



REVIEW ARTICLE OPEN ACCESS

The Effects of Aerobic and Resistance Exercise on Depression and Anxiety: Systematic Review With Meta-Analysis

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ABSTRACT

Exercise can reduce physiological and psychological symptoms associated with depression and anxiety. However, it is unknown which mode of exercise, if any, is more beneficial. To determine whether aerobic, resistance, or aerobic and resistance exercise improves depressive and/or anxiety symptoms in individuals diagnosed with depression or anxiety. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines were followed. Five electronic databases were searched, until February 24, 2024. Studies were included for analysis based on satisfying quality appraisal standards and the established inclusion criteria associated with aerobic or resistance exercise in adults with a diagnosis of depression or anxiety. Random effects meta-analysis was performed where possible. Thirty-two randomised controlled trial studies ($n = 3243$ participants) met the inclusion criteria for this systematic review, and 26 studies ($n = 2681$ participants) were included in the meta-analyses. For the 25 studies assessing the effect of exercise on depressive symptoms, the pooled standardised mean difference (SMD) favoured exercise as a beneficial treatment of depression (-0.97 , 95% confidence interval [CI] -1.28 to -0.66), with a large magnitude of effect. For the 11 studies reporting the effect of exercise on anxiety symptoms, the pooled SMD results revealed that exercise had a significant, moderate magnitude of effect favouring exercise treatment (-0.66 , 95% CI -1.09 to -0.23). No studies excessively influenced the outcomes of depression and anxiety. Aerobic, resistance, or a mixture of aerobic and resistance exercise is beneficial for improving symptoms of depression and anxiety.

Protocol Registration: PROSPERO registration number: CRD42019119341 (date of registration: 5/2/2019).

1 | Introduction

Globally, individuals with mental illnesses experience a significantly reduced life expectancy compared to those without a diagnosed mental health condition (Hu et al. 2020). Common mental health disorders, such as depression and anxiety, are

particularly associated with a higher incidence of chronic health conditions including cardiovascular disease, diabetes and respiratory disorders (Stanton et al. 2019; Heissel et al. 2023). Consequently, this population faces substantially poorer physical health outcomes compared to those without mental illness (Happell et al. 2015). One key factor contributing to the higher

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prevalence of comorbid mental and physical illnesses is low levels of physical activity (Schuch et al. 2017; Stubbs et al. 2017). The World Health Organisation (WHO) Mental Health Action Plan (World Health Organization 2021) recognises that engaging in regular exercise poses unique challenges for individuals with mental health conditions. These challenges are often linked to the symptoms of their illness, compounded by external barriers such as socioeconomic disadvantages.

Depressive disorders are defined in the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) as 'sad, empty or irritable mood, accompanied by somatic and cognitive changes that significantly affect the individual's capacity to function' (American Psychiatric Association 2018). Similarly, anxiety disorders are characterised by 'excessive fear and anxiety and related behavioural disturbances' (American Psychiatric Association 2018). Both depression and anxiety are commonly managed with psychotherapy and pharmacological medication (Kendrick and Pilling 2012). However, antidepressant medications can present challenges, including being cost prohibitive for some individuals and causing adverse effects such as weight gain and insomnia (Stanton et al. 2019).

Although individuals with mental illness may face challenges in engaging in exercise, research has shown that physical activity can alleviate both physiological and psychosocial impacts associated with depression and anxiety (Ren and Xiao 2023; Ramos-Sanchez et al. 2021). Physiological benefits of exercise include enhanced mitochondrial function and reduced fatigue (Lopresti et al. 2013), improved regulation of stress hormones in the brain (Schuch and Stubbs 2019) and better mood and sleep patterns (Hu et al. 2020). Psychosocial benefits, on the other hand, involve increased social interaction and providing a distraction from daily struggles with depressive or anxiety-related issues (Ren and Xiao 2023; Ramos-Sanchez et al. 2021).

Gordon et al. (2018) reported that resistance exercise has a moderate effect on reducing depressive symptoms, while Cooney et al. (Cooney et al. 2013) found that exercise (mixed aerobic and resistance) offers only small mental health benefits, comparable to standard psychological treatments. While there is substantial evidence supporting the role of exercise in managing depression, conflicting findings may arise due to variations in the mode, frequency, intensity and volume of exercise prescribed across studies. Additionally, the relatively recent focus on exercise and depression research highlights the need for further investigation to refine and standardise exercise recommendations for this population.

To achieve substantial health benefits, the WHO (Bull et al. 2020) recommends that adults engage in the following weekly exercise regimen: (i) at least two moderate-intensity strengthening activities (i.e., resistance training) targeting the major muscle groups and (ii) at least 150 to 300 min of moderate-intensity aerobic activity, or 75 to 150 min of vigorous-intensity aerobic activity, or an equivalent combination of both moderate- and vigorous-intensity aerobic activities. In light of these guidelines and the significant impact of depression and anxiety on mental health and the potential benefits of exercise as a non-pharmacological intervention, it is critical to examine the effectiveness of resistance training and aerobic exercise. Therefore, does prescribed

aerobic exercise, resistance exercise, or a combination of both improve depressive and/or anxiety symptoms in individuals diagnosed with depression or anxiety?

2 | Methods

2.1 | Equity, Diversity and Inclusion Statement

Our author team consists of four women and two men that are early career, mid-career and senior researchers from different disciplines, including biostatistics, exercise science and nursing. Our analysis was performed on studies from 17 countries in five continents, with the study population comprising a spectrum of ages, genders and demographics. However, we acknowledge that we did not examine youth or older adult populations.

2.2 | Registration of Systematic Review Protocol

The protocol for this systematic review was prospectively registered in February 2019 with the PROSPERO database (registration number: CRD42019119341) and is reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement (Page et al. 2021).

2.3 | Literature Search

A systematic search of six databases (EBSCOhost, Scopus, Web of Science, PsychNET and PubMed) was conducted from the earliest available record to February 24th, 2024. The search strategy included terms for exercise AND mental health conditions of depression and/or anxiety and was limited to an English language version. Additionally, reference lists of included studies and relevant review articles were searched manually.

A PICO strategy was used to help organise the key terms for the literature search strategy (Santos et al. 2007). The subsequent key terms were used for searching: (('exercise' OR 'physical training' OR 'aerobic training' OR 'circuit training' OR 'strength training' OR 'resistance training' OR 'high intensity interval training' OR 'fitness' OR 'muscular strength' OR 'VO₂ *' OR 'muscular power') AND ('anxiety' OR 'depression' OR 'mood disorder*') AND ('antidepressant*' OR 'anti depressant*' OR 'anxiolytic*' OR 'anti anxiety' OR 'antianxiety' OR 'SSRI*' OR 'second generation' OR 'tricyclic' OR 'self efficacy') AND ('randomi* control* trial*')).

2.4 | Eligibility Criteria

All the studies retrieved were assessed against the inclusion and exclusion criteria detailed in Table 1. When the included and excluded age range overlapped, and we were not able to extract data that matched our population inclusion criteria, the study was excluded.

For the purposes of this review, usual care was considered treatment that is typically offered to people with a diagnosis of depression and/or anxiety as part of their routine care and for example

TABLE 1 | Inclusion and exclusion criteria for the systematic review.

	Inclusion	Exclusion
Population	People aged between 18 and 64 years (adults) who have a diagnosis of depression and/or anxiety	People aged younger than 18 years or older than 64 years People without a diagnosis of depression or anxiety
Intervention	Prescribed (aerobic, resistance, or aerobic and resistance [mixed]) exercise alone or prescribed exercise and the same usual care as the control group	Non prescribed exercise (general public health advice or guidelines rather than exercise prescription) Exercises not aerobic or resistance (i.e., Yoga)
Outcome	Primary: Depression and/or anxiety symptoms Secondary: Physical fitness, self-efficacy, exercise adherence, medication	Studies that did not include a depression and/or anxiety symptoms outcome
Study type	Primary research, Peer reviewed studies, Studies published in English, Randomised controlled trial	Non-research publications (conference papers, educational, commentaries, letter) Other reviews, Guidelines, Thesis or grey literature
Language	Studies written in English	Studies not written in English

included the following: medication, cognitive behavioural therapy (CBT), counselling, or health-based education.

2.5 | Study Selection

Once the duplicate studies were removed, the search results were screened independently by four authors (LG, HB, AB and KLE) against the inclusion criteria identified in Table 1. Once no further articles could be excluded by title or abstract, the full text articles were retrieved and independently assessed for eligibility by two authors (LG and AB). Titles and authors were not masked to the researchers conducting the review. Any disagreements arising between authors regarding the eligibility of studies were resolved through discussion with a third author (HB).

