Review

The Combined Efficacy of Adjunctive Psychological Interventions and Pulmonary Rehabilitation in People With Chronic Obstructive Pulmonary Disease - A Systematic Review and Meta-Analysis

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Running Head: **Adjunctive Psychological Interventions in COPD**

Keywords: chronic obstructive pulmonary disease; cognitive behavioral therapy; psychological intervention; anxiety; depression

Abbreviations: COPD = Chronic obstructive pulmonary disease; PR = Pulmonary rehabilitation; PEDro score=Physiotherapy Evidence Base; HRQoL=Health-related quality of life; CBT=Cognitive behavioral therapy; PR + PSY-INT=Combined PR and Psychological intervention ; PRISMA=Preferred Reporting Items for systematic reviews and meta-analyses; RCTs=Random control trials; GRADE=Grading of Recommendations, Assessment, Development, and Evaluations; SD=Standard deviation; SMD=Standardized mean differences; CI=Confidence intervals; PR=Prediction intervals; HADS=Hospital Anxiety and Depression Scale; BAI=Beck Anxiety Inventory; BDI=Beck Depression Inventory; 6MWD=6-minute walk distance; MCID/MID=Minimal (clinically) important differences

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Abstract

Background: Depression and anxiety exacerbate the pernicious cycle of dyspnea, inactivity, and deconditioning in people with chronic obstructive pulmonary disease (COPD). Pulmonary rehabilitation (PR) is a well-proven management for improving exercise capacity and health-related quality of life in people with COPD. Recently, evidence suggested that adjunctive psychological interventions may enhance the efficacy of PR by targeting the bidirectional dyspnea-anxiety cycle and modifying maladaptive behaviors.

Objective: To evaluate the added benefit of psychological interventions in comparison to conventional PR alone.

Methods: Four electronic databases (PubMed, EMBASE, Web of Science, and CINAHL) were searched from their inception to March 31, 2025. Studies retrieved were screened according to the selection criteria. Statistical analyses were performed using Cochrane RevMan Manager 5.4. Appraisal of study quality and the certainty of evidence were evaluated.

Results: Five studies were included in this meta-analysis. Primary analysis results showed significant improvements in anxiety (Standardized Mean Difference, SMD = -0.55; 95% CI: -0.85 to -0.25, $p = 0.0004$). There was no improvement in depression (SMD = -0.38, 95% CI = -0.97 to 0.22, $p = 0.22$) or physical outcomes (6-minute walking distance: (Mean difference, MD = 16.45, 95% CI = -17.38 to 50.27, $p = 0.34$). Subgroup analysis results demonstrated significantly greater improvement in depression among people with clinical symptoms at baseline ($p = 0.004$).

Conclusions: The addition of adjunctive psychological interventions may enhance the efficacy of PR for people with COPD when compared to those receiving PR alone. The findings suggest that better improvements were observed among patients with clinical psychological symptoms at baseline.

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Introduction

Epidemiology and Psychological Burden of COPD

Chronic obstructive pulmonary disease (COPD) is characterized by airflow limitation and breathlessness, which encompasses emphysema and bronchiolitis.[1] There are more than half a billion cases worldwide, making COPD the third leading cause of global mortality.[2] Aside from physical symptoms such as dyspnea, people with COPD also report anxiety and depression symptoms, or in more severe cases, suffer from psychological disorders.[3] According to a 2023 systematic review, the overall pooled global prevalence of variably defined depression among people with COPD was 34.5% (95% CI: 30.9-38.1),[4] with rates in individual studies varying from 17.0% to 61.7%.[4] A higher prevalence was found among hospitalized individuals (40.4% vs 36.5% in out-patient clinics), females (39.7% vs 28.8% in males), and patients with GOLD III-IV (35.0% vs 28.3% in patients with GOLD I-II).[4] Anxiety disorders are also common among inpatient populations (10-55% vs 13-46% in outpatients).[5]

Mechanisms Underlying Anxiety and Depression in COPD

The mechanism leading to the symptoms of anxiety and depression in people with COPD is believed to be multifactorial and bidirectional, forming a pathological cycle of progressively undermines health status.[6-8] Specifically, this bidirectional relationship manifests as a vicious cycle between physical and psychological symptoms. Psychological symptoms in people with COPD result from multiple interacting biological, behavioral, and social factors.[7-9] Symptoms such as dyspnea, fatigue, cough, and sputum production may induce psychological symptoms.[2] When triggered, negative emotions are associated with physical symptoms, leading to maladaptive behaviors and undermining the individual's perception of their own health status.[10] For instance, dyspnea was frequently interpreted as threatening.[10] Fear could prompt people with COPD to avoid physical activities, leading to a vicious cycle of dyspnea,

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inactivity, and deconditioning.[10, 11] Perpetuation of this vicious cycle exacerbates the psychological symptoms of people with COPD, reduced treatment adherence,[12] and lower self-efficacy.[13, 14] These could in turn diminish physical capacity and worsen disease prognosis, increasing the likelihood of hospitalization and mortality in people with COPD.[15]

Pulmonary Rehabilitation and Psychological Interventions for People with COPD

Pulmonary rehabilitation (PR) is one of the most common non-pharmacological management strategies for people with COPD, which aims to improve the physical and psychological well-being of individuals with chronic respiratory diseases and encourage long-term adherence to health-enhancing behaviours.[16, 17] Based on detailed assessments, patient-tailored therapies, including exercises, education, and behavior modification, are prescribed. According to a systematic review summarizing international pulmonary rehabilitation guidance, the supervised exercise-training component is typically recommended for at least 4 weeks, and extending programs beyond 12 weeks is generally not associated with additional gains.[18] Meta-analyses study showed that PR significantly improves exercise capacity,[18] depression and anxiety symptoms,[19] and health-related quality of life (HRQoL)[18, 20] in people with COPD. Despite evidence supporting the benefits of PR, poor adherence is common (non-completion rate =10-23%). Common barriers include environmental factors, as well as cognitive and behavioral factors such as a lack of perceived benefits of PR, current smoking habits, low motivation, poor physical ability, and psychological problems.[21-23]

Previous studies have demonstrated that symptoms of anxiety and depression are associated with poor disease prognosis in people with COPD. For instance, a meta-analysis by Atlantis and colleagues reported that depression or anxiety symptoms consistently increased the risks of adverse COPD outcomes (RR=1.43; 95% CI: 1.22–1.68)[6]. Another meta-analysis

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found that comorbid anxiety more than doubled the risk of acute exacerbations (AECOPD) within the first year after discharge (HR=2.10, 95% CI: 1.28–3.45), while comorbid depression elevated this risk by 36% (HR = 1.36, 95% CI: 1.10-1.69)[24].

