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REVIEW

Exercise Training Improves Depression and Anxiety in Patients with COPD: A Dose-Response Meta-Analysis of Randomized Controlled Trials

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Objective: To evaluate the effects of exercise training on depressive and anxiety symptoms in patients with chronic obstructive pulmonary disease (COPD).

Methods: We searched PubMed, Embase, Cochrane Library, and Web of Science from inception to May 7, 2025, for randomized controlled trials (RCTs) investigating exercise training for depression or anxiety in COPD patients. Two researchers independently screened literature, extracted data, and assessed methodological quality. To reduce measurement heterogeneity, only studies reporting the Hospital Anxiety and Depression Scale (HADS-D for depression, HADS-A for anxiety) were included as outcome indicators. Meta-analysis was performed using a random-effects model, and subgroup analysis explored the influence of cumulative intervention duration.

Results: Eleven RCTs involving 1208 COPD patients were included. Using HADS-D and HADS-A as outcome measures, exercise training significantly improved depressive symptoms [SMD = −0.35 (95% CI: −0.58, −0.12), $P < 0.05$] and anxiety symptoms [SMD = −0.27 (95% CI: −0.53, −0.01), $P < 0.05$]. Subgroup analysis indicated that improvement in depression was significant when cumulative intervention duration exceeded 1500 minutes ($P < 0.05$). For anxiety, although subgroup differences were not significant, the overall trend supported a positive effect.

Conclusion: Exercise training is an effective non-pharmacological intervention for depression and anxiety in COPD patients. Integrating exercise into comprehensive COPD management is recommended, with exploratory evidence suggesting benefit when cumulative durations exceed 1500 minutes. More high-quality, long-term follow-up RCTs are needed to clarify optimal exercise regimens and mechanisms.

Keywords: COPD, exercise, depression, anxiety, meta-analysis, randomized controlled trial

Introduction

Chronic obstructive pulmonary disease (COPD) is a progressive chronic respiratory condition characterized by airway and/or alveolar abnormalities leading to persistent airflow limitation.[1] Epidemiological data indicate that approximately 300 million people worldwide are affected by COPD,[2] with continuously rising morbidity and mortality rates,[3] posing a significant global burden on patients and healthcare systems. The World Health Organization predicts that by 2030, COPD will become the third leading cause of death and the fifth most economically costly disease globally.[4]

COPD presents with sudden onset, persistent, and recurrent symptoms, which not only impose psychological burdens but also exacerbate anxiety and depression.[5] Clinical observations indicate high comorbidity of anxiety and depression in COPD patients, with prevalence rates ranging from 10% to 65%.[6,7] These psychological disorders lead to poorer clinical

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outcomes, including reduced survival, prolonged hospitalization, and increased mortality risk.[8] Therefore, it is crucial to implement effective interventions to alleviate anxiety and depression symptoms in patients with COPD.

As a non-pharmacological treatment, pulmonary rehabilitation (PR) has become a cornerstone of COPD management, involving exercise, education, and behavior modification.[9] Exercise training is a key component of pulmonary rehabilitation for COPD.[10] In recent years, an increasing number of studies have identified that exercise training can improve negative emotions,[11] exercise tolerance and respiratory function, and reduce exacerbation risks, hospitalizations and deaths in COPD patients.[12,13]

Although recent meta-analyses have examined the effects of exercise on psychological outcomes in COPD patients,[14,15] several critical gaps remain. First, the optimal dosage of exercise interventions, particularly the cumulative duration required for significant psychological benefits, has not been systematically explored. Second, the use of heterogeneous assessment tools across studies may compromise the validity of pooled effect estimates. Identifying this optimal dosage is critical for clinical decision-making in pulmonary rehabilitation, as it would help clinicians prescribe exercise programs with greater precision. Therefore, this meta-analysis specifically investigates the dose-response relationship between cumulative exercise duration and psychological outcomes, using the standardized HADS scale exclusively to ensure methodological rigor and clinical interpretability. Through rigorous analysis, we aim to provide references for practitioners and therapists to develop appropriate treatment strategies for improving mental health and overall therapeutic outcomes in COPD patients.

Materials and Methods

Systematic Review Registration

This systematic review followed the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines[16] and is registered in PROSPERO (CRD420251145664).

Ethics

As this study is a meta-analysis without direct clinical trials, ethics committee approval was not required.

Data Sources

Two researchers (Siyu Chen and Boyi Shang) comprehensively searched English databases (PubMed, Embase, Cochrane Library, and Web of Science) up to May 7, 2025. Search terms included subject headings such as "exercise therapy", "pulmonary disease, chronic obstructive", "anxiety", "depression", and "breathing exercises", along with free terms including "exercise", "physical activity", "chronic obstructive lung disease", "COPD", "Nervousness", "depressive disorder", "randomized controlled trial", and "breathing exercises". The detailed search strategy for each database is provided in Supplementary Material 1.

Study Selection

All identified citations were collated and uploaded into EndNote X9 (Clarivate, Philadelphia, PA, USA), with duplicates removed. Two reviewers (Siyu Chen and Boyi Shang) independently conducted the study selection process according to PRISMA guidelines. Titles and abstracts were initially screened to exclude clearly irrelevant studies. The full texts of potentially eligible studies were then retrieved and assessed against predefined inclusion and exclusion criteria. Disagreements were resolved through discussion or consultation with a third reviewer (Yanze Bi or Shaodan Hu). The study selection process is detailed in the PRISMA flow diagram (Figure 1).

Inclusion and Exclusion Criteria

Inclusion Criteria

1) Population: patients with stable COPD and no other lung diseases.; 2) Intervention: any exercise training (aerobic exercise, endurance training, respiratory training, strength training, calisthenic exercise, Tai Chi, etc.); 3) Comparison:

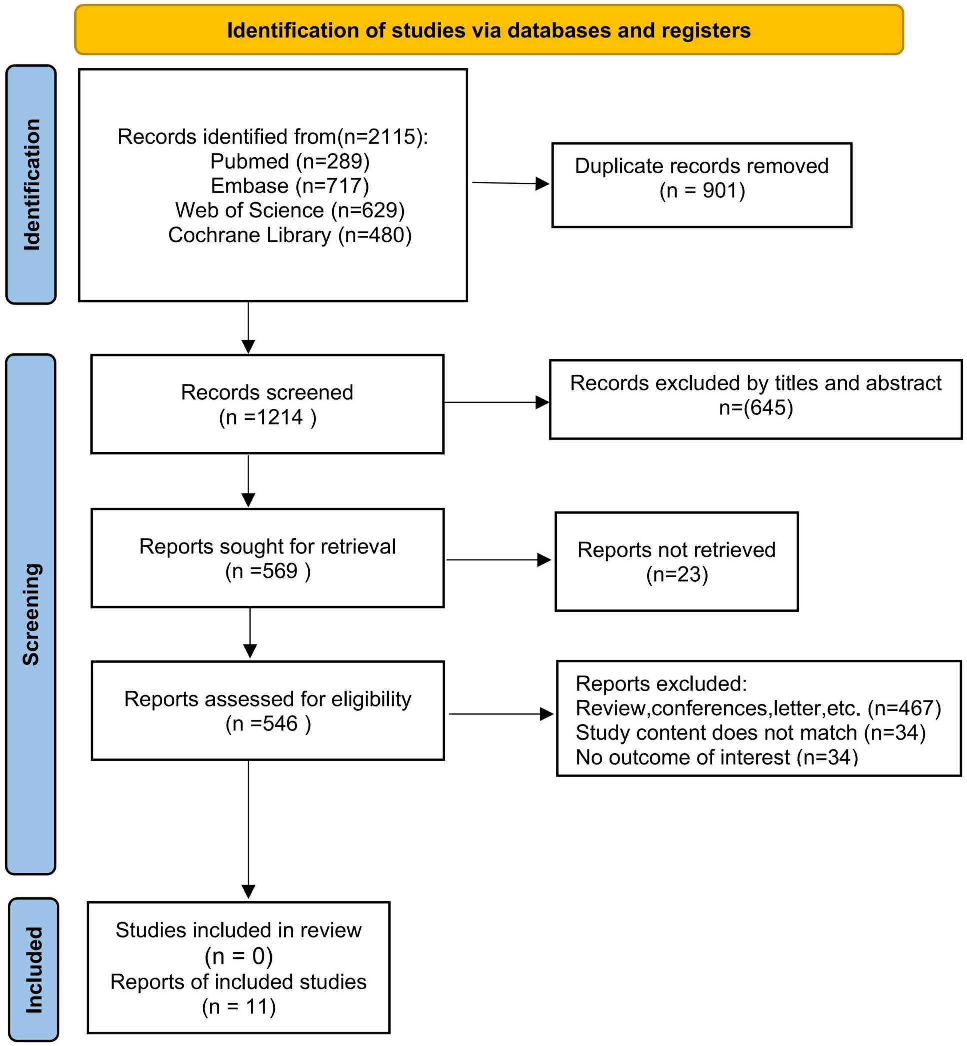

Figure 1 PRISMA flow diagram of the study selection process.

conventional treatment or different exercise methods than the intervention group; 4) Outcome: measured using any depression/anxiety scale; 5) Study design: RCTs.