2.6 | Data Extraction

Data extraction from the original studies was completed by the authors (HB, LG, JS, LA, AB and KLE). Once the studies met the inclusion criteria, the following data were extracted into an Excel spreadsheet (Microsoft Excel, Microsoft Office, Microsoft, Redmond, Washington, USA): (1) study identification information; (2) participant information; (3) country of study; (4) depression outcomes; (5) anxiety outcomes; (6) length of training study; (7) mode of exercise; (8) exercise programmatic variables; (9) exercise setting and (10) additional outcome measures. Within the exercise programmatic variables, exercise intensity was ascertained according to the guidelines detailed by Norton et al. (Norton et al. 2010).

2.7 | Risk of Bias Assessment

The quality of individual studies was assessed using the Cochrane Risk of Bias tool (Higgins et al. 2011). The quality of

evidence for each meta-analysis was assessed according to the GRADE criteria for systematic reviews (Higgins et al. 2019) using the GRADEpro tool. This was undertaken independently by two authors (JS, LA) and if any discrepancies were identified, a third author (HB) would resolve the discrepancy through discussion.

2.8 | Reporting Quality Assessment

The quality of reporting for the included randomised controlled trials was assessed using the consolidated standards of reporting trials (CONSORT) statement (Butcher et al. 2022). A total of 32 articles (Helgadóttir et al. 2016; Abdelbasset and Alqahtani 2019; Abdollahi et al. 2017; Babyak et al. 2000; Bernard et al. 2015; Blumenthal et al. 2021, 2007, 1999, 2012; Brush et al. 2022; Carneiro et al. 2015; Chalder et al. 2012; Cheung and Lee 2018; Doose et al. 2015; Fernandes et al. 2022; Haller et al. 2018; Haffmans et al. 2006; Levin et al. 2018; Mailey et al. 2010; Majumder et al. 2015; Merom et al. 2008; Mota-Pereira et al. 2011; Oeland et al. 2010; Gordon et al. 2023, 2021; Pfaff et al. 2014; Phongsavan et al. 2008; Pulu et al. 2007; Roy et al. 2018; Verhoeven et al. 2023; Henriksson et al. 2022; La Rocque et al. 2021) were examined based on adherence to CONSORT reporting standards, which was undertaken by two authors (HB and LG).

2.9 | Statistical Analysis

Random effects meta-analyses were constructed using the DerSimonian and Laird model. This assumes that the individual studies represent a random sample from a population of studies with a mean treatment effect about which individual study effects vary. The main meta-analyses were based on the primary outcomes and included the depression scores and anxiety scores. Additional secondary meta-analyses were based on the

secondary outcomes of exercise testing, self-efficacy, exercise programme adherence and attendance.

The random effects model was chosen to reflect recognised clinical and methodological heterogeneity across included studies with respect to all primary and secondary outcomes. For primary and secondary analyses of interval-level numerical measures, standardised mean differences, based on intervention minus control treatment, and associated 95% confidence intervals (CIs), were processed due to variation in the instruments used to record outcomes. However, for the secondary outcome of exercise attendance, we assessed risk ratios based on the ratio of attendance proportion in intervention to control treatments, and associated 95% CIs were measured. The analyses were based on summary statistics of post-test scores (sample size, mean and standard deviation for numerical (interval-level) variables; and number of events and non-events for binary variables).

Clinical improvements in depression and anxiety were represented by reductions in reported scores. Clinical improvements in exercise testing, self-efficacy, exercise programme adherence and attendance were represented by increases in reported scores. The tools used to measure depression and anxiety were collated to determine the most frequently used across the included studies. Therefore, when included studies measured depression and/or anxiety using more than one instrument, we defaulted to only include the instrument that was most frequently used to allow for statistical comparison between studies. Where not reported directly, mean values were estimated from reported medians. Similarly, standard deviations were calculated from reported standard errors or confidence intervals for grouped means; and standard errors, confidence intervals, *t*-values or *p*-values for differences in means were estimated from reported ranges or inter-quartile ranges.

Following recommendations of the Cochrane Collaboration (Higgins et al. 2019), any studies reporting statistics from two or more intervention groups which had been pre-identified as suitable for inclusion in the depression and/or anxiety meta-analyses were combined into a single group, leading to single pairwise comparisons. For example, Helgadóttir et al. (Helgadóttir et al. 2016) had participants training in three different intensity exercise groups (light, moderate and vigorous) which were combined into a single exercise group for the meta-analyses.

Forest plots were conducted for meta-analyses of both primary outcomes, reporting synthesised estimates and associated 95% CIs, and a *Z*-test for the standardised mean difference. Heterogeneity statistics were also reported, including Cochran's *Q* test for heterogeneity, the *I*² statistic (the proportion of variation across studies ascribed to heterogeneity) and the τ^2 statistic (an estimate of between study variance). Sensitivity analyses were conducted on the meta-analyses of both primary outcomes to assess the robustness of the derived estimates. Each of the *k* included studies was omitted in turn, and a meta-analysis was conducted based on the remaining *k*–1 studies. Any study that was suspected of excessive influence (considered to be indicated by the point estimate of the 'omitted' analysis of a study lying outside the confidence interval of the 'combined' analysis) was flagged as an influential study.

Funnel plots were generated for the meta-analyses of both primary outcomes to detect small study effect-related bias, including publication bias and other types of bias which may result from the true treatment effect differing between small and large studies, as indicated by asymmetry in the funnel plot. Funnel plots are displayed in line with meta-analytic convention and following recommendations by Sterne and Egger (Sterne and Egger 2001) with study size, as measured by the standard error of the treatment or intervention effect, plotted (on the vertical axis) against the effect of the treatment in each study.

Synthesised effects from meta-analyses of secondary outcomes were reported in tabulated form. Forest plots, influence plots and funnel plots were not constructed for secondary analyses. Subgroup analyses were conducted based on the type of exercise intervention delivered, comparing aerobic exercise with resistance or mixed methods (aerobic and resistance) with respect to both primary outcomes. Synthesised effects from sub-groups were reported in tabulated form.

3 | Results

3.1 | Search Results

The initial search results yielded 38 358 articles which were downloaded into Endnote (version 9.1, Clarivate Analytics, Philadelphia, PA, USA). A total of 22 448 duplicate articles were then removed, leaving 15 908 studies. After records were excluded, 145 full text articles were retrieved with a further 113 articles excluded at full text screening (reasons outlined in the PRISMA flowchart Figure 1), resulting in a total of 32 articles included in the systematic review (Helgadóttir et al. 2016; Abdelbasset and Alqahtani 2019; Abdollahi et al. 2017; Babyak et al. 2000; Bernard et al. 2015; Blumenthal et al. 2021, 2007, 1999, 2012; Brush et al. 2022; Carneiro et al. 2015; Chalder et al. 2012; Cheung and Lee 2018; Doose et al. 2015; Fernandes et al. 2022; Haller et al. 2018; Haffmans et al. 2006; Levin et al. 2018; Mailey et al. 2010; Majumder et al. 2015; Merom et al. 2008; Mota-Pereira et al. 2011; Oeland et al. 2010; Gordon et al. 2023, 2021; Pfaff et al. 2014; Phongsavan et al. 2008; Pilo et al. 2007; Roy et al. 2018; Verhoeven et al. 2023; Henriksson et al. 2022; La Rocque et al. 2021), with 26 included in the meta-analyses (Helgadóttir et al. 2016; Abdelbasset and Alqahtani 2019; Abdollahi et al. 2017; Bernard et al. 2015; Blumenthal et al. 2021, 2007, 1999, 2012; Brush et al. 2022; Carneiro et al. 2015; Chalder et al. 2012; Cheung and Lee 2018; Doose et al. 2015; Fernandes et al. 2022; Haller et al. 2018; Haffmans et al. 2006; Levin et al. 2018; Mailey et al. 2010; Majumder et al. 2015; Merom et al. 2008; Mota-Pereira et al. 2011; Oeland et al. 2010; Pilo et al. 2007; Roy et al. 2018; Henriksson et al. 2022; La Rocque et al. 2021).