In addition, Popa-Velea and Purcarea (2014) summarized key psychological variables that influenced COPD management and highlighted the importance of incorporating interventions addressing the psychological needs of the patients.[25] Therefore, a growing body of evidence has examined the efficacy of psychological interventions defined as purposive and systematic approaches designed to reduce symptoms or modify behavior.[26, 27] Interventions such as cognitive behavioral therapy (CBT) aim to identify and change dysfunctional thinking and maladaptive behavioral patterns[7]. Conversely, mindfulness-based interventions employ an acceptance-based approach to help individuals manage unhelpful thoughts or physical sensations, such as dyspnea.[28] Ultimately, both approaches aim to address the individual's psychological problems.[29] CBT has been shown to improve anxiety- and depression-related symptoms and enhance quality of life when compared with usual care.[27] However, its efficacy in improving physical outcomes remains inconclusive.[7, 30] Conversely, mindfulness-based programs, such as relaxation and meditation[31] have been shown to improve physical outcomes,[30] although their effectiveness in improving psychological outcomes also remains inconclusive.[30-32]

Previous systematic reviews compared the efficacy of psychological intervention[25] employing diverse approaches,[17] e.g., CBT or mindfulness-based cognitive therapy, counseling and psychoeducation. Among these, the majority of evidence reported their beneficial effects on psychological well-being.[7, 15, 30] Exercise training, combined with psychological intervention, demonstrated profound clinical benefits, significantly improving quality of life

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and reducing emotional distress when compared with usual care alone.[26] Although integrating psychological intervention with PR may enhance adherence and treatment efficacy in people with COPD, the synergistic effect is difficult to isolate, making it challenging to determine the exact added value of the psychological component. Standard PR traditionally includes education sessions focusing on understanding the disease and self-management; however, such education often lacks the targeted strategies to overcome the psychological barriers which disrupt the complex dyspnea-anxiety cycle. While standard PR effectively improves functional capacity, its independent impact on psychological symptoms remains inconsistent.[26, 27]

Therefore, the current meta-analytical review aims to address these knowledge gap through synthesizing data from randomized controlled trials that directly compare PR combined with psychological intervention against conventional PR in order to establish whether structured behavioural strategies confer incremental benefits beyond standard care.

Methods

This review was performed in accordance with Preferred Reporting Items for systematic reviews and meta-analyses (PRISMA) guidelines.[33] The protocol for this study was registered in the PROSPERO Systematic Review Protocols Registry under ID: CRD420250651201.

Search strategy

Four databases (i.e., PubMed, EMBASE, Web of Science, and Cumulative Index to Nursing and Allied Health CINAHL via EBSCOhost) were searched for relevant articles from inception to March 31, 2025. All records retrieved from the database searches were exported

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to Microsoft Excel. Duplicates were identified and removed in Excel. The detailed search strategy is listed in Table 1.

Study selection

A detailed list of inclusion and exclusion criteria is provided in Table 2. Inclusion criteria: (1) Population: adults with COPD, (2) Intervention: PR with an adjunctive CBT / psychological intervention (PSY-INT), (3) Comparison: PR alone, (4) Outcomes: all physical and/or psychological outcomes were considered, (5) Study design: true experimental and quasi-experimental studies, (6) Language: English, (6) Information Source: full-text articles published in peer-reviewed journals. Studies were excluded if they did not fulfil the aforementioned inclusion criteria. Two authors (CC and TS screened all studies independently, and discrepancies were resolved through discussion with a third author (GL).

Data extraction

For each included article, article title, study year, and country of publication, demographics of participants, study methodology, intervention details, outcome measures, and results, including scores in specific outcome measures assessed before and after intervention treatment and/ or between-group difference, were extracted independently by two authors (CC and TS). When studies reported multiple instruments for the same outcome domain, the decision of prioritization was based on predetermined clinical and methodological consideration.[34, 35]

Quality assessment

Each study was appraised independently by two authors (TSL and GLN). Disagreement on the scores was resolved by discussion, and a third author (CCC) was consulted when no

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consensus could be reached. Risk of Bias was evaluated using the Cochrane Risk of Bias (RoB) 2 tool for randomized controlled trials (RCTs),[36] and ratings of "low risk", "some concerns" or "high risk" were assigned to each domain. Certainty of evidence was evaluated using the Grading of Recommendations, Assessment, Development, and Evaluations (GRADE) approach[37] and ratings of "high", "moderate", "low", and "very low" were assigned for each outcome. In addition to the quality assessment outlined in the protocol registered at PROSPERO (CRD420250651201), this review incorporated the Physiotherapy Evidence Database (PEDro) scale to evaluate the methodological quality of studies, complementing the Cochrane Risk of Bias tool to provide a comprehensive appraisal of study quality. A cut-off score of ≥6 on the PEDro scale indicated good methodological quality and a lower risk of bias.[38]

Statistical analysis

Statistical and subsequent meta-analyses were performed using RevMan Manager 5.4 software. Quantitative data were expressed in mean ± standard deviation (SD). Effect sizes were reported as standardized mean differences (SMD) with 95% confidence intervals (CI). All meta-analyses were conducted using a random-effects model. Between-study heterogeneity was quantified using the τ^2 (Tau-squared) statistic and the I^2 statistic. In addition to the pooled effect and its CI, 95% prediction intervals (PI) were calculated to estimate the range of true effects that may be expected in future populations. Sensitivity analyses were performed by excluding the study contributing most to statistical heterogeneity and re-estimating the pooled effect to assess the robustness of the findings.

Results

Screening

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Study selection is illustrated in the PRISMA flow diagram (Figure 1). A total of 887 articles were retrieved from all databases. After removing 304 duplicates, an additional 469 articles were excluded during title and abstract screening. The remaining 20 were considered relevant for full-text review. Two articles were retrieved from the reference lists of included articles. After full-text screening, 5 articles met the inclusion criteria and were subjected to quality appraisal.[39-43]

Study characteristics

A total of 276 participants (intervention group, n = 138; control group, n = 138) were included. Subjects were over 50 years of age. Studies were conducted in Australia (20%),[42] Denmark (20%),[40] Canada (20%)[43] and Brazil (40%).[39, 41] COPD severity ranged from moderate to severe. Three studies employed GOLD criteria to classify disease stage,[40, 41, 43] while the remainder used either the Brazilian Society of Pulmonary and Tisiology guidelines[39, 41] or FEV_1/FVC[33] (Table 3). One study did not specify the tool used for classification.[42]

All studies compared PR + PSY-INT with active control groups consisting of PR, education, and a social group.[39-43] The contents of the psychological interventions varied. Most studies included individual or group-based CBT.[39-42] Other approaches (e.g., psychotherapy) were also used.[41] Three studies offered 8-week interventions,[40, 42, 43] while two studies provided 12-week interventions.[39, 41] To evaluate the add-on benefits of psychological interventions on anxiety and depression symptoms, studies utilized the Hospital Anxiety and Depression Scale (HADS),[40, 42, 43] Beck Anxiety Inventory (BAI), and Beck Depression Inventory (BDI) [39, 41] as outcome measures. For physical outcomes, three studies used the 6-minute walk distance (6MWD)[39, 42, 43], while 1 study used the distance walked-weight product (in 6 minutes).[41]

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Quality appraisal

PEDro results are summarized in Figure 2a. Four studies[39-41, 43] scored 6 or above on the PEDro scale, while one study had a score of 3.[42] All five studies had similar baseline characteristics between treatment and control groups and reported at least one key outcome for between-group comparisons. RoB 2 results are summarized in Figure 2b, two studies were considered to have a high risk of bias. These two studies were raised regarding the dominant 4 measurement outcome,[40, 42] and one study had a high risk of the randomization process.[42]

Certainty of evidence

GRADE results are reported in Table 5. Changes in the levels of anxiety, depression, and 6MWD were rated as very low certainty of evidence.

