Running from depression: A systematic review and network meta-analysis of exercise dose and modality in the treatment for depression

Journal:	*BMJ*
Manuscript ID	BMJ-2023-075847
Article Type:	Original research
Date Submitted by the Author:	30-Mar-2023

Complete List of Authors:	Noetel, Michael ; The University of Queensland Sanders, Taren; Australian Catholic University Faculty of Health Sciences, Institute for Positive Psychology and Education Gallardo-Gómez, Daniel; Universidad de Sevilla (Departamento de Educación Física y Deporte) Taylor, Paul; Australian Catholic University Faculty of Health Sciences del Pozo Cruz, Borja; University of Southern Denmark; University of Cádiz, Biomedical Research and Innovation Institute of Cádiz (INiBICA) Research Unit van den Hoek, Daniel; University of the Sunshine Coast Smith, Jordan; The University of Newcastle Mahoney, John; Australian Catholic University Spathis, Jemima; Australian Catholic University Moresi, Mark; Australian Catholic University Vasconcellos, Roberta; Australian Catholic University Arnott, Hugh; Australian Catholic University - North Sydney Campus Varley, Benjamin; The University of Sydney Westmead Clinical School Parker, Philip; Australian Catholic University - North Sydney Campus Biddle, Stuart; University of Southern Queensland - Springfield Campus Lonsdale, Chris; Australian Catholic University Faculty of Health Sciences, Institute for Positive Psychology and Education

Keywords:	Physical and rehabilitation medicine, Mental health, Psychiatry, Public health, Sports medicine

Running from depression: A systematic review and network meta-analysis of exercise dose and modality in the treatment for depression

1. Michael Noetel, PhD, School of Psychology, The University of Queensland, St Lucia, 4072, Australia
2. Taren Sanders, PhD, Institute for Positive Psychology and Education, Australian Catholic University, North Sydney, 2060, Australia
3. Daniel Gallardo-Gómez, MSc, University of Seville, Department of Physical Education and Sport, Seville, Spain.
4. Paul Taylor, PhD, School of Health and Behavioural Sciences, Australian Catholic University, Strathfield, 2135, Australia
5. Borja del Pozo Cruz, PhD, Department of Clinical Biomechanics and Sports Science, University of Southern Denmark, Odense, Denmark, and Biomedical Research and Innovation Institute of Cádiz (INiBICA) Research Unit, University of Cádiz, Spain
6. Daniel van den Hoek, PhD, School of Health and Behavioural Sciences, University of the Sunshine Coast, Petrie, 4502, Australia
7. Jordan J Smith, PhD, School of Education, University of Newcastle, Callaghan, 2308, Australia
8. John Mahoney, PhD, School of Health and Behavioural Sciences, Australian Catholic University, Banyo, 4014, Australia
9. Jemima Spathis, PhD, School of Health and Behavioural Sciences, Australian Catholic University, Banyo, 4014, Australia
10. Mark Moresi, PhD, School of Health and Behavioural Sciences, Australian Catholic University, Strathfield, 2135, Australia
11. Roberta Vasconcellos, MPhEd, Institute for Positive Psychology and Education, Australian Catholic University, North Sydney, 2060, Australia
12. Hugh Arnott, BPsychSci, Institute for Positive Psychology and Education, Australian Catholic University, North Sydney, 2060, Australia
13. Benjamin Varley, BSc, Children's Hospital Westmead Clinical School, University of Sydney, Westmead, 2145, Australia
14. Philip Parker, PhD, Institute for Positive Psychology and Education, Australian Catholic University, North Sydney, 2060, Australia
15. Stuart Biddle, PhD, Centre for Health Research, University of Southern Queensland, Springfield, 4300, Australia, and Faculty of Sport & Health Science, University of Jyvaskyla, Finland
16. Chris Lonsdale, PhD, Institute for Positive Psychology and Education, Australian Catholic University, North Sydney, 2060, Australia

Correspondence to:
Dr Michael Noetel, School of Psychology, The University of Queensland, St Lucia, 4072, Australia
m.noetel@uq.edu.au
+61 7 3365 6230

Summary

Background

Depression is a leading source of global disease burden. Clinical practice guidelines recommend exercise as part of routine care, alongside psychotherapy and antidepressant medication. Our network meta-analysis aims to inform those guidelines with evidence regarding the optimal dose and modality of exercise for alleviating depression.