3.2 | Study Characteristics

A summary of participant and study characteristics of the 32 studies included in the systematic review is presented in Table S1. The majority of studies (seven) were conducted in the United States of America (Babyak et al. 2000; Blumenthal et al. 2021, 2007, 1999, 2012; Brush et al. 2022; Levin et al. 2018),

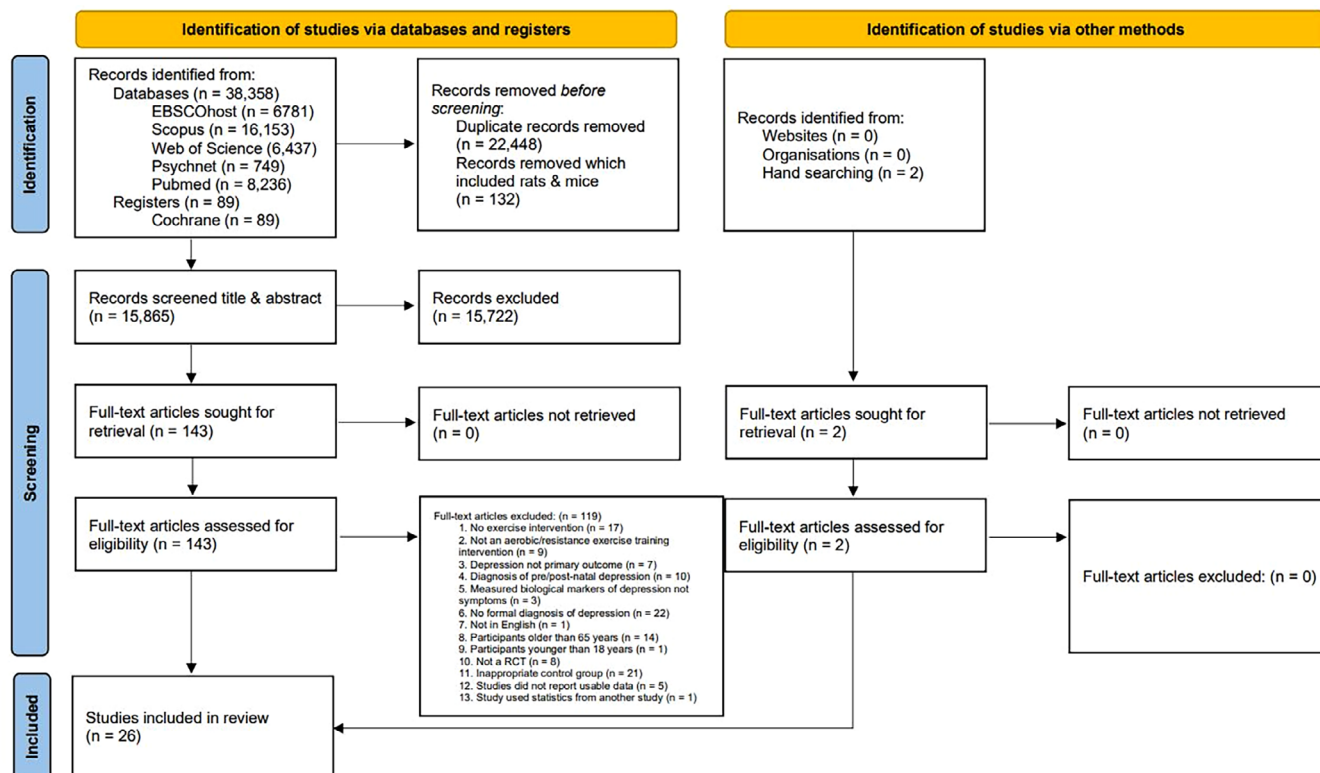


FIGURE 1 | PRISMA flowchart. *n* = number of studies.

four studies in Australia (Levin et al. 2018; Merom et al. 2008; Pfaff et al. 2014; Phongsavan et al. 2008), two studies in Germany (Doose et al. 2015; Haller et al. 2018), India (Majumder et al. 2015; Roy et al. 2018), Ireland (Gordon et al. 2023, 2021), Netherlands (Haffmans et al. 2006; Verhoeven et al. 2023), Portugal (Carneiro et al. 2015; Mota-Pereira et al. 2011) and Sweden (Helgadóttir et al. 2016; Henriksson et al. 2022), with the remaining studies conducted in Brazil (Fernandes et al. 2022), Canada (La Rocque et al. 2021), Denmark (Oeland et al. 2010), France (Bernard et al. 2015), Hong Kong (Cheung and Lee 2018), Iran (Abdollahi et al. 2017), Italy (Pilu et al. 2007), Saudi Arabia (Abdelbasset and Alqahtani 2019) and the United Kingdom (Brush et al. 2022).

Depression was reported in 30 studies; 13 of these studies also reported on anxiety (Bernard et al. 2015; Blumenthal et al. 2021, 1999; Brush et al. 2022; Carneiro et al. 2015; Cheung and Lee 2018; Levin et al. 2018; Mailey et al. 2010; Merom et al. 2008; Oeland et al. 2010; Gordon et al. 2023; Phongsavan et al. 2008; Pilu et al. 2007), and only one study reported on anxiety only (Gordon et al. 2021). Seven different measurement tools were used to measure depression, and four were used for anxiety (Table S2). Twelve studies included various physical fitness outcomes (Bernard et al. 2015; Blumenthal et al. 2007, 1999, 2012; Brush et al. 2022; Carneiro et al. 2015; Doose et al. 2015; Haller et al. 2018; Levin et al. 2018; Oeland et al. 2010; Pfaff et al. 2014; Henriksson et al. 2022) (Table S3). Two studies reported usable data on the 6-min walking test (Bernard et al. 2015; Carneiro et al. 2015). Five studies reported usable data on the VO_2 max test (Blumenthal et al. 1999; Brush et al. 2022; Doose et al. 2015; Haller et al. 2018; Oeland et al. 2010). Usable data was not reported by more than one

study for any other physical fitness outcome. Three studies included outcomes related to self-efficacy (Haller et al. 2018; Haffmans et al. 2006; Mailey et al. 2010) (Table S3), with all reporting usable data. Eleven studies included various outcomes related to exercise adherence (Helgadóttir et al. 2016; Blumenthal et al. 2007, 1999; Carneiro et al. 2015; Chalder et al. 2012; Doose et al. 2015; Mailey et al. 2010; Merom et al. 2008; Mota-Pereira et al. 2011; Phongsavan et al. 2008; Gordon et al. 2021) (Table S3), but usable data was not reported by more than one of these studies for any outcome related to adherence. Fifteen studies included outcomes related to attendance at sessions (Helgadóttir et al. 2016; Bernard et al. 2015; Blumenthal et al. 2007, 1999, 2012; Carneiro et al. 2015; Cheung and Lee 2018; Doose et al. 2015; Haller et al. 2018; Levin et al. 2018; Majumder et al. 2015; Phongsavan et al. 2008; Gordon et al. 2021; Henriksson et al. 2022; La Rocque et al. 2021) (Table S3). Meta-analysis data included three studies with usable data (Chalder et al. 2012; Majumder et al. 2015; Phongsavan et al. 2008). A total of 21 studies prescribed aerobic exercise alone (Helgadóttir et al. 2016; Abdelbasset and Alqahtani 2019; Abdollahi et al. 2017; Babyak et al. 2000; Bernard et al. 2015; Blumenthal et al. 2021, 2007, 1999, 2012; Chalder et al. 2012; Cheung and Lee 2018; Doose et al. 2015; Haffmans et al. 2006; Mailey et al. 2010; Majumder et al. 2015; Merom et al. 2008; Mota-Pereira et al. 2011; Phongsavan et al. 2008; Roy et al. 2018; Verhoeven et al. 2023; La Rocque et al. 2021). Three studies prescribed resistance exercise alone (Gordon et al. 2023, 2021; Pilu et al. 2007), and six studies prescribed combined aerobic and resistance (mixed) exercise (Helgadóttir et al. 2016; Haller et al. 2018; Levin et al. 2018; Oeland et al. 2010; Pfaff et al. 2014; Henriksson et al. 2022). Exercise intensities varied across the studies (Riebe et al. 2018),

Studies	Sequence generation	Allocation concealment	Blinding of participants and researchers	Blinding of outcome assessment	Incomplete outcome data	Selective reporting	Other sources of bias	Summary assessment outcome (across domains) within study
Abdelbasset, et al 2019	✗	1✗	1	2	3	3	2	2
Abdollahi et al 2017	✓	3	3	2	1	2	3	2
Babyak et al 2000	✗	1✗	1	2	2	1	2	2
Bernard et al 2015	✓	3	3	2	1	3	3	3
Blumenthal et al 2020	✗	1✗	1	2	2	2	2	2
Blumenthal et al 2007	✓	3	3	2	3	3	3	3
Blumenthal et al 1999	✗	1✗	1	2	1	3	3	2
Blumenthal et al 2012	✓	3	3	1	3	3	3	3
Carneiro et al 2015	✓	3	3	2	2	2	3	2
Chalder et al 2012	✓	3	3	2	2	3	3	3
Cheung et al 2018	✓	3	3	2	3	3	3	3
Doose et al 2015	✗	1✗	1	2	2	3	3	2
Gordon et al 2021	✗	1✗	1	2	2	3	3	1
Haffmans et al 2006	✗	1✗	1	2	2	2	3	2
Haller et al 2018	✓	3	1	2	3	1	3	1
Helgadóttir et al 2016	✓	3	3	2	3	3	3	3
Henriksson et al 2022	✓	3	3	2	3	2	3	3
La Roque et al 2021	✓	3	3	2	3	3	3	3
Levin et al 2018	✗	1✗	1	2	2	2	3	2
Mailey et al 2010	✗	1✗	1	2	2	2	3	2
Majumder et al 2015	✗	1✗	1	2	2	3	2	2
Meron et al 2008	✗	1✗	1	2	2	3	3	2
Mota-Pereira et al 2011	✗	1✗	1	2	2	1	2	2
Oeland et al 2010	✗	1	2	2	2	2	3	2
Pfaff et al 2014	✓	3	3	1	3	3	3	3
Phongsavan et al 2008	✗	1✗	1	2	2	1	2	2
Pilu et al 2007	✗	1✗	1	2	2	1	2	2
Roy et al 2018	✗	1✗	1	2	2	3	3	3