Exclusion Criteria

1) Inadequate experimental data; 2) Animal studies; 3) Conference abstracts or literature reviews; 4) Irrelevant to exercise intervention; and 5) Duplicate articles.

Data Extraction

Search results were imported and managed using EndNote X9. A standardized data extraction form was developed, two researchers (Siyu Chen and Boyi Shang) independently extracted data from the included literature based on the predefined inclusion and exclusion criteria. Discrepancies were resolved by consulting a third researcher (Yanze Bi or Shaodan Hu).

The following data were extracted:①Study identifiers and characteristics: first author, publication year, and country; ② Participant information: sample size, gender distribution, mean age, and baseline lung function (eg, FEV1, FVC); ③ Intervention details: type of exercise training, program duration (weeks), frequency (sessions/week), session length (minutes), total cumulative intervention duration (minutes); ④ Control group details: components of control condition (eg, routine medical care, education); ⑤ Outcome data: HADS subscale scores (HADS-D for depression, HADS-A for anxiety) at baseline and post-intervention for both groups; ⑥ Methodological quality indicators: randomization methods, allocation concealment, blinding procedures, and documentation of withdrawals and dropouts.

Extracted data on interventions and significant findings are summarized in Tables 1 and 2.

Quality Assessment

Two researchers independently assessed risk of bias using the Cochrane Risk of Bias Tool (Rob 2.0),[28] evaluating: randomization procedures, allocation concealment, blinding of investigators and participants, blinding of outcome assessors, completeness of outcome data, selective reporting, and other potential biases. Studies were classified as low, unclear, or high risk of bias. The modified Jadad scale[29] was also used, evaluating: 1) random sequence generation, 2) allocation concealment, 3) blinding implementation, and 4) documentation of withdrawals and dropouts. Studies scoring 1–3 were classified as low quality, and those scoring 4–7 as good quality.

Data Analysis

Through literature screening, we found that while various scales assess depression or anxiety, studies using HADS-D/HADS-A were most numerous with sufficient data. The number of studies utilizing other types of depression or anxiety scales (which met the inclusion and exclusion criteria) was insufficient to permit a valid quantitative synthesis. Therefore, this meta-analysis only included HADS-D/HADS-A scales. For continuous variables (HADS-A/HADS-D), standardized mean differences (SMD) and 95% confidence intervals (95% CI) were calculated. For studies reporting standard error (SE), we converted to standard deviation (SD) using $SD = SE \times \sqrt{n}$ (where n is sample size). A total of 6 studies were excluded from the quantitative synthesis because they used other depression or anxiety assessment tools (eg, Beck Depression Inventory, Hamilton Depression Rating Scale, Self-Rating Depression Scale, PROMIS) and did not report HADS outcomes. These instruments were each used in only one eligible study, precluding any meaningful subgroup or meta-analysis by scale type. Moreover, these instruments differ substantially in scoring systems, item structures, and measurement constructs, making it methodologically inappropriate to combine them in a meta-analysis. This supports our decision to restrict inclusion to HADS for consistent and interpretable synthesis.

To explore potential sources of heterogeneity and investigate the dose-response relationship between exercise volume and psychological outcomes, subgroup analyses were performed based on cumulative intervention duration (calculated as session duration × frequency per week × total weeks). The cumulative duration thresholds (<1000 minutes, 1000–1500 minutes, >1500 minutes) were post-hoc defined according to the distribution of included studies and the natural terciles of cumulative duration, aiming to ensure balanced group sizes for meaningful comparisons. Given the exploratory nature of these analyses, results should be interpreted as hypothesis-generating rather than confirmatory.

Sensitivity analysis was conducted using the leave-one-out approach, in which the meta-analysis was sequentially repeated after removing each individual study to assess the influence of any single study on the pooled effect estimates.

A fixed-effects model was used when $I^2 < 50\%$ and a random-effects model when $I^2 \geq 50\%$.

Results

Search Results

Based on inclusion and exclusion criteria, 11 RCTs were included for qualitative synthesis and meta-analysis. The PRlSMA flow diagram of the study selection process is shown in Figure 1. After searching various databases and importing into EndNote X9, 2115 English records were identified. We excluded 2104 studies as irrelevant, incomplete, or duplicate, along with non-RCTs, conferences, or reviews.

Study Characteristics

Tables 1 and 2 provide detailed characteristics of the 11 included RCTs,[17–27] totaling 1208 COPD patients. Eight studies reported gender distribution, comprising 658 males and 415 females. Ten studies described specific randomization methods: five used computer-generated sequences[17,19,21,23,27] (three with allocation concealment,[17,19,23] two without[21,27]); two used sealed envelopes administered by independent therapists;[20,24] one used a minimization

Table 1 Basic Characteristics of Included studies[17–27]

Study	Country	Group	Age (Years)	M/F	FEV1% pred	FEV_1/FVC %	Inclusion Criteria	Exclusion Criteria	Jadad Score
(2010) Breyer M-K[27]	Austria	RT:30 CT:30	RT:61.9 ± 8.87 CT:59.0 ± 8.02	RT:14/16 CT:13/17	RT: 48.1 ± 19.1 CT:47.1 ± 16.3	/	Patients with COPD	Self reported exacerbation <12weeks, myocardial infarction <6months, cardiac arrhythmias >Lown IIIb, or walking disturbances due to muscle or bone diseases.	3
(2011) Effing T[26]	The Netherlands	RT:77 CT:76	RT:62.9 ± 8.1 CT:63.9 ± 7.8	RT:45/32 CT:44/32	RT:49.6 ± 14.2 CT:50.5 ± 17.0	/	(1) a clinical diagnosis of COPD according to the GOLD criteria; (2) no exacerbation in the month prior to enrolment; (3) ≥3 exacerbations, defined as respiratory problems that required a course of oral corticosteroids and/or antibiotics, or one hospitalisation for respiratory problems in the two years preceding study entry; (4) (ex) smoker; (5) age 40–75 years; (6)post-bronchodilator FEV_1 25–80% of predicted; (7) able to understand and read Dutch; (8) and written informed consent from the subject prior to participation.	(1) serious other disease with a low survival rate; (2) other diseases influencing bronchial symptoms and/or lung function (eg, cardiac insufficiency, sarcoidosis); (3) severe psychiatric illness; (4) uncontrolled diabetes mellitus during a COPD exacerbation in the past or a hospitalisation for diabetes mellitus in the two years preceding the study; (5) need for regular oxygen therapy (>16 h/day or PO_2< 7.2 kPa); (6) maintenance therapy with antibiotics; (7) known α1-antitrypsine deficiency; (8) disorders or progressive disease seriously influencing walking ability (eg, amputation, paralysis, progressive muscle disease).	3
(2013) Wadell K[25]	Canada	RT:20 CT:28	RT:68 ± 6 CT:66 ± 7	RT: 11/9 CT:16/12	RT:48 ± 12 CT:48 ± 19	RT:44 ± 11 CT: 42 ± 10	Patients with COPD who were 40–80 years of age, had significant activity-related breathlessness (Baseline Dyspnea Index ≤ 8), were on optimal pharmacotherapy in accordance with best practice recommendations, and were clinically stable in the preceding 4 weeks.	Presence of other significant comorbidities that might contribute to dyspnea or exercise limitation; use of supplemental oxygen; or body mass index <18 or >40 kg/m2	2
(2016) Duruturk N[24]	Turkey	RT:15 CT:13	RT:61.2 ± 5.0 CT:63.8 ± 5.7	RT:11/4 CT:11/2	RT:58.4 ± 14.4 CT:63.6 ± 10.8	/	A diagnosis of stage II or III COPD according to the Global Initiative for Chronic Obstructive Lung Disease criteria in a clinically stable patient.	Patients were excluded from participation if they were considered clinically unstable, had cardiovascular disease or malignant disorders, were non-compliant with treatment, or were unable to perform the lung function test, cardiopulmonary exercise testing, or exercise training.	4
(2017) Wang K[23]	China	RT:28 CT:27	RT:70.8 ± 4.5 CT:70.0 ± 6.3	/	RT:49.82 ± 16.14 CT:51.26 ± 18.00	RT:49.60 ± 11.18 CT:47.23 ± 9.90	Age > 40 years; diagnosis of stable COPD based on the Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines; and no participation in any pulmonary rehabilitation program in the previous 2 months.	Patients were excluded if they had acute or chronic airway diseases other than COPD, cardiovascular disorders (such as acute coronary syndrome), metabolic conditions (such as diabetes or hyperthyroidism), or other health problems that would interfere with exercise performance or the testing procedures.	4
(2019) Lavoie KL[22]	Canada	RT:76 CT:76	RT:64.8 ± 6.5 CT:64.9 ± 6.9	RT:45/31 CT:48/28	RT: 49.1 ± 13.3 CT:49.6 ± 12.5	RT:46.5 ± 9.8 CT:48.7 ± 11.8	Patients with COPD, age 40–75years, postbronchodilator forced expiratory volume in 1 s (FEV_1) ≥30% and <80% of predicted normal (Global initiative for chronic Obstructive Lung Disease 2–3) and did not experience acute exacerbations in the month prior to the study, postbronchodilator FEV_1/forced vital capacity <70%, and have a smoking history of >10 pack-years.	Patients with a significant disease other than COPD, a history of asthma, clinically relevant abnormal baseline haematology, blood chemistry or urinalysis, or conditions excluding them from exercise.	3