Effects of combined therapy (PR + PSY-INT) on psychological outcomes

Five studies investigated the effects of PR + PSY-INT on anxiety symptoms compared to PR alone (Figure 3a). Three studies adopted the HADs-A,[40, 42, 43] and two used the BAI.[39, 41] The random-effects model showed heterogeneity I^2 was 30%. The pooled effect demonstrated a statistically significant reduction in anxiety symptoms in the PR + PSY-INT group (SMD = -0.55; 95% CI: -0.85 to -0.25; $p < 0.001$). The 95% PI (-1.35 to 0.25), the effect favors PR + PSY-INT, but the true effects across different settings and populations may range from a substantial reduction in anxiety symptoms to little or no improvement.

The overall effect of PR + PSY-INT on depression symptoms was not statistically significant (SMD = -0.38, 95% CI = -0.97 to 0.22, $p = 0.22$). The 95% PI was wide (-2.52 to 1.76). Four out of five studies measured SMD favoring PR + PSY-INT on depression

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symptoms (Figure 3b).[39-42] The heterogeneity of the overall pooled data was 81%. Three studies used HADs-D[40, 42, 43] and 2 used BDI [39, 41] to assess depression symptoms.

Effects of combined therapy (PR + PSY-INT) on physical outcomes

Three studies compared the effects of PR + PSY-INT versus control conditions on 6MWD.[39, 42, 43] The heterogeneity was 82% PR + PSY-INT did not significantly improve 6MWD relative to control conditions (MD = 16.45, 95% CI = -17.38 to 50.27, $p = 0.34$, Figure 3c).

Sensitivity analysis

Sensitivity analyses were conducted to assess the robustness and consistency of the overall findings. For anxiety symptoms, heterogeneity (I^2) decreased from 30% to 0% after excluding the study by de Godoy & de Godoy,[39] while the adjusted pooled estimate remained statistically significant (SMD = -0.43, 95% CI = -0.69 to -0.18, 95% PI = -0.98 to 0.12, $p < 0.001$, 95%, Figure 4a). This indicates that this study was the main contributor to heterogeneity regardless of the outcome measure used. For depression symptoms, heterogeneity was initially high. A study of Williams and colleagues,[43] which reported an effect in the opposite direction, and its exclusion reduced I^2 from 81% to 38%, and changed the pooled effect from non-significant to statistically significant (SMD = -0.60, 95% CI = -1.01 to -0.19, 95% PI = -2.05 to 0.85, $p = 0.004$, Figure 4b). A similar pattern was observed for the 6MWD. Removing the study of Williams and colleagues,[43] the I^2 reduced from 82% to 0% and yielded a significant improvement (MD = 33.84, 95% CI = 9.43 to 58.25, $p = 0.007$, Figure 4c), suggesting that this study's results were inconsistent with the others. One plausible explanation is the variation in assessment timepoints, most studies measured outcomes immediately post-intervention,[39-42] whereas Williams and colleagues assessed outcomes 1-month after intervention.[43] Given

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uncertainty about how long the intervention effect lasts, differences in follow-up timing may be one reason contributing to the observed heterogeneity.

Subgroup analysis on the factors affecting the effects of PR + PSY-INT

Baseline level of anxiety/ depression symptoms

People with mild and normal anxiety symptom levels at baseline demonstrated significant improvement (Normal: SMD = -0.48, 95% CI = -0.83 to -0.13, p = 0.008; Mild: SMD = -0.70, 95% CI = -1.31 to -0.09, p = 0.03) (Figure 5a). There are no significant differences between the subgroups (p = 0.53). For depression symptoms, only patients with mild symptoms at baseline showed significant improvement (SMD = -1.01, 95% CI = -1.55 to -0.48, p = 0.0002). Significant differences were observed between the subgroups (p = 0.004, Figure 5b).

Intervention dosage

A significant effect that favors PR + PSY-INT was only observed in the subgroup with high volumes of CBT (≥ 50% of total sessions)[39, 41, 42] for outcomes in anxiety symptoms (SMD = -0.59, 95% CI = -0.97 to -0.22, p = 0.002), although the subgroup difference was insignificant (Figure 6a). Depression showed no subgroup difference and effect (Figure 6b).

Discussion

In line with the review by Popa-Velea and colleagues,[25] this meta-analysis contributes new insights by pooling effect estimates of outcome measures and critically appraising study quality to justify the strength of the evidence.[37] Furthermore, this meta-analytical review highlights the added value of psychological interventions (PSY-INT) on both psychological and physical outcomes in people with COPD undergoing pulmonary rehabilitation (PR). By

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comparing the combined intervention of PSY-INT plus PR against PR alone, the incremental effects of PSY-INT can be clarified. The pooled data from included studies demonstrated significant benefits for anxiety symptoms when psychological interventions were incorporated into PR for people with COPD.

Additive effects of psychological intervention on psychological outcomes

This review evaluated the comparative efficacy of PR + PSY-INT and PR alone for improving psychological and physiological outcomes in people with COPD. Overall, PR + PSY-INT demonstrated superior effects on anxiety symptoms compared with PR alone, whereas no clear additional benefit was observed for depression symptoms. For physiological outcomes, PR + PSY-INT did not consistently outperform PR alone, and effects varied across measures and studies. We have also performed additional analyses comparing the mean differences of each outcome measurement with their minimal (clinically) important differences (MCID/MID). For anxiety symptoms, both BAI and HADS-A results showed significant mean differences favoring PSY+PR, but only one study by de Godoy et. al. could meet the respective MCID or MID (BAI: MID = 8.8; HADS-A: MCID = 1.6).[44, 45] This showed that notwithstanding the overall improvements of anxiety symptoms favoring PR + PSY-INT, the clinical importance of such effects was doubtful. In addition, the 95% PI for anxiety symptoms (-1.35 to 0.25) indicates the average effect is a beneficial true effect in future settings may range from a reduction to little or no improvement. The substantial study effect observed for anxiety and depressive symptoms in the present review aligns with recent high-power clinical evidence as reported by Taylor and colleagues.[46] The study evaluated the effect of psychological interventions on people with COPD and found that there was no significant overall effect on depression. Brief psychological approaches often face severe real-world barriers, including deeply entrenched, lifelong comorbidities, complex social situations, and

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poor subsequent uptake of physical rehabilitation. The psychological approach was largely ineffective because it was delivered late in the trajectory of advanced, disabling COPD, acting as 'too little, too late' for entrenched distress. Crucially, the study hypothesized that the efficacy of such behavioral modalities may be contingent upon early-stage deployment. Also, the psychological interventions were profound therapeutic resistance when distress had become clinically entrenched alongside lifelong multicomponent conditions, such as health conditions, complex social backgrounds, and severely attenuated behavioral engagement. The variations in baseline clinical severity and the precise timing of intervention deployment across primary studies naturally explain the wide prediction intervals, which represent the difference between study variability.