Methods

We replicated the most recent Cochrane review on exercise for depression, searching five databases (Cochrane Library, MEDLINE, EMBASE, SPORTDiscus, and PsycINFO). We included any randomised trial with exercise arms for participants meeting clinical cutoffs for depression. We did all screening, data extraction, coding, and risk of bias assessment independently and in duplicate. For our primary analyses, we conducted Bayesian arm-based, multilevel network meta-analyses.

Results

We included 177 studies, with a total of 404 unique arms, and 10,673 participants. Compared with waitlist control, the largest effects on depression were for dance (n = 107, k = 5, g = -1·21 [-1·59, -0·84]), cognitive behaviour therapy with aerobic exercise (n = 198, k = 10, g = -1·04 [-1·36, -0·73]), walking or jogging (n = 914, k = 46, g = -0·92 [-1·08, -0·76]), and strength training (n = 369, k = 16, g = -0·92 [-1·14, -0·70]). Effects were stronger as dose increased until meeting the WHO guidelines for physical activity (~150 min moderate intensity), beyond which there were few additional benefits. Results appeared robust to publication bias, but only one study met Cochrane criteria for low risk of bias.

Discussion

Exercise is an effective treatment for depression, with dance, walking/jogging, and strength training appearing more effective than other exercises. Exercise appeared equally effective for people with and without comorbidities, and of different baseline levels of depression. Many forms of exercise could be considered first-line treatment, alongside psychotherapy and antidepressant medication.

Registration

This review was registered with PROSPERO (CRD42018118040).

Funding

We received no funding for this review.

Key words

Exercise; Depression; Physical activity; Major Depressive Disorder; Behaviour Change Techniques; Yoga; Qigong

Summary

What is already known about this topic

- Depression is a leading cause of disability, and exercise is often recommended alongside first-line treatments, like pharmacotherapy and psychotherapy.
- Treatment guidelines and overviews of reviews disagree on how to prescribe exercise to best treat depression.

What this study adds

- Exercise can be as potent as other first-line treatments for depression: pharmacotherapy and psychotherapy.
- Exercise was most effective when people met WHO guidelines for physical activity, ideally using dance, walking/jogging, strength training, or cognitive behaviour therapy with adjuvant aerobic exercise.

Introduction

Major depressive disorder is a leading cause of disability worldwide.[1] It lowers life-satisfaction more than debt, divorce, or diabetes.[2] It exacerbates comorbidities including heart disease,[3] anxiety,[4] and cancer.[5] It often responds well to medication and psychotherapy,[6,7] but many cases are resistant to treatment.[8]

Exercise may be a cost-effective complement or alternative to medication and psychotherapy.[9,10] Clinical practice guidelines in the US, UK, and Australia recommend physical activity as part of treatment for depression.[11–14] However, these guidelines do not provide clear, consistent recommendations regarding dose or exercise modality. British guidelines recommend group exercise programs,[13,14] and offer general recommendations to increase any form of physical activity.[14] The American Psychiatric Association recommends any dose of aerobic exercise or resistance training.[13]. Australian and New Zealand guidelines suggest a combination of strength and vigorous aerobic exercise modalities, with bouts at least 2-3 times per week.[12]

Authors of guidelines may find it hard to provide consistent recommendations because existing meta-analyses have mostly been pairwise, exploring a specific modality versus a specific comparator in a specific group of participants. A recent overview of these reviews did not find differences between exercise modalities: stretching was as effective as strength training, and as effective as aerobic exercise.[15] However, comparing effect sizes *between* different pairwise meta-analyses in this way can lead to confusion because each meta-analysis can make different analytical decisions. Instead, a better way of precisely quantifying differences between interventions is to use network meta-analyses that simultaneously model the direct and indirect comparisons between interventions.[16]

Network meta-analyses have been used to compare different types of psychotherapy and pharmacotherapy for depression.[6,17,18] For exercise, they have shown that dose and modality influence outcomes for cognition,[19] back pain,[20] and blood pressure.[21] However, no such meta-analysis has been conducted for the use of exercise for depression. In this review, we aim to identify the optimal dose and modality of exercise. We also aim to explore whether those recommendations differ based upon the gender, age, and baseline depression level of participants. for different patients. Given the challenges involved in behaviour change for people with depression,[22] we aim to also identify behaviour change techniques that might improve intervention effects.[23]