(*Continued*)

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Table 1 (Continued).

Study	Country	Group	Age (Years)	M/F	FEV1% pred	FEV_1/FVC %	Inclusion Criteria	Exclusion Criteria	Jadad Score
(2021) Saka S[21]	Turkey	RT:20 CT:20	RT:62.30 ± 7.43 CT: 62.10 ± 7.76	/	RT: 39.30 ± 12.37 CT:40.50 ± 14.92	RT:59.30 ± 9.18 CT:62.35 ± 6.82	Age >18 years, able to read written and understand spoken language; a forced expiratory volume in 1s (FEV_1) to forced vital capacity (FVC) ratio (FEV_1/FVC) lower (<) than 70% in pulmonary function test (PFT).	A history of COPD exacerbation in the last 6 weeks, presence of comorbidities affecting ambulation/activity (eg, severe cardiac or neurological disorders, cancer, musculoskeletal problems) and cognitive disorders (Mini Mental State Examination [MMSE]<24). An exacerbation was defined as worsening of at least two respiratory symptoms requiring hospitalization.	3
(2022) Ismail AMA[20]	Egypt	RT:20 CT:20	RT:60.35 ± 4.35 CT:59.35 ± 3.82	/	RT:64.10 ± 9.71 CT: 63 ± 10	RT:63.07 ± 7.65 CT:62 ± 6.95	Non-smokers, no any physical activity program in the previous six months, and had a cycle or treadmill at home.	Presence of systemic/cardiovascular disorders, previous COVID-19 attacks, neuromuscular problems, and hepato-renal diseases, on a supplemental oxygen therapy or had another chest disease, autoimmune disease, connective tissue disorders, cancer or psychiatric disease.	2
(2023) Liu W[19]	China	RT:30 CT:30	RT:64.70 ± 6.89 CT:60.90 ± 7.44	RT: 21/9 CT:21/9	RT:55.17 ± 14.60 CT:51.55 ± 15.16	/	Age 45–75years, with mild to severe COPD, defined by a postbronchodilator FEV_1 ≥ 30% and<80% of predicted. Participants were clinically stable	(1) coexistence of other chronic respiratory disorders; (2) presence of severe comorbidities such as haematological or solid organ malignancy, symptomatic cardiovascular disease (CVD), musculoskeletal or neurological disease that might affect ambulation or exercise training; (3) presence of cognitive dysfunction, mental disorder or abnormal behaviours; (4) participation in a PR programme in the past 12 months; (5) current practice with Tai Chi; and (6) participation in another clinical trial.	4
(2024) Chen Y[18]	China	RT:158 CT:160	RT:61.52 ± 10.31 CT:61.97 ± 10.91	RT:89/69 CT:88/72	/	/	Patients with COPD and were registered for COPD management, met the 2017 Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines2, volunteered to participate in the study, and signed an informed consent form. Age 40–75 years; COPD grade II or III (grade II: 50% ≤ forced expiratory volume in one second (FEV_1) < 80% of the predicted value; grade III: 30% ≤ FEV_1 < 50% of the predicted value); stable phase of COPD; no respiratory infections or acute exacerbations of COPD during the last four weeks; no engagement in BE or similar Qigong exercises or daily aerobic exercises during the last six months; and the ability to communicate well.	Presence of diabetes mellitus, active tuberculosis, bronchiectasis, lung cancer, congestive heart failure, unstable angina pectoris, or myocardial infarction within 12 months before enrolment; epilepsy within 12 months before enrolment or epileptic seizures; chronic liver and kidney disease; glaucoma; limited physical activity or other reasons why participants could not perform BE training; participation in any other clinical studies in the last six months; and bipolar depression or other serious psychological disorders.	4
(2024) Cui SL[17]	China	RT:122 CT:132	RT:75.02 ± 0.87 CT:73.75 ± 0.63	RT:72/50 CT:109/23	/	RT:0.63 ± 0.04 CT:0.59 ± 0.04	Age 40–80 years, patients with clinically stable COPD in GOLD (Global Initiative for Chronic Obstructive Lung Disease) stage I to I; patients were forced expiratory volume in 1s (FEV_1)/forced vital capacity (FVC) ratio <70%, FEV_1<80% of predicted, resting arterial oxygenation >90%	(1) cardiovascular problem (such as NYHA class IV, ACS), (2) diagnosed psychiatric or cognitive disorders, (3) contraindications to exercise activities (progressive neuromuscular diseases, severe orthopedic problems), (4) resting arterial PaO2 <60mmHg and PaCO2 >55 mmHg, and (5) prior inclusion in a rehabilitation program (<1 year).	4

Note: data are presented as n or mean ± SD.

Abbreviations: M, male; F, female; FEV1, forced expiratory volume in 1 second; FVC, forced vital capacity; RT, experimental group; CT, control group; COVID-19, Coronavirus Disease 2019; PR, pulmonary rehabilitation; GOLD, Global Initiative for Chronic Obstructive Lung Disease; NYHA, New York Heart Association; ACS, Acute Coronary Syndrome.

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Table 2 Interventions Included in studies[17–27]

Study	Duration	Cumulative Intervention Duration (Minutes)	Intervention	Study Design	Outcomes
(2010) Breyer M-K[27]	3 months	2314	RT:Nordic Walking CT:education session	RT:Three months of outdoor Nordic walking training, three times a week, one hour each time.	HADS-D HADS-A
(2011) Effing T[26]	6 months	/	RT:COPE-active programme +self-management sessions CT:self-management sessions	RT:Three times a week, group training (2–3 people per group) guided by community physical therapists, including targeted activities such as cycling, walking, stair climbing and weight lifting.	HADS-D HADS-A
(2013) Wadell K[25]	8 weeks	3600	RT: PR+CTRL CT: CTRL	RT:PR consisted of three supervised 2.5-hour sessions per week over an 8-week period. Sessions included graduated exercise training for upper and lower limbs	HADS-D HADS-A
(2016) Duruturk N[24]	6 weeks	450	RT: cycle exercise +education session CT: education session	RT:Aerobic training was conducted on a bicycle ergometer three times a week for six weeks.	HADS-D HADS-A
(2017) Wang K[23]	8 weeks	1056	RT: CET + IMT CT: CET	RT:Three times a week, each session begins with 30 minutes of CET, followed by 14 minutes of IMT 30 minutes later. The IMT equipment uses threshold load. The initial intensity is 30% of the maximum inhalation pressure. The training is conducted in an intermittent manner (7 sets, each set lasting 2 minutes, with 1 minute of rest between sets).	HADS-D HADS-A
(2019) Lavoie KL[22]	8 weeks	1800	RT:T/O FDC (5/5 μg) +SMBM+ExT CT:T/O FDC (5/5 μg) +SMBM	RT: Three times a week, each session consisted of 30 min aerobic exercise (cycling or walking) and 45 min upper and lower body resistance training	HADS-D HADS-A
(2021) Saka S[21]	8 weeks	1200	RT: IMT CT: sham group	RT:Five days per week, two times per day, 15min each time	HADS-D HADS-A
(2022) Ismail AMA[20]	8 weeks	1920	RT: HBPA CT: no HBPA	RT: Three times per week, each session including 50-minute cycling or treadmill walking, followed by 30-minute upper/lower limb exercises, followed by a 30-minute educational training session	HADS-D HADS-A
(2023) Liu W[19]	2 months	771	RT: Tai Chi CT: usual care	RT: Engage in Tai Chi training three times a week, for 30 minutes each time. Emphasis is placed on the combination of breathing control and body movements.	HADS-D HADS-A
(2024) Chen Y[18]	6 months	7714	RT: usual care+Baduanjin exercise CT: usual care	RT:Baduanjin exercise: 5 days per week, two times per day, 30min each time	HADS-D HADS-A
(2024) Cui SL[17]	12 months	1440	RT: medical treatments +endurance training CT: medical treatments	RT:Running on a treadmill, 20minutes, once a day+three sets of 30 repetitions of free weightlifting	HADS-D HADS-A