Apart from the overall effect, one study compared the discriminant validity of HADS and BDI-II/BAI in detecting depression in people with COPD and suggested that after the removal of "question 4: I feel as if I am slowed down" and adjusting the cut-off point to ≥5, the HADS-D sensitivity/specificity would improve from 78%/81% to 100%/83%.[47] It was suggested that the feeling of "slowed down" could be universal in people with COPD, hence, lowering the sensitivity of the scale to detect changes in depressive symptoms.[47] A similar problem was identified in BDI-II in "question 21: loss of interest in sex".[47] Additionally, a subgroup analysis showed that only those studies employing BDI as outcome measure for depression symptoms showed statistically and clinically significant added effect favoring the PR + PSY-INT (BDI: MD= -8.44)[44] but not in HADS-D ($Chi^2 = 6.13$, $p= 0.01$, $I^2 = 83.7\%$). Considering the above-discussed questionable sensitivity in detecting the changes of depressive symptoms in people with COPD, plus the relatively high heterogeneity and lack of significant overall effects of the PR + PSY-INT on outcomes of depression symptoms in this study, the corresponding summarized result warrants cautious interpretation. Consistently, the

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95% PI for the outcome of depression symptoms was very wide (-2.52 to 1.76), implying substantial between-study heterogeneity. These results implied the necessity to adjust assessment items in future studies to augment the specificity of outcome measurement for this disease population.

Nonetheless, disease-specific fears also play an important role in the subjective experience of people with COPD that exceeds the effects of general, unspecific forms of anxiety.[48] It is mentioned that generic measurements such as HADS and BDI are fundamentally insufficient to capture the specific emotional burdens of specific disease populations. Consequently, the widespread reliance on these generic scales across the studies may present a profound psychometric limitation that attenuates evaluative sensitivity, which naturally explains the lack of statistically significant overall treatment effects and the substantial study heterogeneity observed in our review. In short, future research with more robust designs and consistent outcome measures is required to confirm and provide evidence of the effects of PR + PSY-INT on depression in people with COPD.

Additive effects of psychological intervention on physical outcomes

In terms of physical outcomes, PR is well established for improving the 6MWD. As PR alone already substantially improves physical capacity, there are limited additional gains when adding psychological intervention. While the addition of psychological intervention may offer some extra benefit, the net change in 6MWD did not reach statistical significance compared to PR alone. Nonetheless, the sensitivity analysis for the 6MWT showed a wide 95% PI (–99.35 to 154.25 m). This suggests considerable clinical and methodological heterogeneity, meaning that while some subgroups may experience meaningful gains, others may not. Previous systematic reviews reported that psychological intervention could significantly improve

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exercise capacity and dyspnea in people with COPD compared to passive or active control.[15, 26, 30] This improvement might be a result of the interrelationship of physical and psychological factors in COPD.[15] For instance, people with dyspnea might undergo cognitive and emotional processes, which potentially lead to the development of anxiety and/or depression symptoms.[15] Having these psychological issues prompts the avoidance of physical activities, leading to deterioration in physical capacity.[24,26] However, the data on changes in dyspnea level from the included studies are insufficient to substantiate the correlation between physical and psychological outcomes. Hence, we could not conclude if such an effect is due to the dyspnea-inactivity-deconditioning cycle as discussed in the introduction. Meanwhile, the wide PI is consistent with this rationale, as the functional response may vary if psychological burden, dyspnea severity, or program intensity differs across studies. Nevertheless, it was observed that the 3 studies that had the largest effect on anxiety symptoms, favoring PR + PSY-INT,[39, 41, 42] also demonstrated a greater improvement on physical outcomes, favoring the experimental group. This indicates a possible link between anxiety symptoms and physical outcomes. Future research should standardize 6MWT procedures and report intervention fidelity to reduce dispersion in effects and clarify which subgroups derive clinically meaningful improvements. Future research could investigate the proposed correlation by measuring the change in dyspnea level alongside physical and psychological outcomes.

Factors that influence the outcome measures

With reference to the defined cut-offs,[49, 50] the mean severity of anxiety and depression symptoms of the subjects in the included studies ranged from minimal to mild. The subgroup analysis revealed that patients with clinically observed anxiety & depressive symptoms at baseline demonstrated significant changes in psychological outcomes, although the between-group difference in anxiety was insignificant. Acknowledging the higher responsiveness by

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participants with baseline psychological symptoms, PR + PSY-INT might not be recommended for all patients, rather only limited to the abovementioned subgroup for resource concerns. Nonetheless, no study included subjects with severity of anxiety/depression symptoms graded as moderate or severe, hence the added effects of psychological intervention on these patient populations are unclear. Future studies could therefore analyze the added benefits of psychological intervention on improving psychological outcomes for subjects with different severities of anxiety/ depression symptoms accordingly.

According to the dosage of programs, weekly sessions demonstrated a significantly larger effect on anxiety symptoms. In contrast, programs by Luk et al (2017),[42] where only 3 or 6 sessions were delivered in 8 weeks, respectively, showed insignificant improvements on psychological outcomes. This suggested that weekly psychological intervention may be more favorable to facilitate improvement in health outcomes. However, the insignificant subgroup difference indicated that weekly sessions may not impose significantly different effects on psychological outcomes compared to less frequent sessions. For the duration of each session, only Farver-Vestergaard et. al. (2018) stated the length of psychological intervention as 45 minutes;[40] no statistical analysis could therefore be conducted. These uncertain and inconsistent findings warrant more studies to examine the relationship between program duration and the effectiveness of the intervention.

Study limitations

There are several limitations in this review. First, the limited number of studies included reduces statistical power, which affects subsequent interpretation and recommendations. Secondly, the low quality of studies and the certainty of outcome measurements based on the GRADE analysis limited our confidence when generating clinical recommendations. Thirdly,

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insufficient data were acquired for each subgroup analysis, which restricted the confidence of our results. Hence, conclusions regarding the optimal treatment duration and long-term effects of psychological intervention on an existing PR program could not be made. Fourthly, the comparison design of this review does not allow for direct comparison with active control. This comparison limits to rule out non-specific therapeutic effects. As highlighted by Williams and colleagues, the intervention shows significant benefits when compared to inactive controls, but these benefits disappear when compared to active controls. [27] Consequently, this comparison design on this review may have led to an overestimation of the specific incremental effect size of PSY-INT. Fifth, blinding of patients and therapists is structurally impossible due to the active nature of the interventions.

One point to take note of was that one study reported multiple outcomes to assess the domain of depression.[42] In that study, both HADS and DASS demonstrated trends of favoring PSY-INT + PR than PR only. However, only DASS demonstrated a statistically significant difference. Such a phenomenon could probably be associated with the differences in tool sensitivity. Although both scales are comparable instruments for evaluating depression, their item content differs, which can result in varying sensitivities.[51] Despite these variations, in this meta-analytical review, only HADS-D was extracted for data synthesis due to the predetermined prioritization of outcomes, which potentially reduced any potential selection bias. Consequently, this approach may result in an underestimation of the intervention effect on the pooled data.

Conclusions

Combining psychological intervention with PR for COPD has become an increasingly popular research topic in recent years owing to its proposed effect on breaking the dyspnea-

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inactivity-deconditioning vicious cycle. Our study revealed that psychological intervention complementary to PR provides additional benefits on anxiety symptoms in people with COPD (SMD = -0.55, 95% CI: -0.85, -0.25, P = 0.0004), although no statistically significant improvement was observed for depression (SMD = -0.38, 95% CI: -0.97, 0.22, P = 0.22). However, greater treatment effects were found in patients with clinically observed psychological symptoms at baseline. Regarding the intervention dosage, a higher volume psychological intervention possibly induces greater improvement in anxiety and depression symptoms based on the limited data provided by the included studies. Further research could supplement the mechanism through which psychological intervention induces an additive effect in psychological and physical outcomes when added to PR and investigate the possible correlation between psychological intervention volume and baseline psychological symptoms severity with treatment effectiveness.