Methods

We registered this review with PROSPERO (CRD42018118040) and present the findings according to the PRISMA-NMA guidelines.[24] Our methods replicated and extended the most recent Cochrane review on the topic.[25]

Eligibility Criteria

We included all randomised controlled trials including exercise as a treatment for depression. We included participants diagnosed with Major Depressive Disorder via a diagnostic interview or via cut-points on a depression measure. We used the following definition of exercise: "planned, structured and repetitive bodily movement done to improve or maintain one or more components of physical fitness".[26] Unlike the most recent Cochrane review,[25] we included studies with more than one exercise arm and multifaceted interventions (e.g., health and exercise counselling) as long as they contained a substantial exercise component. We included these trials because network meta-analysis methods allowed us to group those interventions into homogenous nodes. Unlike the previous review, we also included participants with physical comorbidities (e.g., arthritis), and participants with postpartum depression because the DSM5 removed the postpartum onset specifier after that analysis was completed.[27] We excluded studies with interventions shorter than 1 week, and studies not reporting depression as an outcome. We excluded studies with insufficient data to calculate an effect size for each arm. We included published or unpublished studies, with any comparison, in any language.

Information Sources

We replicated the search from the most recent Cochrane review,[25] adding keywords for yoga, tai-chi, and qigong, because we judged them to meet our chosen definition of 'exercise'. We conducted database searches in The Cochrane Library (all years), MEDLINE (1950 to date), EMBASE (1974 to date), SPORTDiscus (all years), and PsycINFO (1967 to date). We conducted our last searches in August, 2020. The full search strategy for each database is available on the Open Science Framework (OSF S0; https://osf.io/nzw6u).

Study Selection

We screened each title and abstract independently and in duplicate, with conflicts resolved via discussion or consultation with a third reviewer. We then conducted full-text screening using the same methods.

Data Collection Process

We used the Extraction 1.0 RCT data extraction forms in Covidence.[28] We extracted all data independently and in duplicate, with conflicts resolved through discussion with a third reviewer.

Data Items

We extracted a description of each intervention, including the frequency, intensity, type and time for each exercise intervention. Using the Compendium of Physical Activities,[29] we calculated the energy expenditure dose of exercise for each arm in terms of METs-min/week. Coders evaluated each exercise intervention using the Behaviour Change Taxonomy v1[23] for behaviour change techniques explicitly described in each exercise arm. Coders also rated the level of autonomy offered to participants, on a scale from 1–10. We also extracted descriptions of each other arm within the randomised trial, including all other treatment or control conditions. We extracted participants' age, gender, comorbidities, and baseline depressive symptom severity. We also extracted each trial's location and funding source.

Risk of Bias in Individual Studies

We used Cochrane's Risk of Bias tool for RCTs.[30] We rated risk of bias independently and in duplicate, with conflicts resolved through discussion with a third reviewer.

Summary Measures and Synthesis

We used Bayesian arm-based multilevel network meta-analysis models.[31] These analyses allowed us to assess the effects of each exercise modality, compared against other modalities and other interventions (e.g., cognitive behaviour therapy). The Bayesian arm-based components of our models allowed us to assess potential non-linear dose-response associations between energy expenditure and depressive symptoms. Many network meta-analyses use 'contrast-based' methods comparing post-test scores between arms of a study.[31] Arm-based meta-analyses instead describe the population-averaged absolute effect size for each treatment arm (i.e., each arm's change-score).[31] As a result, the summary measure we used was the standardised mean change from baseline, calculated as standardised mean differences as Hedges' g. In keeping with the norms from the included studies, effect sizes describe treatment effects on depression, such that larger negative numbers mean stronger effects on symptoms. Using NICE Guidelines, [32] we standardised change scores for different depression scales (e.g., BDI, HAM-D) using an internal reference standard for each scale (for each scale, the average of pooled standard deviations at baseline) reported in our meta-analysis. Because depression scores generally show regression to the mean, even in waitlist control conditions, we present effect sizes as 'improvements beyond waitlist control'. This convention makes our results comparable with existing, contrast-based meta-analyses. We conducted Bayesian meta-analyses in R[33] using the brms package.[34] We preregistered informative priors based on the distributional parameters of our meta-analytic model: $\mu \sim N(0, 1)$ and □ ~ HC(0, 1). We nested effects within arms to manage dependence between multiple effect sizes from the same participants. Finally, we compared absolute effect sizes against a standardised minimum clinically important difference, defined as 0·5 standard deviations of the average change score.[35]