Abbreviations: RT, experimental group; CT, control group; PR, pulmonary rehabilitation; COPE-active, community-based physiotherapeutic exercise; CTRL, usual care control group; CET, cycle ergometer training; IMT, inspiratory muscle training; HBPA, home-based physical activity; T/O FDC, tiotropium/olodaterol fixed-dose combination; SMBM, self-management behavior modification; Ext, exercise training; HADS-D, Hospital Anxiety and Depression Scale - Depression subscale; HADS-A, Hospital Anxiety and Depression Scale - Anxiety subscale.

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program;[26] one used a pseudo-random number generator with block randomization;[22] and one used a random number table for 1:1 allocation.[18]

All participants were adults (age ≥ 18 years), predominantly male. Eight studies reported gender ratios, while three did not. Studies were conducted in China (n = 4), Canada (n = 2), Turkey (n = 2), Austria (n = 1), the Netherlands (n = 1), and Egypt (n = 1). Interventions involved 3–10 sessions per week, each lasting 15–150 minutes, over 6–26 weeks. Exercise types included physical and mental exercise (Tai Chi, n = 1; Baduanjin, n = 1), aerobic exercise (n = 5), and strength training (n = 4). Control groups received routine medical care, education, self-management, placebo, no intervention or single exercise training.

Risk of Bias

Figures 2 and 3 summarize risk of bias and overall judgment for each included study's relevant results. We found that all the data loss and selection bias in the studies were at a low risk, and the risks of other biases were unclear. During the generation of randomization sequences, most of the studies were at a low risk. Five studies included blinded outcome assessment.[17–19,23,24] Additionally, Lavoie et al[22] used double-blind methods for all groups except the exercise training group. This is because existing exercise training studies cannot be double-blind. Based on our findings, 9 studies explicitly mentioned the number of dropouts and the reasons for dropout,[17–19,21,23–27] while 2 studies only mentioned the number of dropouts but did not clarify the reasons for dropout.[20,22]

Figures 2 and 3 summarize domain-level risk of bias and overall judgments. All studies showed low risk in data loss and selection bias, with unclear risks in other biases. Most studies had low risk in randomization sequence generation. Five studies included blinded outcome assessment.[17–19,23,24] Lavoie et al[22] used double-blinding for all groups except the exercise training group, as double-blinding is not feasible in exercise training studies. Nine studies explicitly reported dropout numbers and reasons,[17–19,21,23–27] while two reported dropout numbers without specifying reasons.[20,22]

Meta-Analysis Results

Depression

All 11 RCTs reported effects of exercise training on depression using HADS-D. As shown in Figure 4, high heterogeneity existed among studies (I^2 = 65.6%, p = 0.001), so a random-effects model was used. Meta-analysis showed significantly lower depression scores in the exercise training group compared to controls [SMD = −0.35 (95% CI: −0.58, −0.12)], with statistical significance ($P < 0.05$).

Subgroup analysis of 10 studies based on cumulative intervention duration (minutes) is shown in Figure 5. In the <1000 minutes subgroup (n = 2), heterogeneity was low (I^2 = 0.0%, P = 0.519), with no significant difference between groups [SMD = −0.05 (95% CI: −0.49, 0.39), $P > 0.05$]. In the 1000–1500 minutes subgroup (n = 3), heterogeneity was high (I^2 = 71.7%, P = 0.029), still showing no significant difference [SMD = −0.42 (95% CI: −0.93, 0.09), $P > 0.05$]. In

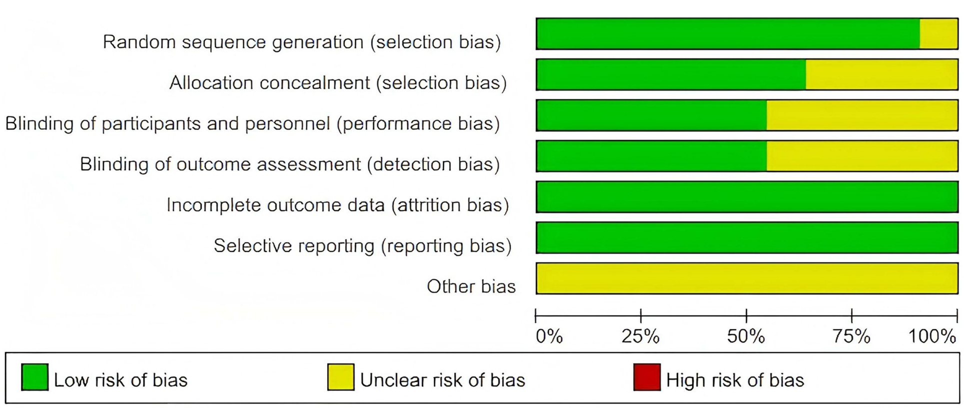

Figure 2 Risk of bias graph:[17–27] review authors' judgments about each risk of bias item presented as percentages across all included studies.

Figure 3 Risk of bias summary:[17–27] review authors' judgments about each risk of bias item for each included study.
Notes: + = low risk; ? = unclear risk; - = high risk.

the >1500 minutes subgroup (n = 5), heterogeneity was high (I^2 = 74.6%, P = 0.003), with significantly lower depression scores in the exercise group [SMD = −0.56 (95% CI: −0.97, −0.14)], and statistical significance ($P < 0.05$).

Substantial heterogeneity persisted in the >1500 minutes subgroup (I^2 = 74.6%), suggesting that beyond cumulative duration, other intervention characteristics, such as exercise type, intensity, supervision mode, or patient baseline characteristics, may contribute to variability in treatment effects.