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Author contributions:

CCC, GLN, and TSL were responsible for study screening, data extraction, and the initial drafting of the manuscript. FFW, TKF, and TM contributed to data analysis and interpretation, visualization, and manuscript revision and editing. XCF, BY, JNC, and BWL contributed to data validation and the critical review of the manuscript. SPN served as the senior author and provided overall study conceptualization, supervision, and oversight of the entire review process, including systematic manuscript writing and revision.

Declaration of Interests:

The authors confirm they have no conflicts of interest.

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Table 1. Search strategy and keywords.

	Synonyms/ short forms
Disease-related (S1)	• COPD • COAD • COBD • Chronic Obstructive Pulmonary Disease • Chronic Obstructive Airway Disease • Chronic Obstructive Lung Disease • Chronic Obstructive Respiratory Disease • Chronic Airflow Obstruction • Chronic Airway Obstruction • Pulmonary Disease, Chronic Obstructive • Lung Diseases, Obstructive • Emphysema* • (Obstruct* and (pulmonary or lung or airway* or airflow* or bronchitis* or respirat*)) • Chronic airflow limitation • CAL
Pulmonary rehabilitation (S2)	• Pulmonary rehab* • PR • PRP • Respiratory rehab* • ((Pulmonary OR Respiratory) AND (physiotherapy OR Physical therapy))

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	• Exercise
Psychological intervention (S3)	• Cognitive behavioural therap* • Behaviour* therapy • CBT • Mindfulness* • Psychosocial intervention • Psychotherapy* • Psychoeducation OR psycho-education • Stress reduction • Relaxation • Meditation • Imagery • Hypnos*
S4	S1 AND S2 AND S3

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Table 2. Study selection criteria

Inclusion criteria	Exclusion criteria
Population: ● Adults (>40y/o) with an objective diagnosis of COPD according to spirometry or Global Initiative for Chronic Obstructive Lung Disease (GOLD) criteria or by a physician (any severity) ● COPD must be the primary diagnosis *Intervention:* ● Must include CBT/psychological intervention as a stand-alone or a component of intervention in the experimental group (irrespective of type and mode of delivery) *Comparison:* ● Must include a control group with pulmonary rehabilitation as a stand-alone or a component *Outcome:* ● Physical outcome = dyspnea, functional capacity ● Psychological outcome = (HR)QoL, depression, and/or anxiety	*Population:* ● Individuals with other chronic lung conditions as primary diagnosis (e.g., lung cancer, asthma) ● Individuals have physical comorbidities and cognitive impairment that impact their ability to actively engage in interventions/leading to severe deterioration of physical and/ or psychological conditions *Intervention:* ● Does not include CBT/psychological intervention *Comparison:* ● No comparator intervention *Outcome:* ● Does not include data for all 1° outcomes *Study characteristics:* ● Protocols, pilot studies, theses, unpublished articles, conference proceedings/abstracts, on-going studies,

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• Must include data for psychological outcomes ± physical outcomes *Study characteristics:* • Randomized control trials, non-randomized control trials • English language • Published in peer-reviewed journals • Full-text available	editorials, research letters, posters that described trials, reviews, studies that cannot provide data for analysis *Other:* • Languages other than English • Full-text unavailable through open sources

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Table 3. Characteristics of included studies

Author	Country	Sample size (F:M)		Age(years)		Diseases severity			Baseline Anxiety score (severity)		Baseline Depression score (severity)		Data collection/ follow-ups	Psychological outcome measures	Physical outcome measures
		Gp1	Gp2	Gp1	Gp2		Gp1	Gp2	Gp1	Gp2	Gp1	Gp2			
de Godoy & de Godoy, 2003	Brazil	14 (2:12)	16 (6:10)	62.1 ± 14.9	58.8 ± 11.8	Severe COPD	12 (85.7%)	11 (68.8%)	12.9 ± 6.9 (Mild)	10.9 ± 9.9 (Mild)	13.7 ± 18.9 (Mild)	14.9 ± 11.6 (Mild)	Baseline and end of intervention	BAI, BDI	6MWD
de Godoy et al., 2005	Brazil	19	CG 1 = 16 CG 2 = 14*	>50 years old	CG 1 >50 CG 2 >50	%pred FEV_1	33 ± 18	CG1: 34 ± 12 CG2 =34 ± 15	15.2 ± 7 (Mild)	13.0 ± 11.0 (Mild)	17.0 ± 10.0 (Mild)	10.0 ± 10.0 (Mild)	Baseline and end of intervention	BAI, BDI	Distance walked-weight product (in 6 mins)
Farver-Vestergaard et al., 2018	Denmark	39 (24:15)	45 (24:21)	66.7 ± 8.0	67.7 ± 7.5	%pred FEV_1	37.5 ± 12.09	37.94 ± 11.62	7.7 ± 4.7 (Mild)	7.6 ± 4.1 (Mild)	6.3 ± 3.7 (Normal)	5.9 ± 4.1 (Normal)	Baseline, Mid, and end of intervention, 3- and 6-month follow-ups	HADs	daily physical activity level recorded by accelerometer (not reported in results) CAT as physical outcome
Luk et al., 2017	Australia	14 (7:7)	14 (8:6)	74.2 ± 7.2	70.5 ± 7.5	%pred FEV_1	49 (37-77)	61.5 (39-67)	5.5 (Normal)	4.5 (Normal)	4.0 (Normal)	3.5 (Normal)	Baseline, end of intervention, 3 months post-intervention	HADs	6MWD

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Williams et al., 2023	Canada	52 (28:24)	49 (19:30)	71.0 ± 6.0	69.0 ± 10.0	%pred FEV_1	48 ± 14	47 ± 19	7.1 ± 4.5 (Normal)	6.8 ± 4.5 (Normal)	5.9 ± 4.0 (Normal)	6.6 ± 4.2 (Normal)	Baseline, 1-, 6-, and 12-months follow-ups	HADs	6MWD

Note. Gp = Group; Gp1 = PR+PSY-INT group (receiving pulmonary rehabilitation combined psychological interventions); Gp2 = PR only (receiving pulmonary rehabilitation without psychological interventions); %predFEV_1 = percentage of predicted value of Forced Expiratory Flow Volume; 6MWD = six-minute walk distance; BAI = Beck Anxiety Inventory; BDI = Beck Depression Inventory; CAT = COPD Assessment Test; DASS = depression anxiety stress scale; HADs = Hospital Anxiety and Depression scale; CG1 = control group with Psychotherapy + physical therapy; CG2 = physical exercise + physical therapy; PR= pulmonary rehabilitation; baseline severity based on the cut-off [41-43] to categorize in : Normal and Mild

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Table 4. Intervention protocol of included studies

