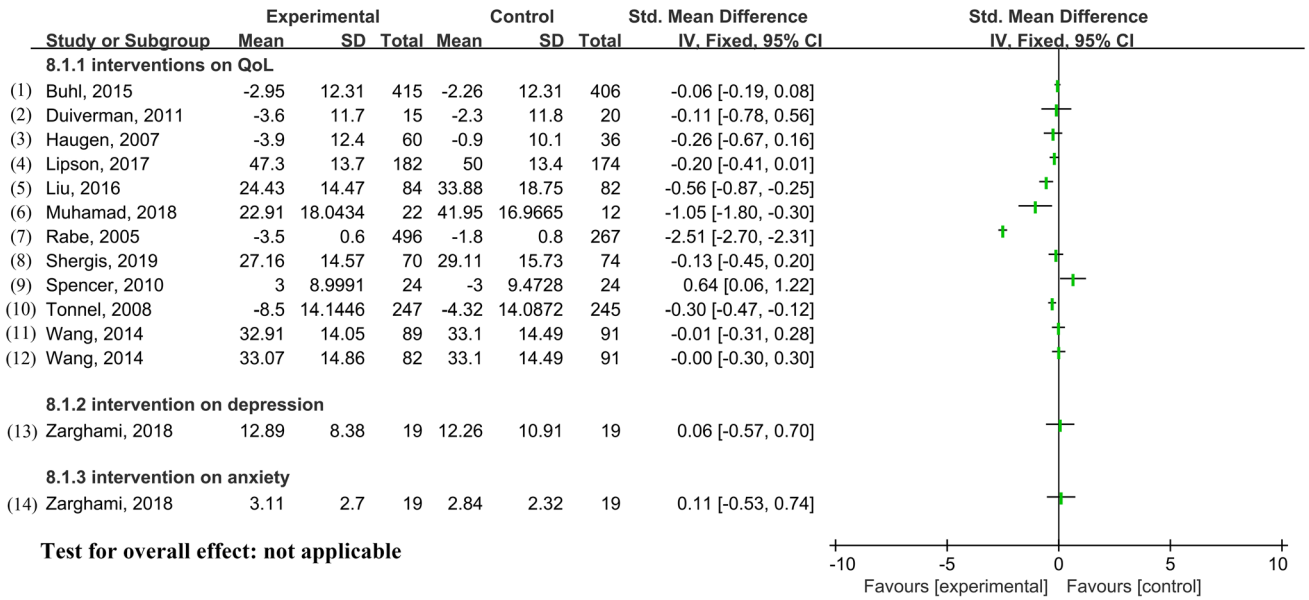

Fig. 5 Effects of other interventions on long-term QoL, depression, and anxiety. Comparisons presented in figure are (1) Indacaterol/glycopyrronium 110 μg/50 μg once daily VS Tiotropium 18 μg once daily plus formoterol 12 μg twice daily; (2) Home-based nocturnal non-invasive ventilation plus PR VS PR alone; (3) Rehabilitation in cold VS in warm climate; (4) fluticasone furoate/umeclidinium/vilanterol 100 μg/62.5 μg/25 μg once daily VS budesonide/formoterol 400 μg/12 μg twice daily; (5) Sugarcane bagasse dietary fiber VS placebo; (6) Honey supplementation VS usual care; (7) Roflumilast 250 mg or 500 mg once daily VS placebo; (8) Ginseng capsules 100 mg twice daily VS placebo; (9) Supervised, outpatient-based exercise plus unsupervised home exercise following PR VS standard care of unsupervised home exercise training; (10) Tiotropium 18 mg once daily VS placebo; (11) Bushen Fangchuan tablets VS placebo; (12) Bushen Yiqi granule VS placebo; (13) and (14) Guided self-change sessions plus nicotine replacement therapy VS nicotine replacement therapy alone

Effect of other interventions on long-term depression

There was limited evidence from one study that a guided self-change combined with nicotine replacement therapy (NRT) did not add more benefits compared with NRT alone in improving long-term depression in patients with COPD [30] (Fig. 5).

Effects of CBT on anxiety

There was limited evidence from three studies [24, 40, 47] (264 participants) that CBT was not effective compared to usual care in improving long-term anxiety in patients with COPD (Fig. 4B).

Effects of other interventions on long-term anxiety

There was limited evidence that a guided self-change combined with NRT was not superior to NRT alone in improving long-term anxiety in patients with COPD [30] (Fig. 5).