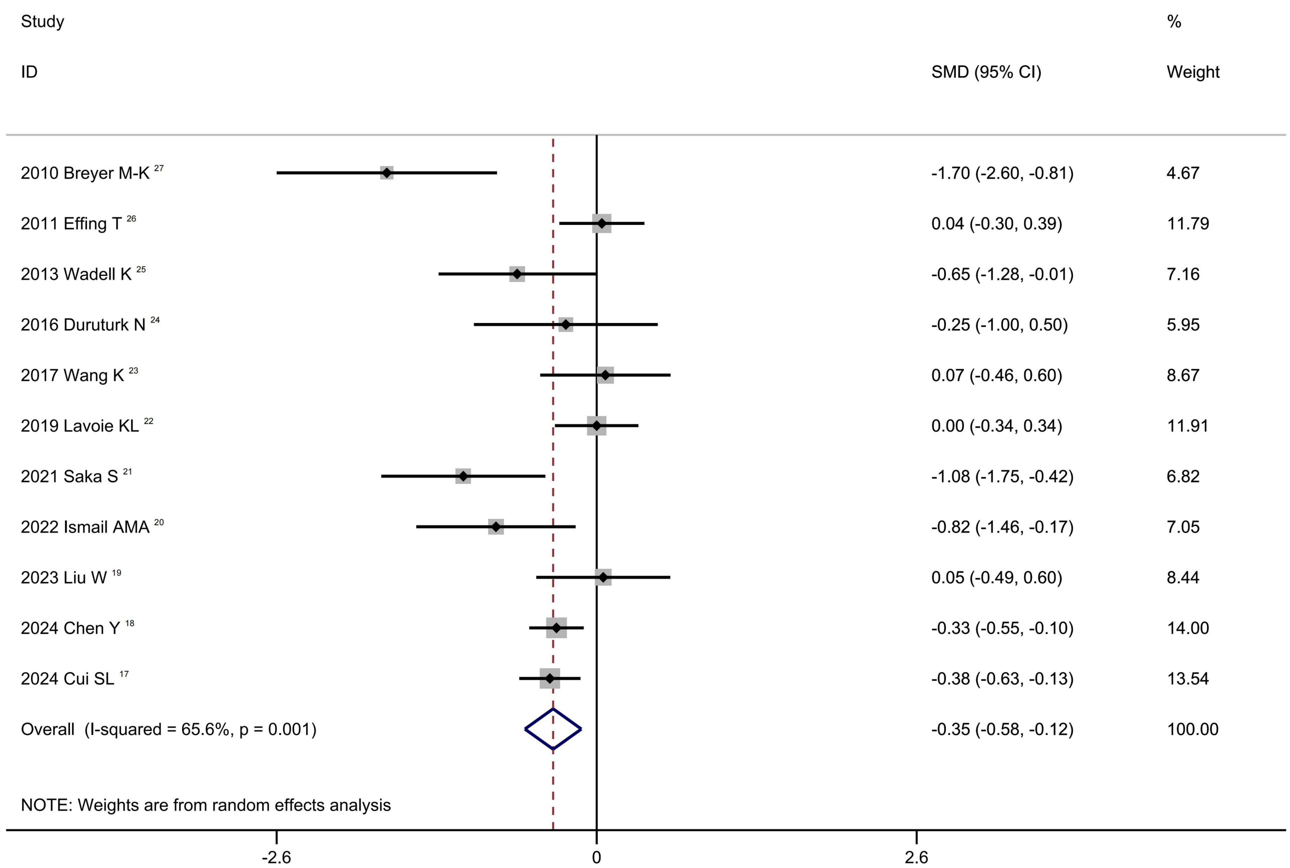

Figure 4 Forest plot of the effect of exercise training on depression (Hads-D).[17–27] A random-effects model was used.

Anxiety

All 11 RCTs reported effects on anxiety using HADS-A. As shown in Figure 6, high heterogeneity existed ($I^2 = 74.5\%$, $P < 0.001$), so a random-effects model was used. Meta-analysis showed significantly lower anxiety scores in the exercise training group [SMD = −0.27 (95% CI: −0.53, −0.01)], with statistical significance ($P < 0.05$).

Subgroup analysis of 10 studies by cumulative duration is shown in Figure 7. In the <1000 minutes subgroup (n = 2), heterogeneity was low ($I^2 = 0.0\%$, $P = 0.512$), with no significant difference [SMD = −0.32 (95% CI: −0.77, 0.12), $P > 0.05$]. In the 1000–1500 minutes subgroup (n = 3), heterogeneity was moderate ($I^2 = 50.9\%$, $P = 0.130$), with no significant difference [SMD = −0.08 (95% CI: −0.45, 0.29), $P > 0.05$]. In the >1500 minutes subgroup (n = 5), heterogeneity was high ($I^2 = 83.3\%$, $P < 0.001$), still showing no significant difference [SMD = −0.47 (95% CI: −0.96, 0.02), $P > 0.05$]. The overall combined effect across all studies showed high heterogeneity ($I^2 = 75.2\%$, P < 0.001), with lower anxiety scores in the exercise group [SMD = −0.31 (95% CI: −0.60, −0.03)], and statistical significance ($P < 0.05$).

Publication Bias

Funnel plots and Egger's test assessed publication bias. Funnel plots for depression and anxiety (Figures 8 and 9) appeared visually symmetrical. Egger's test results were not statistically significant (depression: $P = 0.259 > 0.05$; anxiety: $P = 0.778 > 0.05$), indicating no significant publication bias.

Sensitivity Analyses

Sensitivity analysis using the leave-one-out method was conducted to assess the impact of individual studies on meta-analysis results (Figures 10 and 11). Results showed that sequentially removing any single study did not substantially

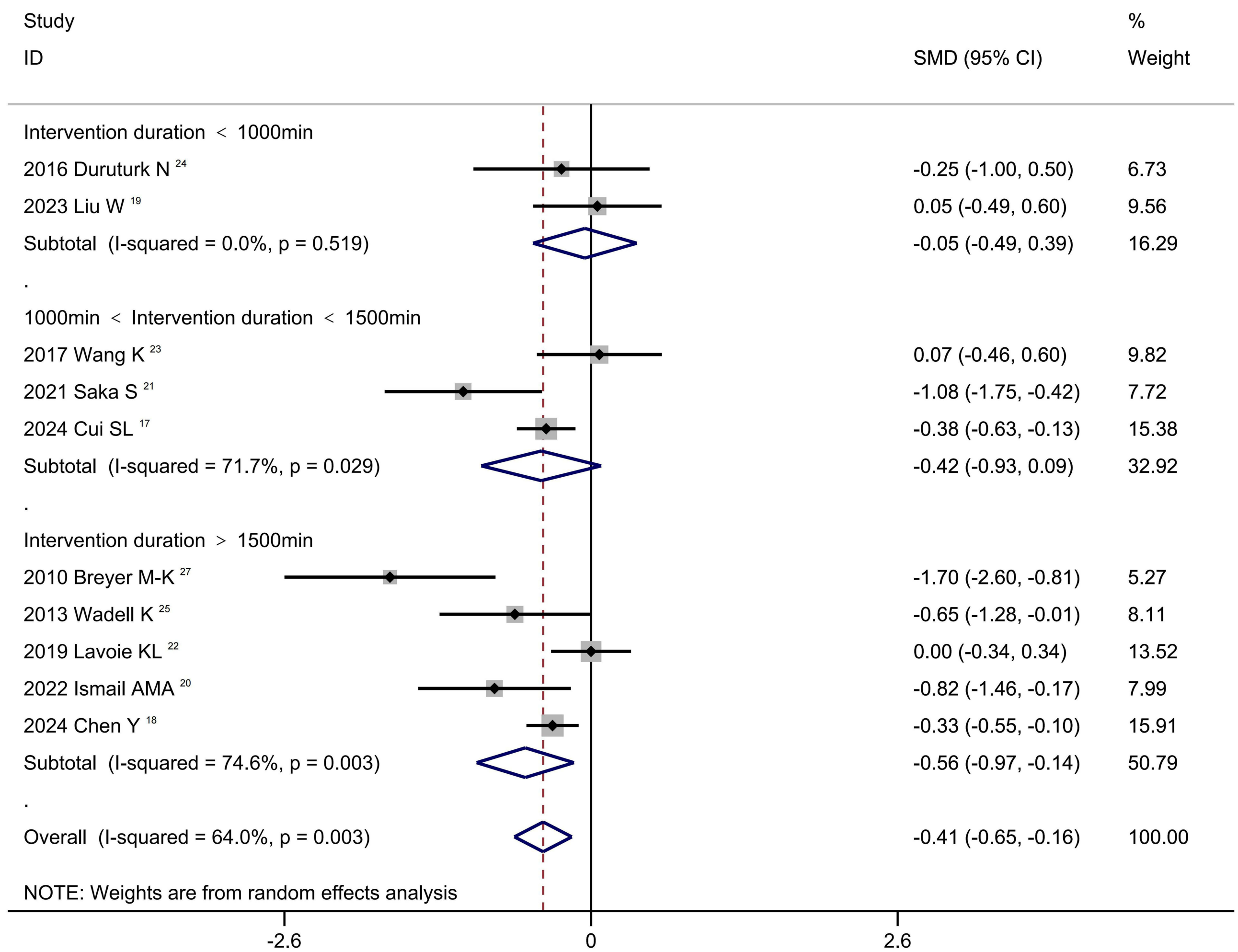

Figure 5 Subgroup analysis of the effect of exercise training on depression by cumulative intervention duration.[17–25,27]

change the combined effect size estimate, and the 95% CI extensively overlapped with the original total effect size CI, indicating robust meta-analysis results.

Discussion

Summary of Main Findings

This systematic review and meta-analysis confirm that exercise training effectively improves depression and anxiety in COPD patients. Our core results show that exercise training significantly alleviates depressive symptoms [Figure 4, SMD = −0.35 (95% CI: −0.58, −0.12), $P < 0.05$] and anxiety symptoms [Figure 6, SMD = −0.27 (95% CI: −0.53, −0.01), $P < 0.05$]. Using the HADS scale exclusively helped minimize measurement heterogeneity, as it is the most widely used tool in this field and effectively distinguishes physical from emotional symptoms. Although high heterogeneity remained (Figures 4 and 6, mainly due to intervention variations and patient baseline differences), focusing on HADS ensured purity of the combined effect size, allowing internally consistent and interpretable conclusions on exercise's impact on depression and anxiety in COPD patients under rigorous methodology.