FIGURE 2 | Risk of bias assessment for all included studies. 3 = Low risk of bias; 2 = High risk of bias; 1 = Unclear.

which included light-to-moderate (Chalder et al. 2012; Mailey et al. 2010; Roy et al. 2018; Gordon et al. 2021), light-to-moderate-to-vigorous (Helgadóttir et al. 2016; Henriksson et al. 2022; La Rocque et al. 2021), moderate (Abdelbasset and Alqahtani 2019; Abdollahi et al. 2017; Cheung and Lee 2018; Haller et al. 2018; Levin et al. 2018; Merom et al. 2008; Mota-Pereira et al. 2011; Oeland et al. 2010; Gordon et al. 2023; Phongsavan et al. 2008; Pilu et al. 2007), moderate-to-vigorous (Bernard et al. 2015; Carneiro et al. 2015; Doose et al. 2015; Pfaff et al. 2014; Verhoeven et al. 2023) and vigorous (Babyak et al. 2000; Blumenthal et al. 2021, 2007, 1999, 2012; Haffmans et al. 2006; Majumder et al. 2015).

3.3 | Risk of Bias Assessment

The quality assessment of the 32 studies included was outlined by the Cochrane Effective Practice and Organisation of Care risk-of-bias tool for randomised controlled trials (Higgins et al. 2011). Eleven of the included studies (34%) were considered to have a low risk of bias (Helgadóttir et al. 2016; Bernard et al. 2015; Blumenthal et al. 2021, 1999; Brush et al. 2022; Carneiro et al. 2015; Merom et al. 2008; Gordon et al. 2023; Phongsavan et al. 2008; Pilu et al. 2007), while 19 of the studies (59%) were considered to have a high risk of bias (Sterne and Egger 2001; Abdelbasset and Alqahtani 2019; Abdollahi et al. 2017; Bernard et al. 2015; Blumenthal et al. 2007, 2012; Chalder et al. 2012; Doose et al. 2015; Fernandes et al. 2022;

Haller et al. 2018; Haffmans et al. 2006; Levin et al. 2018; Mailey et al. 2010; Majumder et al. 2015; Mota-Pereira et al. 2011; Oeland et al. 2010), and two (6%) were unclear (Cheung and Lee 2018; Pfaff et al. 2014). Figure 2 shows the risk of bias assessment for all included studies. The main risk of bias was blinding of participants and researchers (performance bias), with all studies considered high or uncertain risk. The second was blinding of outcome assessor, with 69% of the studies considered high or uncertain risk.

3.4 | Reporting Quality Assessment

The average adherence of the 32 studies according to the 25 checklist items of the CONSORT statement was 67%, ranging from 38% to 84%. Thirteen studies (41%) had high reporting quality ($\geq 75\%$ adherence) (Helgadóttir et al. 2016; Blumenthal et al. 2007; Brush et al. 2022; Carneiro et al. 2015; Chalder et al. 2012; Cheung and Lee 2018; Fernandes et al. 2022; Haller et al. 2018; Gordon et al. 2023; Pfaff et al. 2014; Verhoeven et al. 2023; Henriksson et al. 2022; La Rocque et al. 2021), with a further 15 studies (47%) reporting adequate quality (between 50% and 75% adherence) (Abdelbasset and Alqahtani 2019; Abdollahi et al. 2017; Bernard et al. 2015; Blumenthal et al. 2021, 1999, 2012; Doose et al. 2015; Levin et al. 2018; Mailey et al. 2010; Merom et al. 2008; Mota-Pereira et al. 2011; Oeland et al. 2010; Phongsavan et al. 2008; Roy et al. 2018; Gordon et al. 2021). All studies reported the

abstract, introduction and discussion sections. Most studies reported appropriate information pertaining to the interventions (94% adherence) and statistical analyses (97% adherence). However, key methodological aspects such as sample size calculations (28% adherence), randomised allocation sequence (44% adherence) and blinding (53% adherence) were frequently underreported.

3.5 | Depression Outcome

Thirty studies including the outcome of depression were assessed for meta-analyses (Helgadóttir et al. 2016; Abdelbasset and Alqahtani 2019; Abdollahi et al. 2017; Babyak et al. 2000; Bernard et al. 2015; Blumenthal et al. 2021, 2007, 1999, 2012; Brush et al. 2022; Carneiro et al. 2015; Chalder et al. 2012; Cheung and Lee 2018; Dose et al. 2015; Haller et al. 2018; Haffmans et al. 2006; Levin et al. 2018; Mailey et al. 2010; Majumder et al. 2015; Merom et al. 2008; Mota-Pereira et al. 2011; Oeland et al. 2010; Gordon et al. 2023; Pfaff et al. 2014; Phongsavan et al. 2008; Pilu et al. 2007; Roy et al. 2018; Henriksson et al. 2022; La Rocque et al. 2021). One study did not report an independent piece of research but referred to statistics reported in another study (Abdollahi et al. 2017). Four further studies did not report usable data (Brush et al. 2022; Fernandes et al. 2022; Pfaff et al. 2014; Phongsavan et al. 2008). Usable post-test or change statistics in one or more intervention groups and a control group were obtained from the remaining 26 studies (Helgadóttir et al. 2016; Abdelbasset and Alqahtani 2019; Abdollahi et al. 2017; Bernard et al. 2015; Blumenthal et al. 2021, 2007, 1999, 2012; Carneiro et al. 2015; Chalder et al. 2012; Haller et al. 2018; Haffmans et al. 2006; Levin et al. 2018; Mailey et al. 2010; Majumder et al. 2015; Merom et al. 2008; Mota-Pereira et al. 2011; Oeland et al. 2010; Gordon et al. 2023; Pilu et al. 2007; Roy et al. 2018; Verhoeven et al. 2023; Henriksson et al. 2022; La Rocque et al. 2021). Eighteen studies were included based on a pairwise comparison between a control treatment and a single reported intervention group (Abdelbasset and Alqahtani 2019; Abdollahi et al. 2017; Babyak et al. 2000; Bernard et al. 2015; Blumenthal et al. 2012; Carneiro et al. 2015; Chalder et al. 2012; Cheung and Lee 2018; Dose et al. 2015; Haller et al. 2018; Majumder et al. 2015; Merom et al. 2008; Mota-Pereira et al. 2011; Oeland et al. 2010; Gordon et al. 2023; Pilu et al. 2007; Roy et al. 2018; Verhoeven et al. 2023). Eight studies reported statistics from two or three exercise intervention groups which had been pre-identified as suitable for inclusion in the meta-analysis (Helgadóttir et al. 2016; Blumenthal et al. 2021, 2007, 1999; Haffmans et al. 2006; Levin et al. 2018; Henriksson et al. 2022; La Rocque et al. 2021); all such pairs of intervention groups were combined, again leading to single pairwise comparisons.

As seen in Figure 3, 13 studies reported a statistically significant effect (at the 5% significance level) in favour of intervention methods on depression outcomes (Helgadóttir et al. 2016; Abdelbasset and Alqahtani 2019; Abdollahi et al. 2017; Dose et al. 2015; Levin et al. 2018; Majumder et al. 2015; Merom et al. 2008; Mota-Pereira et al. 2011; Oeland et al. 2010; Gordon et al. 2023; Pilu et al. 2007; Verhoeven et al. 2023; La Rocque et al. 2021). A further 11 studies reported a non-significant

effect in favour of intervention methods on depression outcomes (Blumenthal et al. 2021, 2007, 2012; Carneiro et al. 2015; Chalder et al. 2012; Cheung and Lee 2018; Haller et al. 2018; Haffmans et al. 2006; Mailey et al. 2010; Roy et al. 2018; Henriksson et al. 2022). No studies reported a statistically significant effect (at the 5% significance level) in favour of control treatment on depression outcomes. Two studies reported a non-significant effect in favour of control treatment on depression outcomes (Bernard et al. 2015; Blumenthal et al. 1999). Individual estimates for the standardised mean difference ranged from -6.32 (95% CI: -7.85 to -4.79) (favouring intervention methods), reported by Merom et al. (Merom et al. 2008) to 0.18 (95% CI: -0.16 to 0.52) (favouring control treatment), reported by Blumenthal et al. (Blumenthal et al. 1999).