Author	Program duration	Comparison		Pulmonary rehabilitation protocol				Psychological intervention protocol	
				PR – Exercise content		PR – Education content		PSY-INT content	
		PR + PSY-INT	PR Control	Frequency	Content	Frequency	Content	Frequency	Content
de Godoy & de Godoy., 2003	12 weeks	PR (PT + PE + education) + PSY-INT	PR (PT+PE+ education)	2x/week	*PT session:* - Dyspnea management, diaphragmatic & pursed lip breathing, secretion removal treatment (postural drainage, chest percussion, vibration, directed cough, and the forced expiratory technique) (Conductor not reported) *PE sessions:* - Arm and leg exercises, aerobic conditioning with an ergometric treadmill, and flexibility training (Conductor not reported)	1x/ month	*Educational session:* - Lectures and discussions about several topics that enable patients to integrate therapies into their lives. (The importance of compliance; Coping with illness; Stress management; Normal anatomy and physiology of the lungs; Drug actions, side effects, and proper techniques of administration; Relaxation and energy-saving techniques; Good nutrition; Indications for the benefits of, and optimum use of, oxygen; Environmental control;	1x/week	*PSY-INT session:* - Addressed the patient's psychosocial needs and included his/her social, marital, work, health, and interpersonal philosophy and habits. - Cognitive therapy and logotherapy techniques were used during these sessions. (Conductor not reported)

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								Intimacy and sexuality; The doctor-patient relationship; Smoking cessation; Benefits of exercise) (Conductor not reported)		
de Godoy, 2005	12 weeks	PR (PT + PE + education) + PSY INT	CG1: PR (PT + education) + PSY INT CG2: PR (PE + PT + education)	2x/week	*PT session:* - Diaphragmatic breathing, pursed-lip breathing, postal drainage, coughing, percussion, vibration (Conducted by physical therapist) *PE sessions:* - Upper body, lower body, and flexibility exercises, as well as aerobic exercises using a treadmill. 75-85% of maximum heart rate (Conducted by physical education instructors)	1x/ month	*Education session:* - Group educational session about COPD by a pulmonologist (Conducted by physical therapist)	1x/week	*PSY-INT session:* - Address difficulties in social life, work & health. CBT and logotherapy techniques used - Maintenance of anxiety control - Evaluate QoL, seeking alternatives (Conducted by psychologist)

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Farver-Vestergaard et al., 2018	8 weeks	PR (PE + education) + PSY INT (MCBT)	PR (PE + education)	2x/week	*PE session:* First weekly session lasted 90 min; other weekly sessions lasted 150 min, including physical exercise and disease- and lifestyle-oriented education. (Conductor not reported)	1x/week	*Education session:* -Physical exercise, disease and lifestyle-oriented education following guidelines of ATS & ERS (Conductor not reported)	1x/week	*PSY-INT session:* Mindfulness-based CBT by a clinical psychologist (105mins): - Single individual telephone interview - Group-based medication and educational cognitive exercises session (Conductor not reported)
Luk et al., 2017	8 weeks	PR (PE + education) + PSY-INT (CBT)	PR (PE + education)	2x/week	*PE session:* - 45 mins exercise session, including treadmill/ walking, cycling and circuit exercise, 15min each (Conductor not reported)	2x/week	*Education session:* -2 hours education session about the lungs, COPD, dyspnea, nutrition, medication, and advanced care planning Issues such as how the lungs work, nutrition, advanced care planning and medication management, and link between dyspnea and COPD. -No specific information was provided in relation to recognizing triggers of dyspnea or the use specific breathing strategies.	6 sessions	*PSY-INT session:* -Group-based CBT program to fit the exercise and education program in PR (Conducted by psychologist)

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					(Conductor not reported)					
Williams et al., 2023	8 weeks	PR (PE + education) + PSY-INT (CBT)	RP + SC	2x/week	*PE session:* - Minimum 30 min of combined aerobic and resistance circuit training (Conductor not reported)	2x/week	*Education sessions*: - 1 hour self-management education sessions (Conductor not reported)	1x/week	*PSY-INT session:* - Group-based sessions involving Breathing: Recognize sensations, explore thoughts and beliefs, validate whether thoughts are useful or harmful, Evolve and change behavior (Conducted by psychologist)

Note. CBT= cognitive behavioral therapy; CPRP = comprehensive pulmonary rehabilitation program; GOLD = Global Initiative for Chronic Obstructive Lung Disease; MCBT= Mindfulness-based cognitive therapy; PA = Physical activity; PE= physical exercise; PR= pulmonary rehabilitation; PR+PSY-INT = group receiving pulmonary rehabilitation combined psychological interventions; PSY-INT = psychological interventions; PT= physical therapy; SC= social group control; x = times.

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Table 5. The GRADE analysis

Primary outcome measures for COPD

Patient or population: people with COPD
Settings:
Intervention: Primary outcome measures

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	Control	**Primary outcome measures**				
Anxiety		The mean anxiety in the intervention groups was **0.55 standard deviations lower** (0.85 to 0.25 lower)		276 (5 studies)	⨁⨁⨀⨀ **low**[1,2]	SMD -0.55 (-0.85 to -0.25)
Depression		The mean depression in the intervention groups was **0.38 standard deviations lower** (0.97 lower to 0.22 higher)		276 (5 studies)	⨁⨀⨀⨀ **very low**[1,2,3]	SMD -0.38 (-0.97 to 0.22)
6MWD		The mean 6mwd in the intervention groups was **16.45 higher** (17.38 lower to 50.27 higher)		157 (3 studies)	⨁⨀⨀⨀ **very low**[4,5,6]	MD +16.45 (-17.38 to 50.27)

*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: Confidence interval; SMD: standardized mean difference; 6MWD: 6-minute walk distance.

GRADE Working Group grades of evidence
High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

[1] 3 studies are in high risk of bias.
[2] The CI of 3 included studies crosses the line of no effect, making the estimate imprecise.
[3] Substantial heterogeneity across studies (I^2 = 81%)
[4] 1 studies are in high risk of bias.
[5] Substantial heterogeneity across studies (I^2 = 82%)
[6] No explanation was provided

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Figure 1. Flow diagram of study selection.