Comparison with Existing Literature and Interpretation of Results

Our findings align with recent studies.[14,15] For example, Zhaoying Yan et al[15] reported that physical and mental exercises effectively alleviate anxiety and depression, improving patients' quality of life; Tiying Liu et al[14] also found that exercise

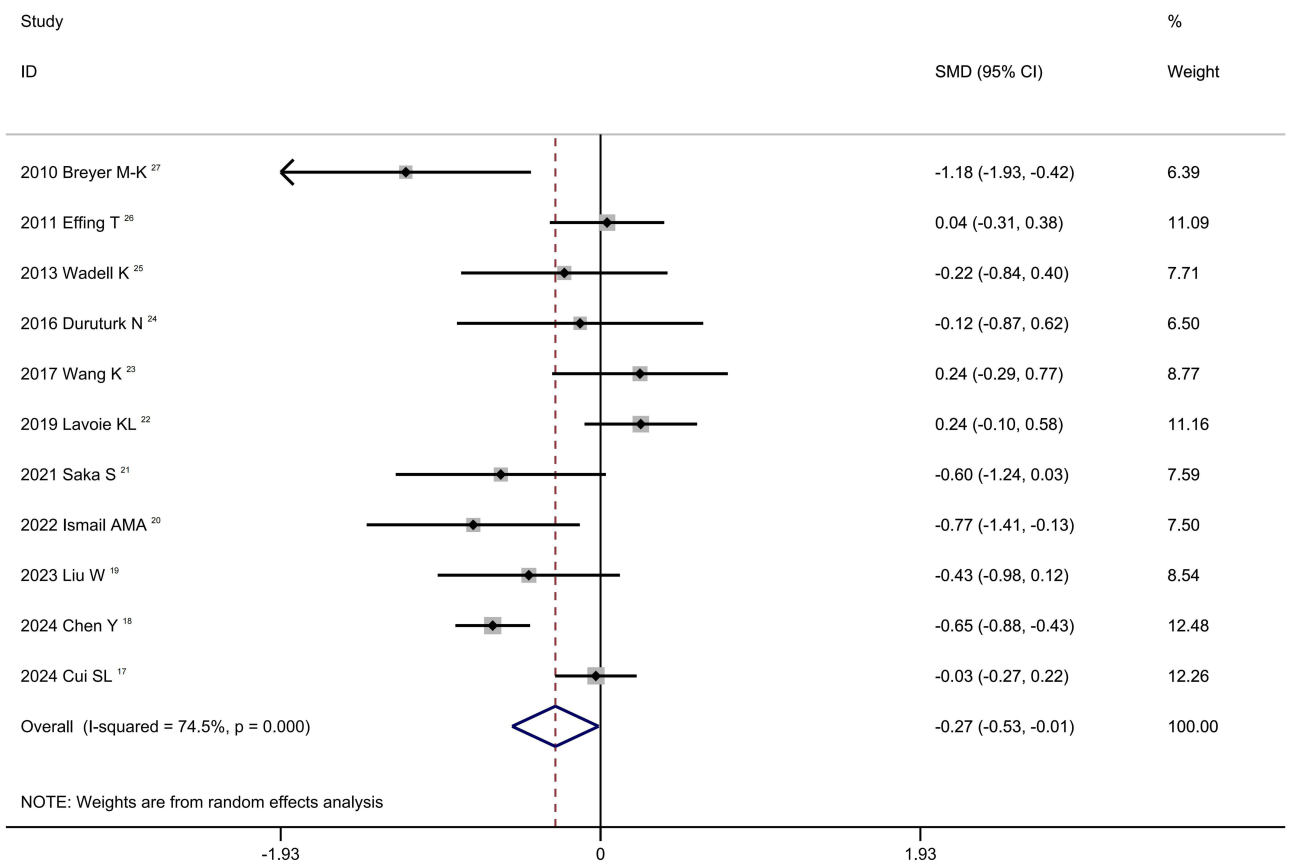

Figure 6 Forest plot of the effect of exercise training on anxiety (Hads-A).[17–27] A random-effects model was used.

reduces psychological distress in COPD patients. Using a unified scale based on HADS, our study further demonstrates the psychological benefits of exercise as a non-pharmacological intervention. Although the overall effect size is small, its clinical significance should not be overlooked. For COPD patients trapped in a vicious cycle of negative emotions, even slight symptom relief may help break the cycle of breathlessness, reduced activity, and worsening emotions.[2] Therefore, integrating exercise training into routine COPD management is a safe, feasible strategy offering both physical and mental benefits.

Interpretation of the Subgroup Analysis Results

Subgroup analyses based on cumulative intervention duration (Figures 5 and 7) provided further insights. For depression (Figure 5), longer cumulative duration (>1500 minutes) showed a clear, consistent antidepressant effect (SMD = −0.56). However, in the medium duration range (1000–1500 minutes), although the average effect size indicated moderate benefit (SMD = −0.42), results were not statistically significant, with high heterogeneity within this subgroup. Notably, within the 1000–1500 minutes subgroup, we observed variations from highly effective to inconsistent effects (eg, Saka S's 2021 study showed a very large effect size). This suggests that beyond a certain duration, other factors such as intervention content, intensity, or patient characteristics may influence effects more than cumulative duration alone. In other words, intervention "quality" may be equally or more important than "quantity". Ensuring adequate duration (>1500 minutes) is a reliable strategy for stable effects, while within medium duration (1000–1500 minutes), optimizing the intervention plan (eg, adopting more efficient exercise patterns) may also achieve significant clinical benefits.

For anxiety (Figure 7), none of the subgroup analyses reached statistical significance (all $P > 0.05$), although effect sizes consistently favored the intervention group. Despite the lack of statistical significance, the consistently favorable effect sizes suggest exercise training may have a positive effect direction across different durations, consistent with Zhaoying Yan et al's findings.[15] This may be partly due to reduced statistical power from smaller sample sizes. These null findings highlight the need for further high-quality studies to clarify the effects of exercise on anxiety in COPD

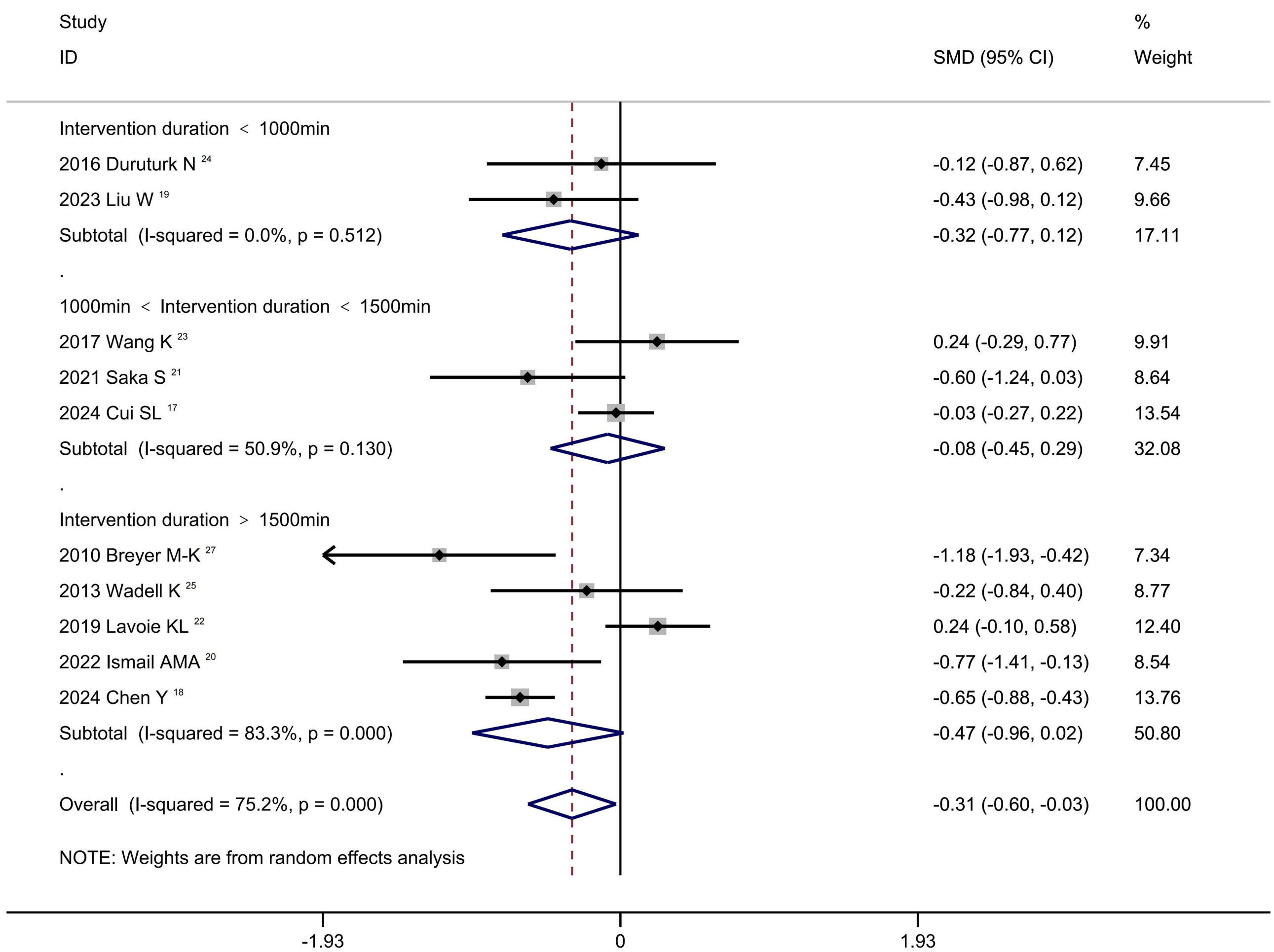

Figure 7 Subgroup analysis of the effect of exercise training on anxiety by cumulative intervention duration.[17–25,27]