A meta-analysis on the outcome of depression revealed that a synthesised estimate of the standardised mean difference in depression scores from intervention treatment methods and control treatment methods was -0.97 (95% CI -1.28 to -0.66); i.e., favouring intervention methods. A Z-test of the standardised mean effect revealed strong evidence (at the 5% significance level) for a non-zero effect ($Z = 6.10$; $p < 0.001$). Cochran's χ^2 test for heterogeneity revealed strong evidence (at the 5% significance level) for statistical heterogeneity ($\chi^2_{(25)} = 253.5$; $p < 0.001$). The I^2 statistic was 90.1%, indicating high levels of heterogeneity (high proportion of variation across studies ascribed to heterogeneity). The τ^2 statistic (an estimate of between study variance) was revealed to be 0.531. The data is summarised in a forest plot (Figure 3).

A sensitivity analysis revealed no individual study to be exerting excessive influence on the meta-analysis, with all point estimates of the omitted analyses lying within the 95% CI associated with the estimate of the combined analysis. Estimates and associated CIs are plotted on an influence plot (Figure 4).

The funnel plot for the depression outcome (Figure 5) displayed some evidence for small-study effects, with some included studies lying outside pseudo-95% confidence limits.

3.6 | Anxiety Outcome

Fifteen studies including the outcome of anxiety were assessed for meta-analyses (Bernard et al. 2015; Blumenthal et al. 2021, 1999; Brush et al. 2022; Carneiro et al. 2015; Cheung and Lee 2018; Levin et al. 2018; Mailey et al. 2010; Merom et al. 2008; Oeland et al. 2010; Gordon et al. 2023, 2021; Phongsavan et al. 2008; Verhoeven et al. 2023; Henriksson et al. 2022). Three studies did not report usable data (Brush et al. 2022; Oeland et al. 2010; Phongsavan et al. 2008). Usable statistics in one or more intervention groups and a control group were obtained from the remaining 12 studies (Bernard et al. 2015; Blumenthal et al. 2021, 1999; Carneiro et al. 2015; Cheung and Lee 2018; Levin et al. 2018; Mailey et al. 2010; Merom et al. 2008; Mota-Pereira et al. 2011; Verhoeven et al. 2023; Gordon et al. 2021; Henriksson et al. 2022). Eight studies were included based on a pairwise comparison between a control treatment and a single reported intervention group (Bernard et al. 2015; Carneiro et al. 2015; Cheung and Lee 2018; Mailey et al. 2010; Merom et al. 2008; Gordon

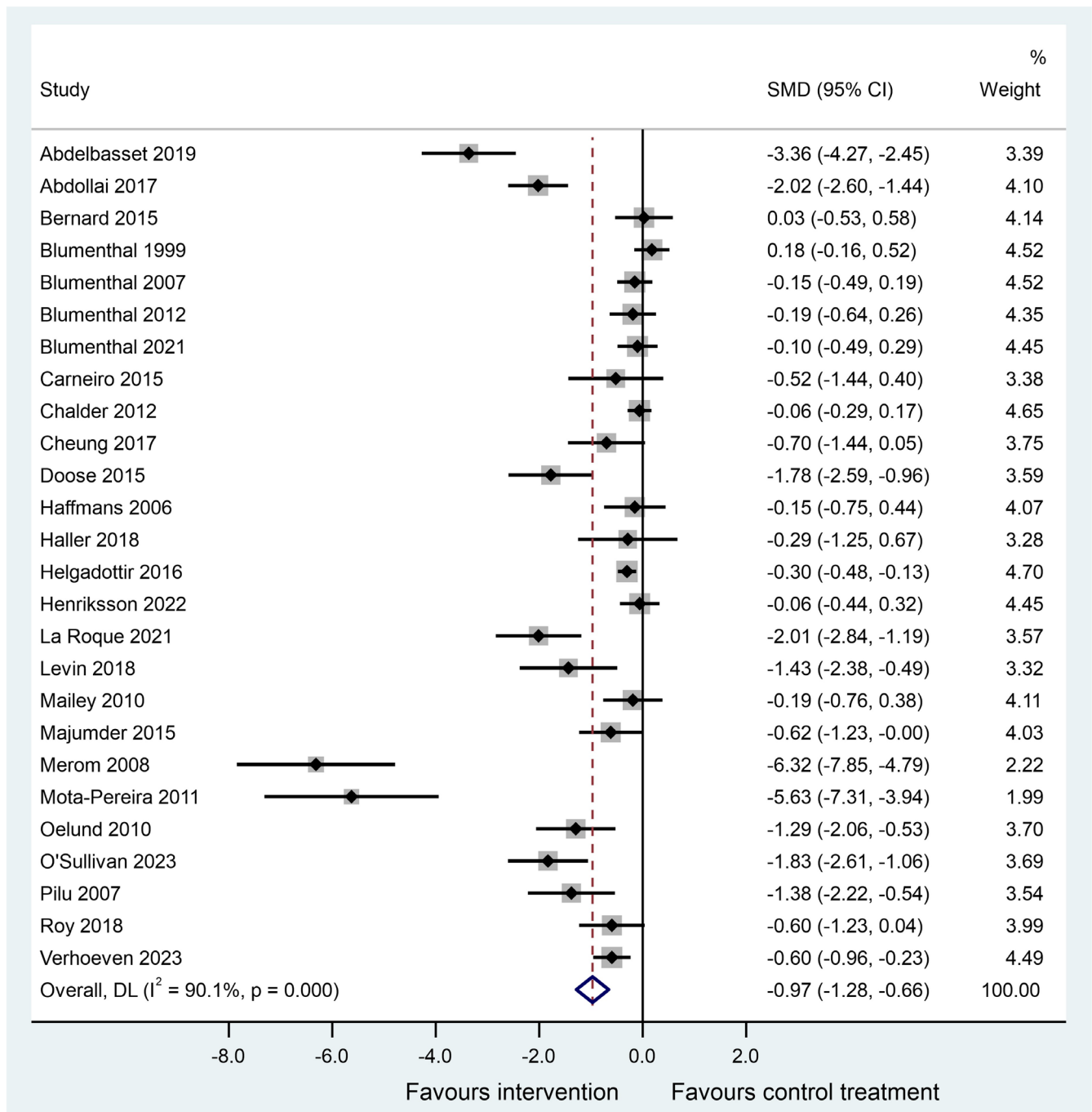


FIGURE 3 | Forest plot for meta-analysis of depression outcome.

et al. 2023, 2021; Verhoeven et al. 2023). Four studies reported statistics from two intervention groups which had been pre-identified as suitable for inclusion in the meta-analysis (Blumenthal et al. 2021, 1999; Levin et al. 2018; Henriksson et al. 2022); all such intervention groups were combined, again leading to single pairwise comparisons.

Two studies reported a statistically significant effect (at the 5% significance level) in favour of intervention methods on anxiety outcomes (Merom et al. 2008; Gordon et al. 2021). Eight studies reported a non-significant effect in favour of intervention methods on anxiety outcomes (Blumenthal et al. 2021, 1999; Carneiro et al. 2015; Levin et al. 2018; Mailey et al. 2010;

Gordon et al. 2023; Verhoeven et al. 2023; Henriksson et al. 2022). Two studies reported a non-significant effect in favour of control treatment on anxiety outcomes (Bernard et al. 2015; Cheung and Lee 2018). Individual estimates for the standardised mean difference ranged from -1.94 (95% CI: -2.36 to -1.52) (favouring intervention methods), reported by Verhoeven et al. (Verhoeven et al. 2023), to +0.12 (95% CI: -0.58 to 0.81) (favouring control treatment), reported by Cheung et al. (Cheung and Lee 2018).

A meta-analysis on the outcome of anxiety revealed that a synthesised estimate of the standardised mean difference in anxiety scores from intervention treatment methods and control