Discussion

This SR identified 38 studies that investigated the effects of interventions on QoL and/or depression and/or anxiety as primary outcomes in patients with COPD. The main findings were as follows: regarding long-term depression, there was moderate evidence supporting the use of CBT compared with usual care in patients with COPD; regarding the long-term QoL of patients with COPD, there was limited evidence supporting the use of walking programs, supplementary sugarcane bagasse dietary fiber, roflumilast, and tiotropium compared with control interventions.

In a meta-analysis by Ma et al. [55], CBT was reported to be effective in improving depression and anxiety in individuals with COPD. However, that study did not specify how long the benefits could be maintained. Our SR extended these findings with a moderate level of evidence that CBT was more effective than usual care in improving long-term depression in patients with COPD. While in regard to the benefits for long-term anxiety, current evidence is insufficient to support the superiority of CBT to usual care.

The latest report of the Global Strategy for the Diagnosis, Management, and Prevention of Chronic Obstructive Pulmonary Disease (GOLD) has recommended active lifestyle and exercise, self-management, and pulmonary rehabilitation in the management of stable COPD [1]. To our surprise, the results of this SR did not support exercise, self-management and education or PR in improving long-term QoL in stable COPD. One possible reason is that the benefits of these interventions diminish over time in COPD if activity and other positively adaptive behaviors are not continued after the completion of the interventions [56]. This finding highlights the importance of a maintenance program following the intervention that encourages sufficient activity and positively adaptive behaviors in daily life. However, the level of evidence was generally weak (most were rated as "limited" or "very limited") due to the low number of studies for the same intervention or the tremendous heterogeneity in the pooled data. Therefore, caution must be taken when interpreting the results.

Pharmacological therapies are another important component in the management of stable COPD. They can reduce symptoms and the risk and severity of exacerbations, as well as improve exercise tolerance and the health status and of patients with COPD [1]. This SR demonstrated that roflumilast, a phosphodiesterase-4 inhibitor, and tiotropium, a long-acting anticholinergic bronchodilator, are more effective in improving the long-term QoL than placebo. However, many studies that investigated the effects of pharmacological therapies on COPD were not included in the current study. One important reason was that these studies did not employ QoL, depression, or anxiety but spirometry parameters, exacerbation rate, or hospitalizations as their primary outcomes; therefore, they did not meet our inclusion criteria.

Our study focused on three important outcomes of COPD patients, i.e., quality of life, depression, and anxiety. However, except for quality of life, studies measuring the depression and anxiety as their primary outcomes were scarce. Although many studies took them as secondary outcomes, considering the pivotal role of a primary outcome in an RCT, the scarcity of studies primarily examining depression and anxiety has partly proved the notion that mental health of COPD patients was overlooked by the medical community. Besides the physical problems, the improvement of patients' mental health is as well an important goal in the treatment of COPD, therefore, future studies focusing on the efficacy of interventions on long-term depression and anxiety are in need.

Limitations

There were several limitations in this study. First, the limited number of studies for each intervention reduced the power of the meta-analysis. Second, we set strict eligibility criteria in an attempt to raise the methodological quality of our study. For example, only the studies that employed QoL, depression, and anxiety as the primary outcomes were included. This could lead to missing some studies that considered QoL, depression, and anxiety as secondary outcomes, and some interventions could be omitted. Third, although we only compared studies with similar interventions, we still cannot neglect the heterogeneity of interventions and their corresponding control conditions among different studies.

For example, in some RCTs included in the present study, subjects in the control group were assigned to usual care, a term most commonly refers to routine care provided for the target problem in the trial setting. However, usual care can range depending on different settings, from guideline-driven, gold-standard care, to highly variable care to no care [57]. The variability of usual care among trials is a potential source of clinical heterogeneity and merits attention when interpreting the results. Last, due to language restriction, we only included articles written in English. These limitations could reduce the power of this study.

Conclusions

CBT is effective in improving long-term depression in patients with COPD. There was limited evidence that the walking program, supplementary sugarcane bagasse dietary fiber, roflumilast, and tiotropium may be effective in improving long-term QoL in patients with COPD. Evidence for other interventions was insufficient, making it difficult to draw conclusions in terms of their effectiveness on the long-term QoL, depression, and anxiety.

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Data availability Data available within the article or its supplementary materials.

Declarations

Conflict of interest The authors declared no conflict of interests.

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