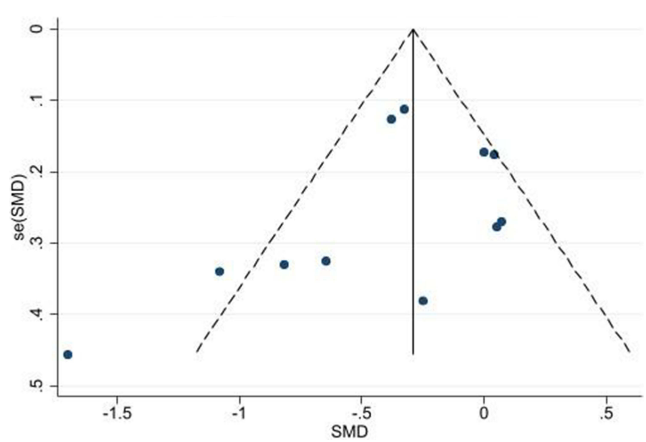

Figure 8 Funnel plot for publication bias assessment of depression outcomes.[17–27]

patients. While Zhaoying Yan et al[15] reported a higher threshold of 3080 minutes specifically for mind-body exercises, our finding of a 1500-minute threshold across diverse exercise modalities presents a more feasible and generalizable clinical target. Achieving 1500 minutes of cumulative exercise is more practical in real-world settings, especially for

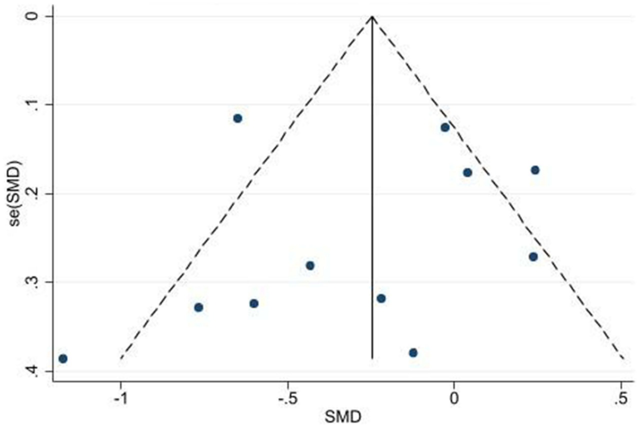

Figure 9 Funnel plot for publication bias assessment of anxiety outcomes.[17–27]

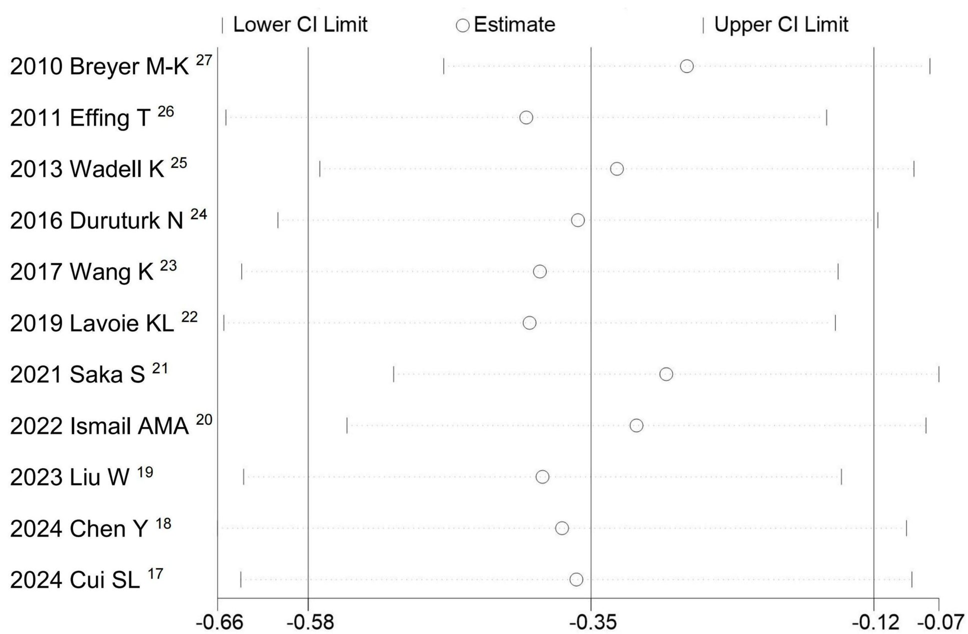

Figure 10 Sensitivity analysis for depression using the leave-one-out method.[17–27]

elderly or frail COPD patients, enhancing the translational potential of our findings. Although current evidence strength is insufficient to definitively conclude the optimal duration, these results provide useful references for clinical practice and directions for future large-sample studies.

Importantly, the observed threshold of >1500 minutes for significant antidepressant effects was exploratory and post-hoc in nature. This finding should therefore be interpreted as hypothesis-generating rather than a definitive clinical cutoff. While it provides a useful reference for clinical practice and future study design, it does not preclude the possibility that shorter durations with optimized intervention characteristics (eg, higher intensity or better adherence) may also yield meaningful benefits.

Heterogeneity Analysis and Publication Bias

This study exhibited substantial heterogeneity for both depression (Figure 4, I^2 = 65.6%) and anxiety (Figure 6, I^2 = 74.5%), which is not unexpected given the diversity of exercise interventions and patient populations. Subgroup analysis by cumulative duration partially explained this heterogeneity, yet high heterogeneity persisted within certain subgroups

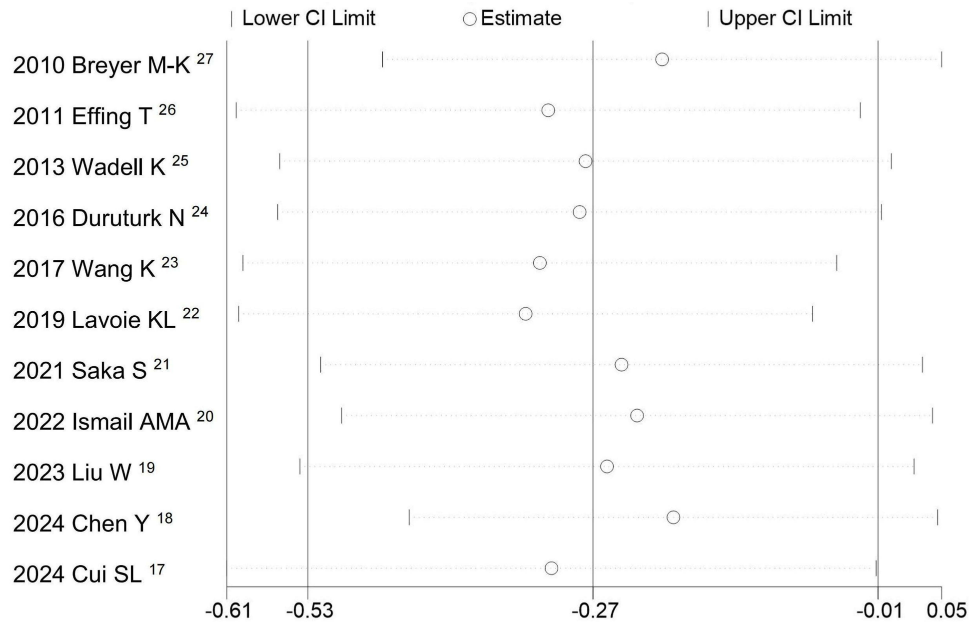

Figure 11 Sensitivity analysis for anxiety using the leave-one-out method.[17–27]