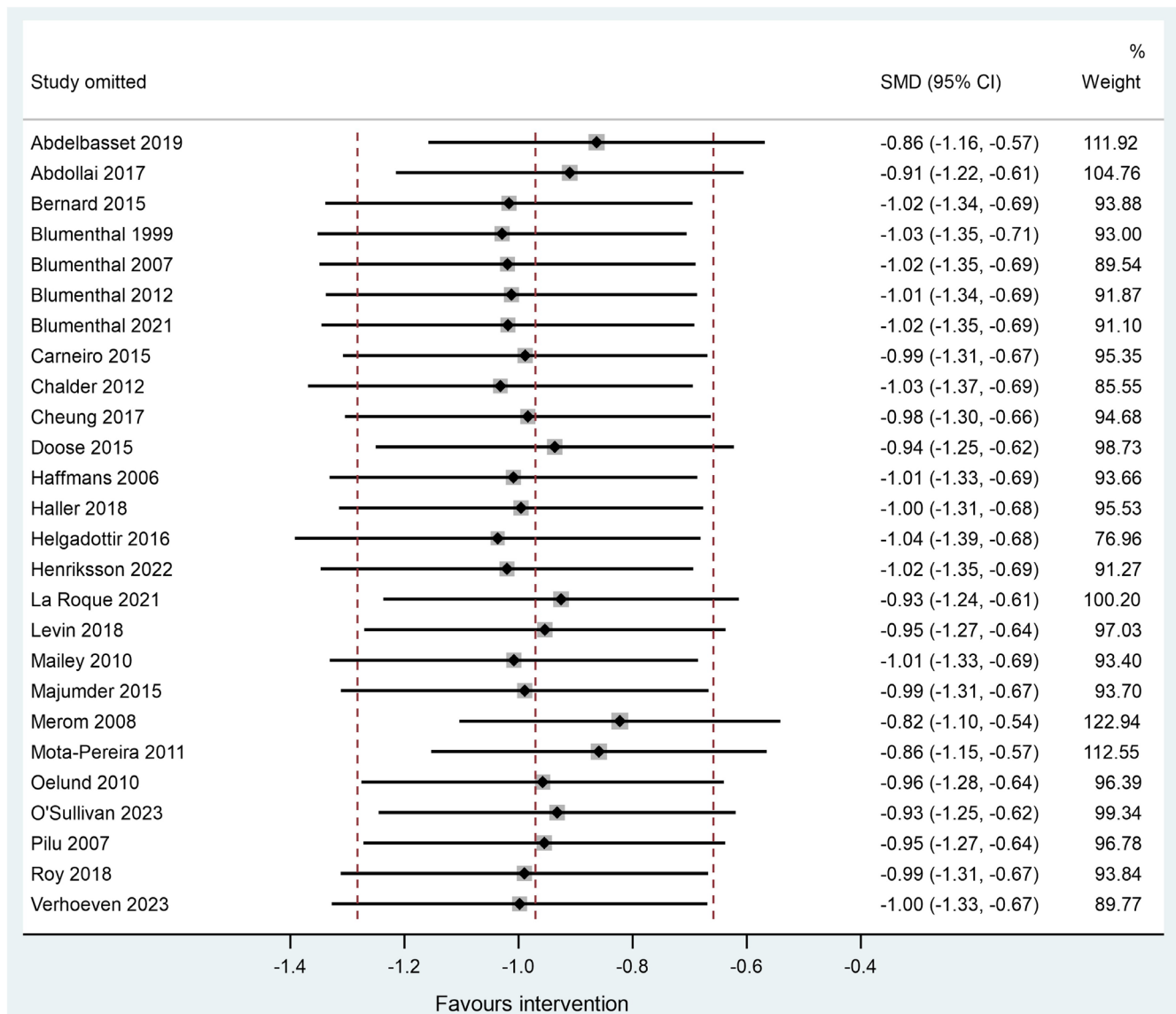


FIGURE 4 | Influence plot for meta-analysis of depression outcome.

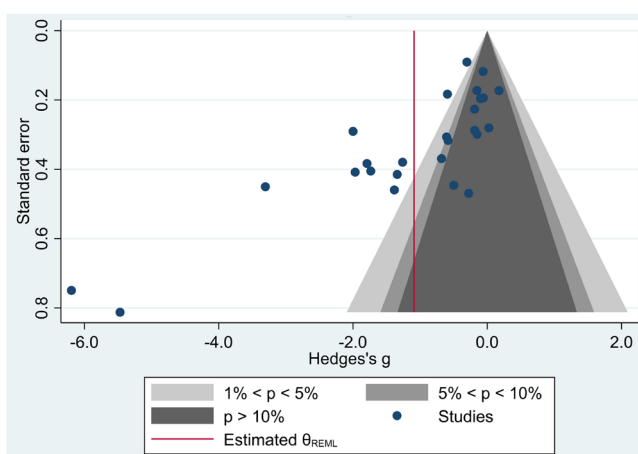


FIGURE 5 | Funnel plot for meta-analysis of depression outcome (with pseudo-95% confidence limits).

treatment methods was -0.66 (95% CI -1.09 to -0.23); i.e., a significant effect favouring intervention methods. A Z-test of the standardised mean effect revealed no evidence (at the 5% significance level) for a non-zero effect ($Z = 3.000$; $p = 0.003$). Cochran's χ^2 test for heterogeneity revealed strong evidence (at the 5% significance level) for statistical heterogeneity ($\chi^2_{(11)} = 77.5$; $p = 0.005$). The I^2 statistic was 85.8%, indicating high levels of heterogeneity (high proportion of variation across studies ascribed to heterogeneity). The τ^2 statistic (an estimate of between study variance) was revealed to be 0.468. The data is summarised in a forest plot (Figure 6).

A sensitivity analysis revealed no individual study to be exerting excessive influence on the analysis, with all point estimates of the omitted analyses lying within the 95% confidence interval associated with the estimate of the combined analysis. Estimates and associated confidence intervals are plotted on an influence plot (Figure 7).

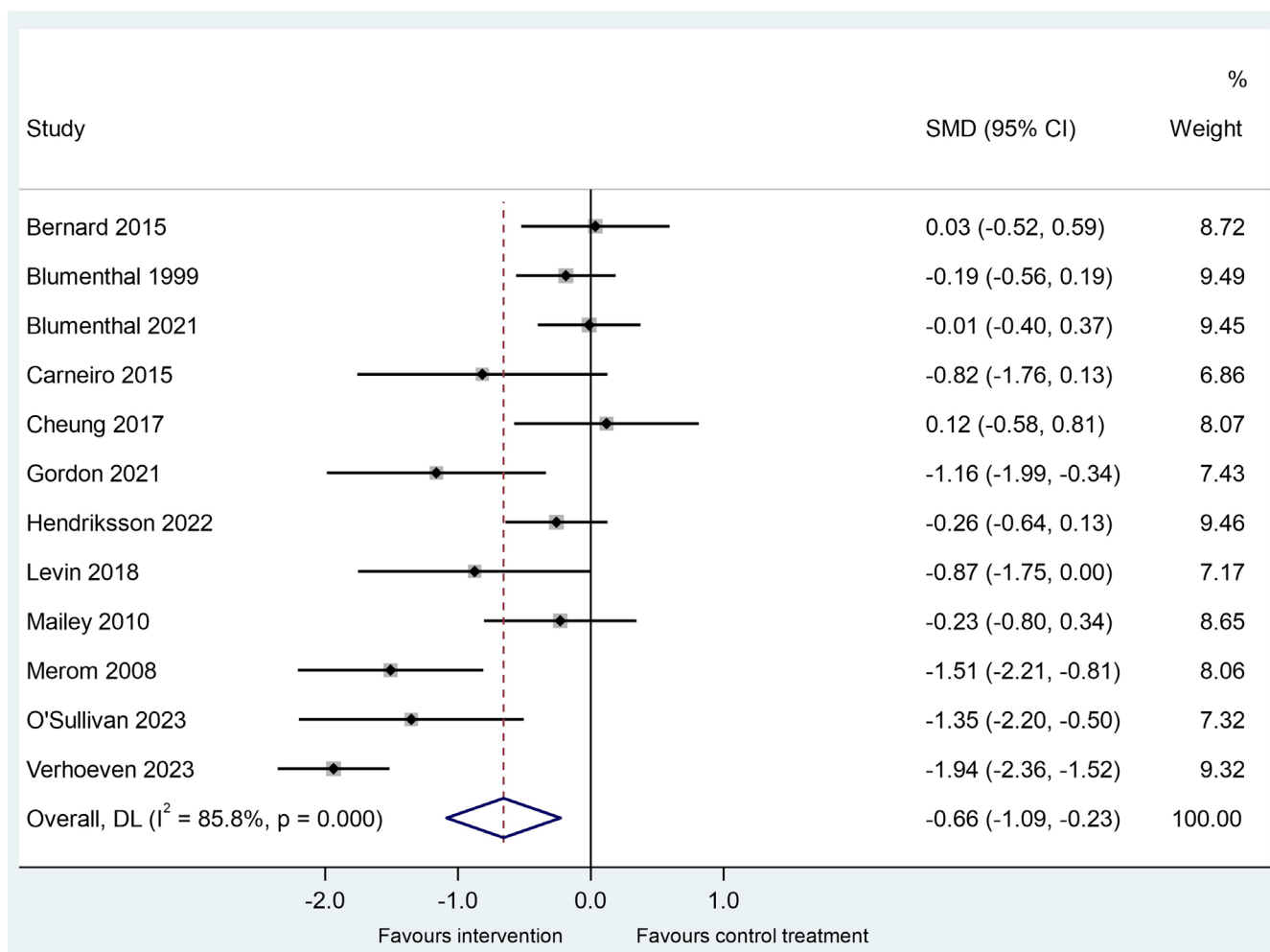


FIGURE 6 | Forest plot for meta-analysis of anxiety outcome.

The funnel plot (Figure 8) for the anxiety outcome displayed some evidence for small-study effects, with some of the included studies lying outside pseudo-95% confidence limits.