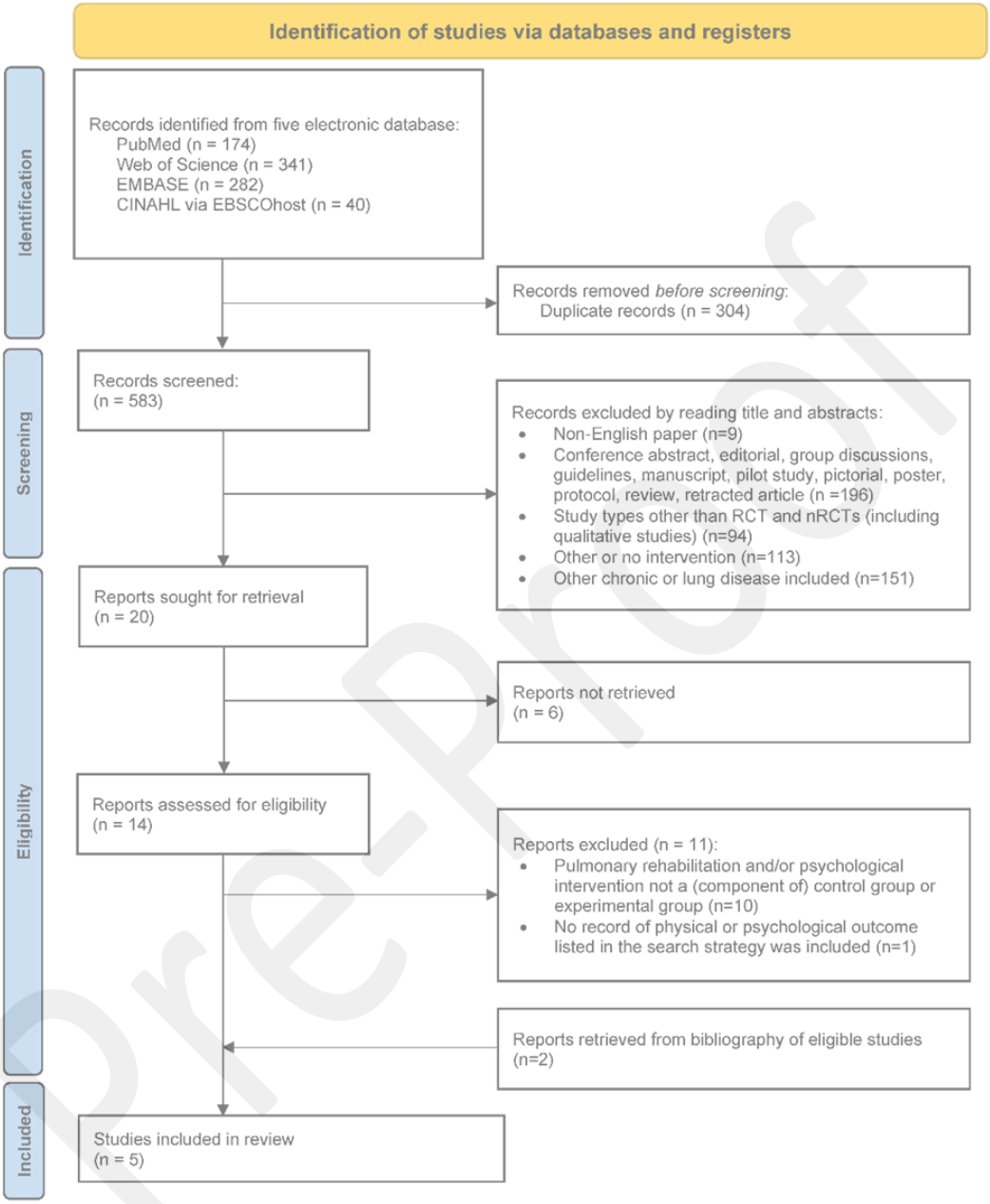

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Figure 2. Quality appraisal in (a) PEDro analysis, (b) Risk of bias

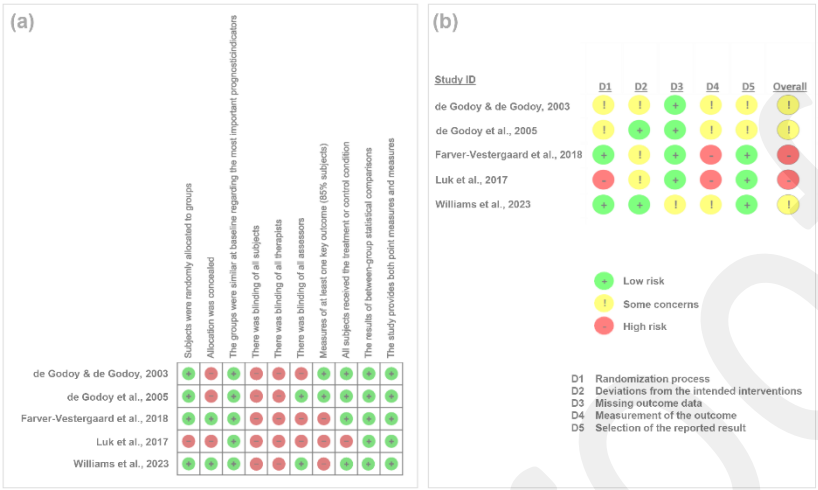

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Figure 3. Forest plot showing the association of combined therapy (PR + psychological intervention) with levels of (a) anxiety, (b) depression and (c) 6 minutes walking distance, 6MWD across included studies.

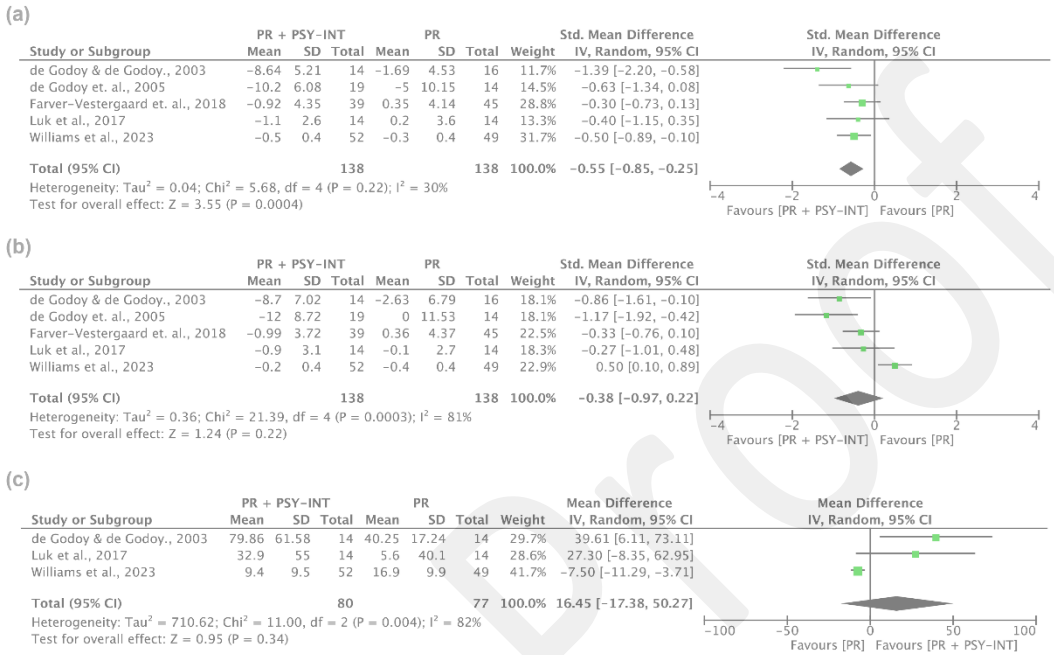

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Figure 4. Forest plot showing the sensitivity analysis of (a) anxiety, (b) depression and (d) 6MWD.