Risk of Bias Across Studies

For this review, we judged that publication bias was most likely when comparing an active exercise condition with an inactive or placebo control condition. So, for assessments of publication bias, we constructed a data set of studies comparing exercise (only) vs. these control conditions. Then, to assess risks of publication bias we:

1. Created funnel plots, including estimates of effect sizes after removing significant studies (i.e., 'worst case' estimates);[36]
2. Calculated an s-value, representing how strong publication bias would need to be to nullify meta-analytic effects;[36] and
3. Conducted PET-PEESE, which tests whether the standard error is a good predictor of effect sizes, which would be indicative of small-study bias.[37]

Additional Analyses

We conducted all prespecified moderation and sensitivity analyses. We moderated for participant characteristics, including the participant gender, age, baseline symptom severity, and presence/absence of comorbidities. We moderated for the length of the intervention (in weeks) and the weekly dose of the intervention. We moderated for the amount of autonomy provided in the exercise prescription and the presence of each behaviour change technique. As pre-registered, we moderated for behaviour change techniques in three ways: the primary analyses were a meta-regression including all behaviour change techniques simultaneously; exploratory analyses included one behaviour change technique at a time (using 99% CIs to somewhat control for multiple comparisons), and meta-analytic classification and regression trees (metaCART) which allowed for interactions between moderating variables (e.g., if goal-setting + feedback had synergistic effects).[38] We conducted sensitivity analyses for risk of bias, assessing whether studies with low vs. unclear/high risk of bias on each domain demonstrated significantly different effect sizes.

Patient and Public Involvement

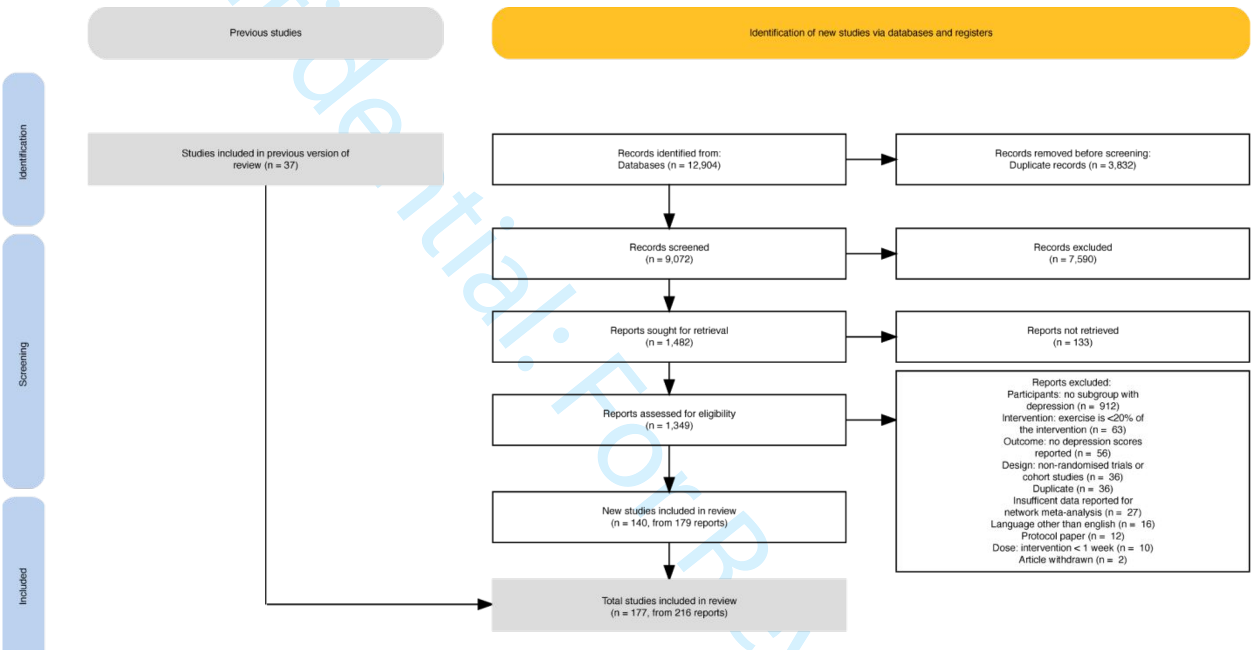
We discussed the aims and design of this study with the public, including those who had experienced depression. A number of our authors have experienced major depressive episodes, but beyond that, we did not include patients in the conduct of this review.