3.7 | Secondary Analyses

Secondary meta-analyses were conducted on the 6-min walking test (Bernard et al. 2015; Carneiro et al. 2015) and VO_2 max test physical fitness outcomes (Blumenthal et al. 1999; Doose et al. 2015; Haller et al. 2018; Oeland et al. 2010; Verhoeven et al. 2023); on the self-efficacy outcome (Haller et al. 2018; Haffmans et al. 2006; Mailey et al. 2010), and on the attendance outcome (Chalder et al. 2012; Majumder et al. 2015; Phongsavan et al. 2008). The parameters of these meta-analyses are summarised in Table 2.

3.8 | Subgroup Analyses

Subgroup analyses conducted on exercise mode revealed that interventions were significantly associated (at the 5% significance level) with changes in depression scores when delivered in either the aerobic mode, resistance mode, or mixed mode; and interventions were significantly associated with changes in anxiety

scores when delivered in resistance/mixed mode, but not aerobic mode. No significant between-subgroup effects were revealed (Tables 3 and 4).

4 | Discussion

The main findings from this systematic review with meta-analysis are that exercise-based interventions are beneficial for improving symptoms of depression and anxiety in people with a clinical diagnosis of depression and/or anxiety. These beneficial effects of exercise were not influenced by the mode of exercise delivery on depressive symptoms, with some influence on anxiety symptoms. Therefore, aerobic, resistance, or a mixture of aerobic and resistance (mixed) modes of exercise can be prescribed to individuals with depression to improve their depressive symptoms, or for those with anxiety, resistance or aerobic and resistance (mixed) modes. However, some caution when interpreting the anxiety data is warranted given the smaller number of studies in this analysis.

The large beneficial effect ($SMD = 0.97$) of exercise for improving depressive symptoms can be observed after analysis of 26 studies; 50% of these studies significantly favoured the exercise intervention in the treatment of depression (Figure 3).

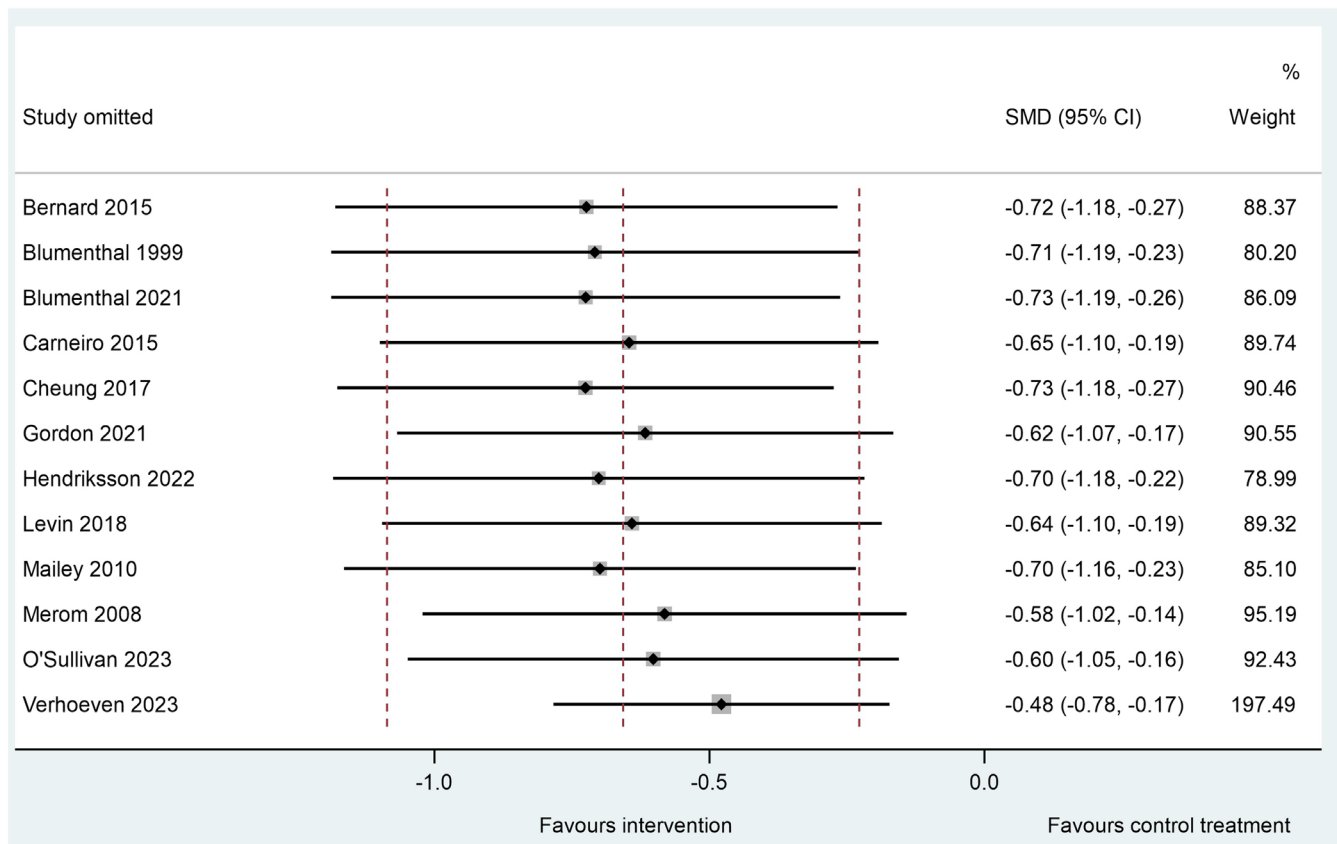


FIGURE 7 | Influence plot for meta-analysis of anxiety outcome.

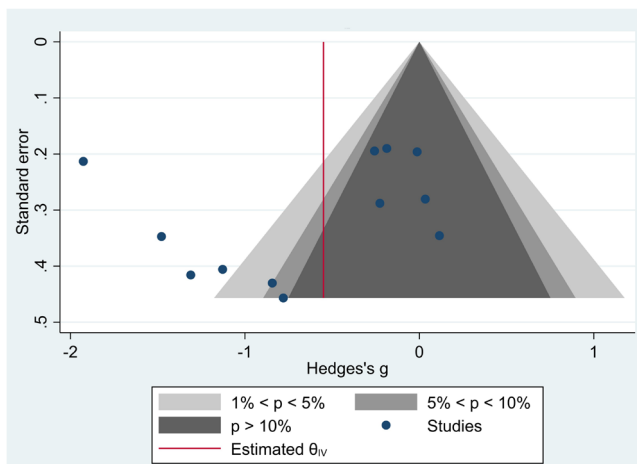


FIGURE 8 | Funnel plot for meta-analysis of anxiety outcome (with pseudo-95% confidence limits).

This significant beneficial exercise effect occurred in aerobic ($n=9$) and resistance or mixed ($n=4$) modes of exercise delivery (Figure 3), with no between-group effect, indicating the mode of exercise prescription did not influence the beneficial effect. These findings are similar to those of Cooney et al. (Cooney et al. 2013) who found exercise had a moderately beneficial effect on depression symptoms compared to the control group ($SMD = -0.62, -0.81$ to -0.42). Despite the benefits of exercise to ameliorate depressive symptoms, it is often underused and/or undervalued as part of standard treatment models for people with mental illnesses such as depression (Kleemann et al. 2020;

McKeon et al. 2022). Some of these barriers to exercise prescription may relate to the mode of exercise prescribed, access to appropriately trained personnel such as exercise scientists/therapists or exercise physiologists (Korman et al. 2020) as well as a lack of understanding or confidence by health professionals related to appropriate exercise recommendations.

There is also evidence that exercise-based interventions are moderately beneficial for improving symptoms of anxiety ($SMD = 0.66$), although the number of studies used for analysis was limited. From the 12 studies examining the effects of exercise on anxiety symptoms, eight were favourable towards exercise, yet only 4 were statistically significant. Notably, of the 12 studies, only one study (which was favourable towards exercise) met the WHO criteria (Bull et al. 2020) for the weekly minimum physical activity levels. Therefore, it could be hypothesised that if the exercise prescribed in the remaining seven studies at least met the minimum physical activity guidelines for intensity and volume, then perhaps the magnitude of mental health benefits from exercise could have been strengthened (Pearce et al. 2022).

Despite the findings from this review favouring the use of exercise to reduce symptoms of depression and anxiety, only three studies, from 30 studies included in this review, met the WHO weekly physical activity guidelines (volume and intensity) for both aerobic and resistance exercise. Fifteen studies had sufficient aerobic exercise, and seven had sufficient resistance exercise. This suggests that health professionals should promote increasing exercise volume, above being sedentary, to improve mental health, even if the volume and intensity do not meet the

TABLE 2 | Secondary meta-analysis parameters.