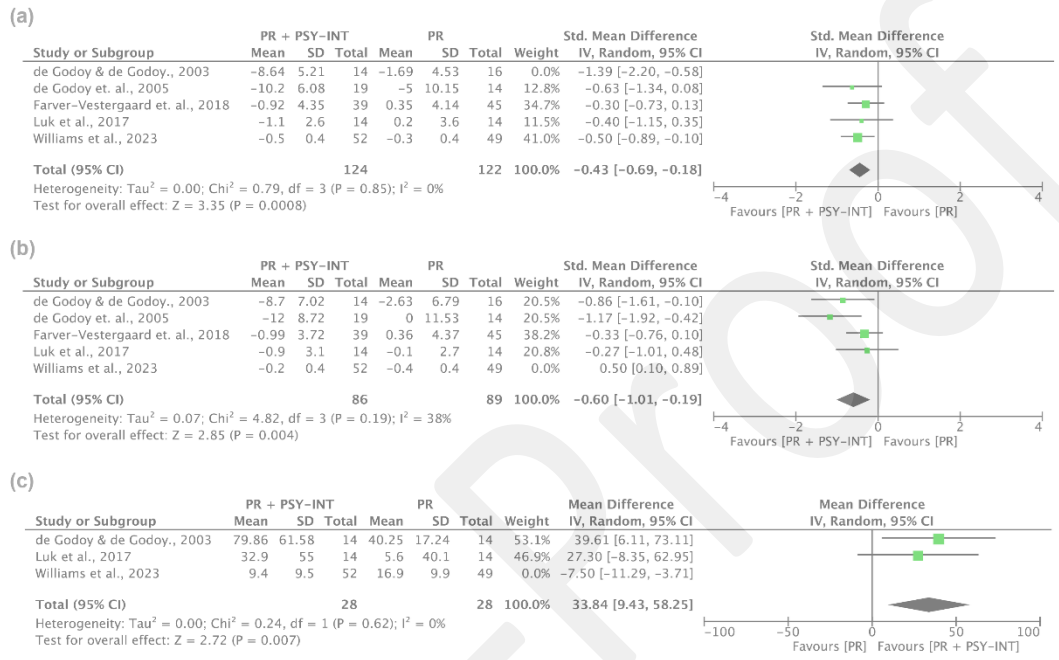

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Figure 5. Forest plot of subgroup analysis based on baseline (a) anxiety level and (b) depression level.

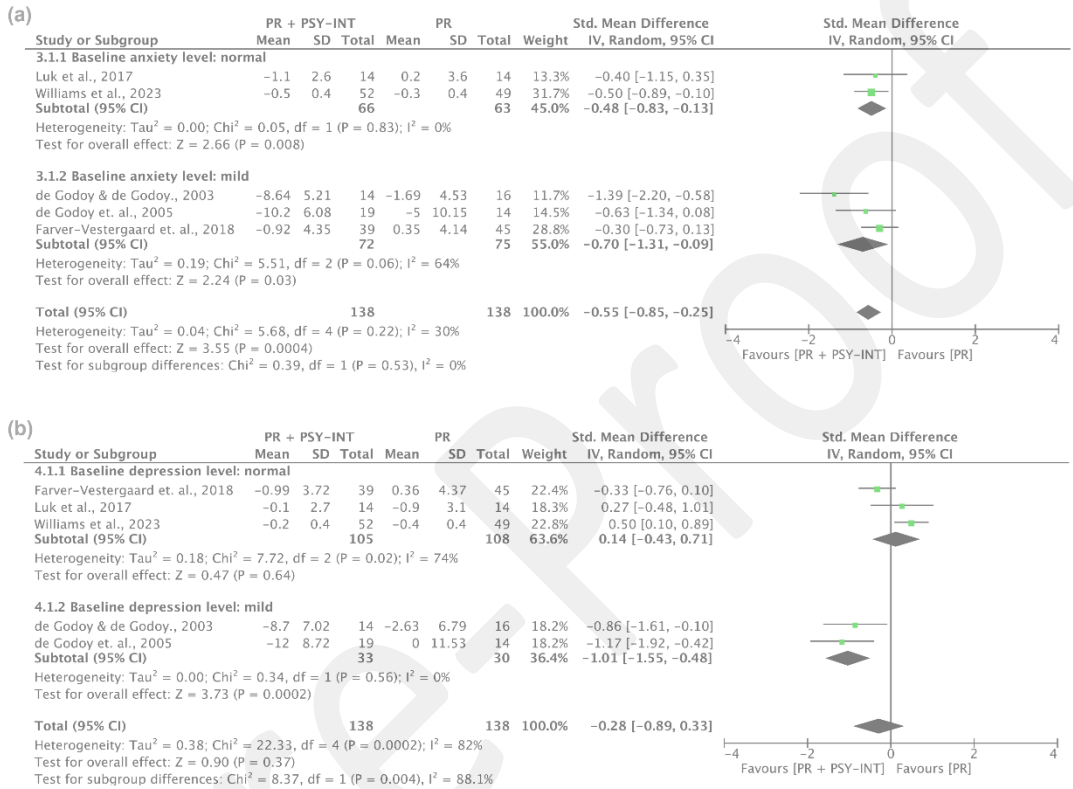

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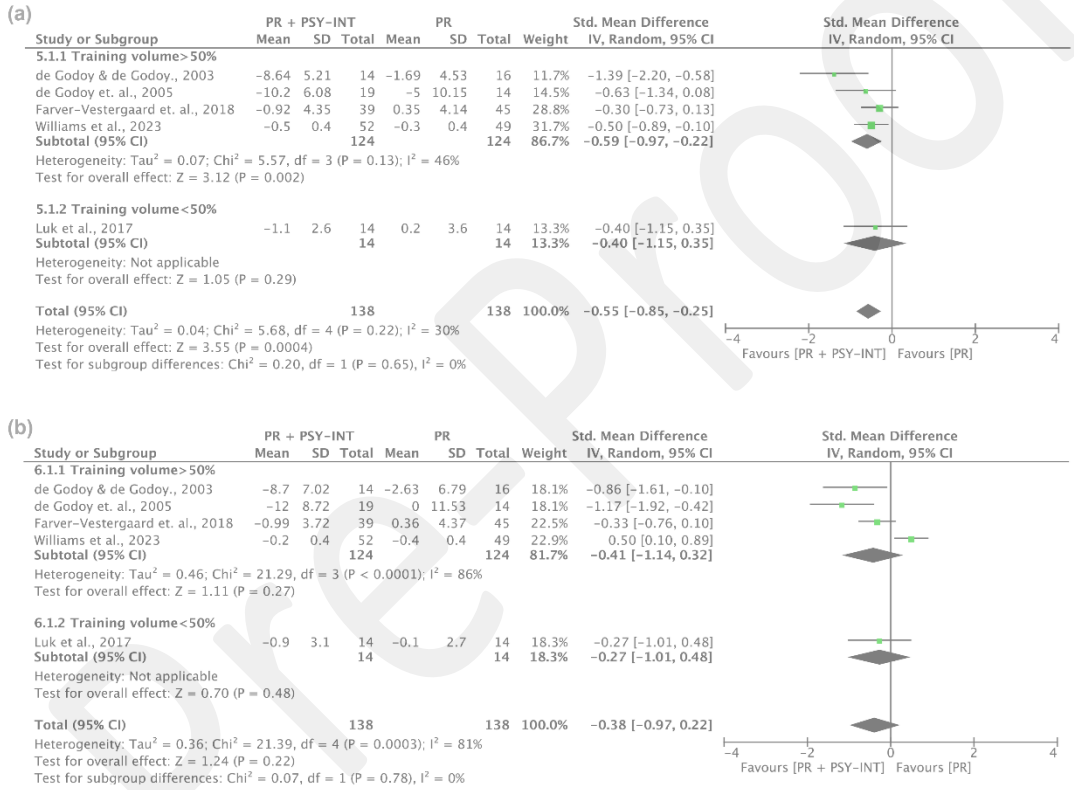
Figure 6. Forest plot showing the effect on (a) anxiety level and (b) depression level from the subgroup analysis based on different volumes of PSY.



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