Results

Study Selection

The PRISMA flow diagram (Figure 1) outlines the study selection process. Through database searching we identified 12,941 possible reviews. After removing 3,832 duplicates, two reviewers independently screened each of 9,072 titles and abstracts. After screening titles and abstracts, two reviewers independently reviewed each of 1,349 full-text articles. Consensus reasons for exclusion are documented on the OSF (S1). Combining these new studies with the 37 included in the latest Cochrane review,[19] we included a combined total of 177 studies. These reviews include a combined total of 404 arms and 10,673 participants. The characteristics of each arm in each included study are available on OSF (S2), as are the references for each included report.

Figure 1. PRISMA2020 Flow Diagram



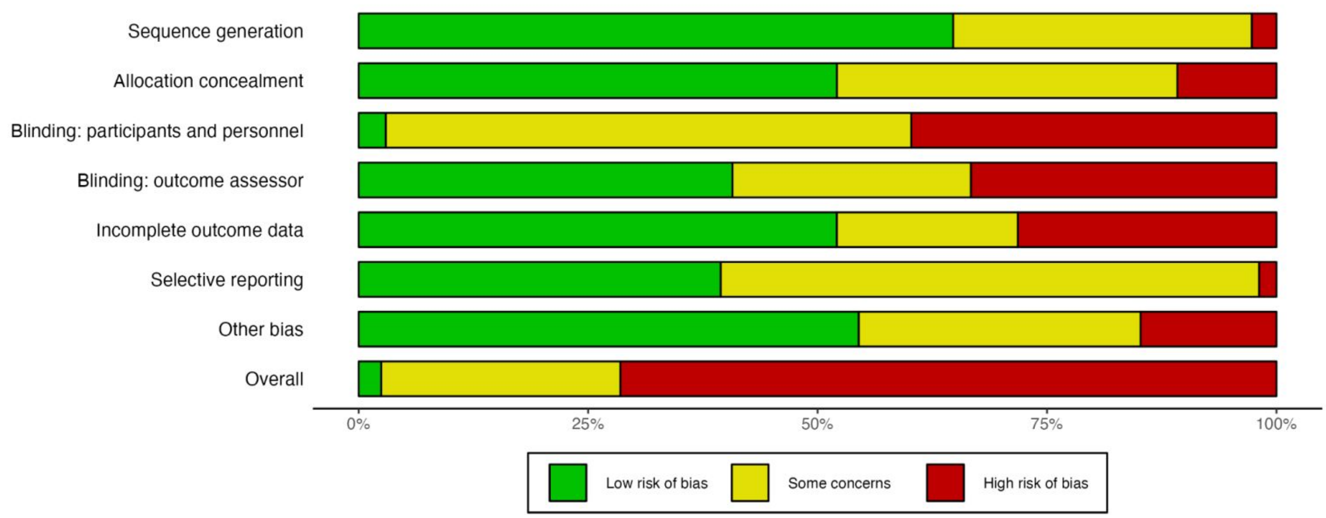
Network Geometry

As pre-registered, we removed nodes with fewer than 100 participants. Following that filter, the network geometry showed most interventions contained comparisons to at least 4 other nodes (see OSF, S3). Using net splitting, there was no evidence that the model violated the assumption of transitivity: there were no significant differences between effect sizes informed by direct or indirect evidence (all $p > 0{\cdot}05$, $p_{min} = 0{\cdot}09$).

Risk of Bias Within Studies

The risk of bias ratings for each study are available on the OSF (S4). As shown in Figure 2, few studies explicitly blinded participants and personnel. As a result, most studies were unclear- or high-overall risk of bias, and effect sizes may include expectancy effects, among other biases. However, sensitivity analyses suggested that effect sizes were not influenced by any risk of bias criteria (see OSF, S5).