Outcome	Estimate (95% CI) ^a	Heterogeneity	Z-test for effect
Physical fitness—6-min walking test (<i>n</i> = 2)	3.39 (2.48, 4.30) ^a <i>Favours intervention</i>	<i>I</i> ² = 0.0%	<i>Z</i> = 7.31; <i>p</i> < 0.001
Physical fitness—VO ₂ max test (<i>n</i> = 5)	0.40 (−0.35, 1.10) ^a <i>Favours intervention</i>	<i>I</i> ² = 88.7%	<i>Z</i> = 1.02; <i>p</i> = 0.306
Self-efficacy (<i>n</i> = 3)	0.35 (−0.37, 1.08) ^a <i>Favours intervention</i>	<i>I</i> ² = 68.4%	<i>Z</i> = 0.95; <i>p</i> = 0.341
Attendance (<i>n</i> = 3)	1.11 (0.93, 1.32) ^b <i>Favours intervention</i>	<i>I</i> ² = 35.9%	<i>Z</i> = 1.19; <i>p</i> = 0.235

^aStandardised mean difference.^bRisk ratio.**TABLE 3** | Subgroup analysis of effect estimates of exercise interventions on depression scores.

Subgroup	Estimate (95% CI) ^a	Heterogeneity	Z-test for effect
Exercise mode			
Aerobic (<i>n</i> = 18)	−1.60 (−2.22, −0.98) <i>Favours intervention</i>	<i>I</i> ² = 92.2%	<i>Z</i> = 4.74; <i>p</i> < 0.001
Resistance or mixed (<i>n</i> = 6)	−0.89 (−1.36, −0.42) <i>Favours intervention</i>	<i>I</i> ² = 79.6%	<i>Z</i> = 3.72; <i>p</i> < 0.001
Between-groups effect			<i>Z</i> = 0.538; <i>p</i> = 0.591

^aStandardised mean difference.**TABLE 4** | Subgroup analysis of effect estimates of exercise interventions on anxiety scores.

Subgroup	Estimate (95% CI) ^a	Heterogeneity	Z-test for effect
Exercise mode			
Aerobic (<i>n</i> = 8)	−0.56 (−1.15, −0.03) <i>Favours intervention</i>	<i>I</i> ² = 89.9%	<i>Z</i> = 1.88; <i>p</i> = 0.090
Resistance or mixed (<i>n</i> = 4)	−0.83 (−1.42, −0.25) <i>Favours intervention</i>	<i>I</i> ² = 63.5%	<i>Z</i> = 2.79; <i>p</i> = 0.005
Between groups effect			<i>Z</i> = 0.408; <i>p</i> = 0.683

^aStandardised mean difference.

physical activity guidelines. This is in accordance with a recent review establishing that significant mental health benefits can be achieved from performing physical activity levels below the WHO recommendations (Pearce et al. 2022). It also suggests that perhaps initial training and education or professional development opportunities for health professionals working in mental health may benefit from a better understanding of the physical activity guidelines and WHO recommendations.

There were no studies that excessively influenced the outcomes of the primary analyses (Figures 4 and 7). However, it must be noted that many of the included studies had a relatively small sample size, with 18 studies conducted with 50 participants or less, and seven of these conducted on 30 participants or less, not uncommon in exercise-based intervention studies (Abt et al. 2020). Despite all included studies being randomised, some substantive baseline imbalances in both depression and

anxiety scores were observed. An additional challenge with the analysis in this review included some studies that reported medians and inter-quartile ranges rather than means and standard deviations, which were estimated using standard methods for analysis. And finally, some studies did not report exact values but presented data in graphical form only that required manual extraction using a high-resolution scanner. The difficulties we identified are not uncommon in exercise and sport science research with calls encouraging an improvement in the quality of methodological rigour and statistical analysis (Sainani and Chamari 2022).

The effects of aerobic and resistance exercise on depression and anxiety often vary across different countries and regions due to cultural, socioeconomic and healthcare system differences (de la Arias- Torre et al. 2021). Populations with better access to exercise facilities and greater awareness of the mental health

benefits of physical activity might be expected to experience more substantial reductions in depression and anxiety symptoms compared to those facing limited resources, infrastructure challenges, or cultural barriers to engaging in structured exercise programs (Salmi et al. 2023). However, our review revealed mixed results, underscoring the difficulty of making direct comparisons due to variations in study design, sample characteristics and intervention protocols. For example, studies conducted in Australia (Levin et al. 2018; Merom et al. 2008) consistently demonstrated the beneficial effects of exercise in reducing depressive symptoms. In contrast, research from the USA (Blumenthal et al. 2021, 2007, 1999, 2012) found little to no benefit from 16 weeks of vigorous intensity walking and running in improving depressive symptoms. Studies from Saudi Arabia (Abdelbasset and Alqahtani 2019) and Iran (Abdollahi et al. 2017), however, reported significant benefits from 12 weeks of moderate intensity walking for reducing depressive symptoms. Similarly, studies from India (Majumder et al. 2015; Roy et al. 2018) showed that exercise had a moderate effect on reducing depression. These contrasting findings highlight the complex nature of exercise interventions and the need for further investigation into how regional and contextual factors influence outcomes.

When assessing the quality of the randomised controlled trials included in this review, 67% met the 25 checklist items outlined in the CONSORT statement. This adherence rate is comparable to other meta-analyses evaluating the quality and compliance of randomised controlled trials in cancer (68%) (Süt et al. 2008), ischaemic stroke (68%) (Kodounis et al. 2020) and multiple sclerosis research (68%) (Rikos et al. 2016), while being notably higher than in diabetic retinopathy research (45%) (Mozetic et al. 2019). Key methodological aspects, such as sample size calculations, were often underreported, with only 28% adherence. Recruiting participants for randomised controlled trials is inherently challenging, with barriers such as strict eligibility criteria, reluctance towards randomisation, healthcare provider limitations and logistical burdens related to time and financial commitment. Consequently, many studies recruit as many participants as possible within a set timeframe, rather than reporting their sample size calculations. However, this approach can often result in underpowering their research. Researchers should be strongly encouraged to adhere to the CONSORT statement when conducting randomised controlled trials.

Meta-analyses have limitations (LeLorier et al. 1997) and inherit any limitations of the individual studies that are included within them and the potential bias of selection of those included studies. However, the use of broad terms in the search strategy for both exercise and the outcomes of depression and anxiety limited the number of missing studies, evident from the large volume of returned studies. Despite our inclusion criteria being randomised controlled studies, the quality of reporting was varied. Many studies sparsely reported methodological information pertaining to the exercise prescription that would enable replication (Schulz et al. 2010). This makes it challenging for future reviews to broaden their research questions to determine the optimum frequency, duration, intensity, nature of supervision, mode of exercise and cost effectiveness of the exercise. Furthermore, the meta-analyses were challenging since there was substantial diversity in intervention prescription, including exercise intensity

(low, moderate, vigorous, combined) exercise mode (swimming, walking, running, resistance etc.), session delivery (individual, group, combined), length of training (2 weeks, 12 months, etc.) supervision models (supervised, self-reported, mixed); hence random effects meta-analyses were judged to be required in all cases. Providing information on session attendance, which was limited to three studies in this review, and adherence to the exercise prescription as well as medication adherence, which was not always provided, would further enhance the ability to translate the data for clinical use.

A wide range of instruments have been used to measure depression and anxiety, which makes direct comparisons difficult, with the need to conduct all analyses based on standardised measures. Despite this, all measures used in the analyses were globally recognised valid and reliable tools to measure symptoms of depression and anxiety. While a standardised measurement tool may have provided more opportunity for direct comparison, this is unlikely to occur given the broad range of clinically accepted tools available and utilised internationally.

5 | Conclusions

In conclusion, despite the benefits of exercise to ameliorate depressive symptoms, it is often an underused and/or undervalued part of standard treatment models for people with mental illnesses such as depression and should be considered as an isolated or adjunctive treatment option. Future research should consider improving the quality of the reporting of the exercise prescription and adhering more closely to the CONSORT statement of reporting of trials.

6 | Relevance for Clinical Practice

Aerobic exercise is largely beneficial for improving symptoms of depression, and moderately beneficial for reducing anxiety symptoms. Resistance, or a mixture of aerobic and resistance (mixed) exercise, is moderately beneficial for improving depression and anxiety symptoms. The beneficial effects of exercise were not influenced by the mode of exercise delivery on depressive symptoms, with some influence on anxiety symptoms. Therefore, aerobic, or resistance, or a mixture of aerobic and resistance (mixed) modes of exercise can be prescribed to individuals with depression and anxiety to improve their depressive and anxiety symptoms.

Author Contributions

A.B., H.B., K.L.E. and L.G. conceptualised the review criteria, and completed the screening. Data extraction was completed by all authors. J.S. and L.A. conducted the risk of bias assessment. J.S. conducted the meta-analysis. All authors contributed to the writing, reviewing and refinement of the manuscript.

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Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

All data and information reported in this systematic review are from peer-reviewed publications.

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Supporting Information

Additional supporting information can be found online in the Supporting Information section.