(eg, as Figure 5, depression in the 1000–1500 minutes subgroup, I^2 = 71.7%; depression in the >1500 minutes subgroup, I^2 = 74.6%). This suggests that factors beyond total exercise volume—including exercise modality (aerobic, resistance, or mind-body), intervention intensity (eg, percentage of maximal heart rate), supervision format (supervised vs. home-based), and baseline disease severity (FEV_1 % predicted)—may independently influence psychological outcomes. Moreover, different exercise types may exert their effects through distinct mechanisms, such as cardiorespiratory

Table 3 Clinical Implications and Exercise Prescription Considerations for COPD Patients[17–27]

Category	Summary
Target population	Patients with stable COPD, typically aged 40–80 years, with no acute exacerbation in the preceding 4–6 weeks. Most included studies enrolled patients with moderate to very severe COPD (GOLD stages II–IV)
Exercise modalities evaluated	Aerobic exercise (eg, walking, cycling, Nordic walking), strength training, mind-body exercises (Tai Chi, Baduanjin), and inspiratory muscle training
Cumulative duration	Interventions ranged from 450 to 7714 minutes across studies. Exploratory finding: cumulative duration >1500 minutes was associated with significant improvement in depressive symptoms (SMD = −0.56, 95% CI: −0.97 to −0.14)
Clinical recommendations	(1) Integrate exercise training into comprehensive COPD management
	(2) Encourage patients to achieve a cumulative exercise duration of at least 1500 minutes (approximately 30 minutes, 3–5 times weekly, over 3–6 months)
	(3) Select exercise modalities based on patient preference and physical capacity; both aerobic and mind-body exercises demonstrated benefits
	(4) For patients with prominent anxiety, consider complementing exercise with cognitive-behavioral strategies to address dyspnea-related catastrophic thinking
Key evidence gaps	(1) Optimal exercise type, intensity, and frequency remain unclear
	(2) The 1500-minute threshold is exploratory and requires confirmation in prospective trials
	(3) Long-term maintenance effects beyond intervention periods are understudied

adaptation, neuromuscular strengthening, or mind-body awareness. However, the limited number of included studies precluded reliable subgroup analyses by these factors.

Publication bias was assessed using funnel plots (Figures 8 and 9) and Egger's test, with no evidence of significant bias (as Figure 8, depression: $P = 0.259$; as Figure 9, anxiety: $P = 0.778$). Sensitivity analyses using the leave-one-out method (Figure 10: depression and Figure 11: anxiety) confirmed the robustness of the pooled effect estimates, as sequential removal of individual studies did not substantially alter the overall results. These findings support the stability of our conclusions.

Future large-scale RCTs should standardize reporting of intervention parameters to enable more robust exploration of heterogeneity sources, including meta-regression analyses to examine the influence of disease severity and intervention characteristics (eg, intensity, supervision format) on psychological outcomes. Head-to-head comparisons of different exercise modalities are also warranted to clarify whether specific exercise types confer superior benefits.

Potential Mechanisms

Depression and anxiety in COPD patients are closely related to pulmonary-specific symptoms like breathing difficulties and coughing.[30] Patients often avoid activities due to exercise fear, leading to further physical decline, worsened breathing difficulties, increased hospitalization and mortality, and varying degrees of depression and anxiety.[31,32]

Regular exercise training improves cardiopulmonary function and muscle oxygen utilization efficiency, effectively relieving breathing difficulties and fatigue,[32] and enhancing exercise self-efficacy (confidence in completing tasks and achieving goals)[33] These improvements directly help alleviate depressive emotions and helplessness,[34] and strongly counteract anticipatory anxiety (fear of impending shortness of breath).[35,36] However, exercise may not directly improve catastrophic misinterpretation of physical symptoms caused by "shortness of breath" anxiety.[37,38] Therefore, as shown in Figure 7, compared to depression, exercise's improvement in anxiety was relatively unstable with a smaller effect size, possibly because exercise cannot directly reverse catastrophic thinking patterns triggered by dyspnea.

Chronic inflammation plays a significant role in COPD development. Inflammatory factors (eg, TNF-α, CRP) not only affect lung parenchyma and airways, exacerbating lung lesions[39] but also influence the central nervous system via the blood-brain barrier, reducing brain-derived neurotrophic factor (BDNF) production in brain regions like the hippocampus.[40] BDNF is crucial for neuronal survival, differentiation, and growth, and is a key protein for emotional regulation.[41–43] Substantial evidence indicates BDNF is closely related to depression pathophysiology and antidepressant treatment mechanisms, representing an important target for antidepressant therapy.[44–50] Low BDNF levels are closely associated with depression.[40] Studies show exercise training effectively reduces inflammation and upregulates BDNF, possibly alleviating or reversing inflammation's negative brain impact and promoting emotional health.[51,52] Concurrently, exercise regulates hypothalamic–pituitary–adrenal (HPA) axis function, normalizes cortisol secretion rhythms, alleviates chronic stress responses,[51,53,54] improves cardiac autonomic regulation, increases vagal tone, and counteracts autonomic dysfunction associated with anxiety and depression.[55]

In summary, exercise training benefits depression and anxiety in COPD patients through multiple synergistic pathways, including improving cardiopulmonary function, enhancing self-efficacy, regulating inflammation, and modulating neuroendocrine function. Exercise directly improves depression by addressing self-efficacy and helplessness in COPD patients but may not effectively alleviate anxiety-related catastrophic thinking. This may be a key reason for the differential effects on depression versus anxiety observed in this study.

Clinical Significance

This study confirms that exercise training (eg, physical and mental exercise, aerobic training, strength training) effectively alleviates depression (SMD = −0.35) and anxiety (SMD = −0.27) in COPD patients. We recommend integrating diverse exercise training modalities into the comprehensive management plan for COPD, particularly for patients presenting with depressive or anxiety symptoms. For those with anxiety, exercise regimens should be complemented by cognitive-behavioral strategies designed to reduce catastrophic thinking associated with dyspnea. Patients should be encouraged to maintain long-term exercise, with a suggested cumulative duration exceeding 1500 minutes, and may select suitable modalities such as Baduanjin, Tai Chi, or other aerobic or mind-body exercises. The main clinical implications and exercise prescription considerations are summarized in Table 3. Future high-quality RCTs should focus on exercise dose-response relationships, long-term follow-up effects, and mechanism research. Efforts should identify key factors maximizing intervention efficiency beyond mere duration accumulation.

Limitations

Several limitations should be acknowledged. First, the number of included RCTs was relatively small (n = 11), with limited sample sizes in certain subgroups. Additionally, the geographic distribution of included studies was limited, with the majority conducted in China and Europe. These factors may affect the stability and generalizability of the findings. Second, to reduce measurement heterogeneity and ensure valid quantitative synthesis, we restricted inclusion to studies using the HADS scale. While this approach enhances internal validity, it may introduce selection bias and limit generalizability to studies using other validated instruments. Six eligible studies were excluded because they employed other depression or anxiety assessment tools (eg, Beck Depression Inventory, Hamilton Depression Rating Scale). Each of these instruments appeared in only one study, precluding subgroup analysis by scale type. Moreover, they differ substantially in scoring systems and measurement constructs, making it methodologically inappropriate to combine them in a meta-analysis. Third, substantial heterogeneity was observed across studies, and although we conducted subgroup analyses by cumulative duration, other intervention characteristics (eg, exercise type, intensity, supervision mode) and patient factors (eg, baseline disease severity, comorbidities) could not be fully explored due to the limited number of studies. Fourth, the threshold of >1500 minutes for subgroup analysis was defined post-hoc; thus, this finding should be considered exploratory rather than confirmatory. Fifth, the nature of exercise interventions precludes blinding of participants and personnel, introducing potential performance and detection bias, particularly for self-reported psychological outcomes. Finally, methodological quality varied across studies, with some failing to report allocation concealment or blinding of outcome assessors, which may introduce bias.

Conclusion

This meta-analysis suggests that exercise training is associated with improvements in depression and anxiety symptoms in patients with COPD, with effects potentially related to cumulative intervention duration. Although the overall effect sizes were modest, the consistent direction of benefit supports exercise training as a valuable non-pharmacological component of comprehensive COPD management. The exploratory finding that cumulative durations exceeding 1500 minutes may confer greater antidepressant effects warrants confirmation in future well-designed, long-term RCTs, which should also investigate optimal exercise modalities, intensity, and adherence strategies to maximize psychological benefits in this population.

Declaration of Generative AI and AI-Assisted Technologies

The authors used AI-assisted tools for language refinement during the preparation of this work and take full responsibility for the content of the publication.

Data Sharing Statement

The data that support the findings of this study (including Tables 1 and 2) are available from the corresponding author upon reasonable request.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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