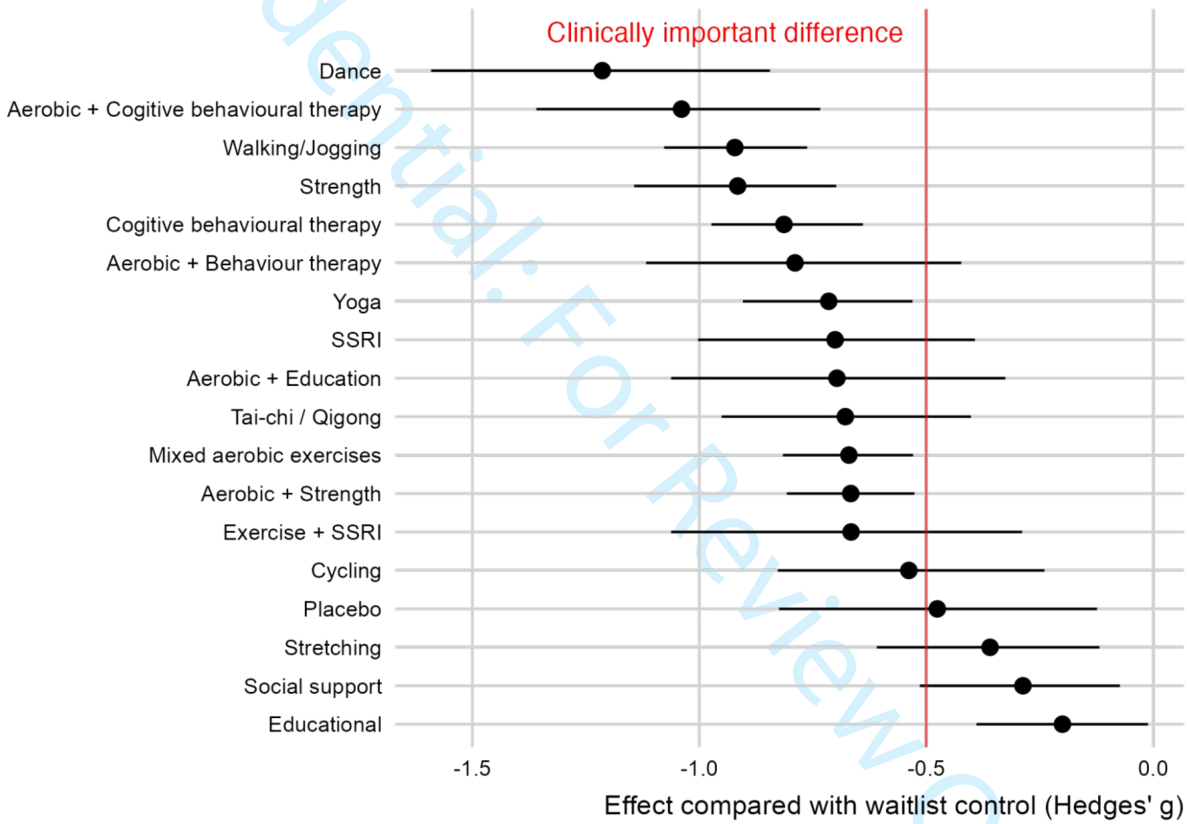
Figure 2. Risk of Bias Summary Plot



Synthesis of Results

Hedges' *g* for each study is presented in a forest plot on the OSF (S6). The predicted effects of each treatment, when compared against usual care, are presented in Figure 3. The largest effect sizes were for dance (*n* = 107, *k* = 5, *g* = -1·21 [-1·59, -0·84]), cognitive behaviour therapy with aerobic exercise (*n* = 198, *k* = 10, *g* = -1·04 [-1·36, -0·73]), walking or jogging (*n* = 914, *k* = 46, *g* = -0·92 [-1·08, -0·76]), and strength training (*n* = 369, *k* = 16, *g* = -0·92 [-1·14, -0·70]). All these interventions were significantly stronger than the standardised minimum clinically important difference ($g_{absolute}$ = -1·16, $g_{vs\ usual\ care}$ = -0·50). Consistent with other meta-analyses, there were also strong effects for cognitive behaviour therapy alone (*n* = 652, *k* = 16, *g* = -0·81 [-0·97, -0·64]), yoga (*n* = 477, *k* = 22, *g* = -0·71 [-0·90, -0·53]), and selective serotonin reuptake inhibitors (SSRIs; *n* = 386, *k* = 16, *g* = -0·70 [-1·00, -0·39]). Dance, cognitive behaviour therapy with aerobic exercise, and aerobic exercise with behaviour therapy were also most likely to perform best when modelling the surface under the cumulative ranking curve (SUCRA; see OSF, S7).

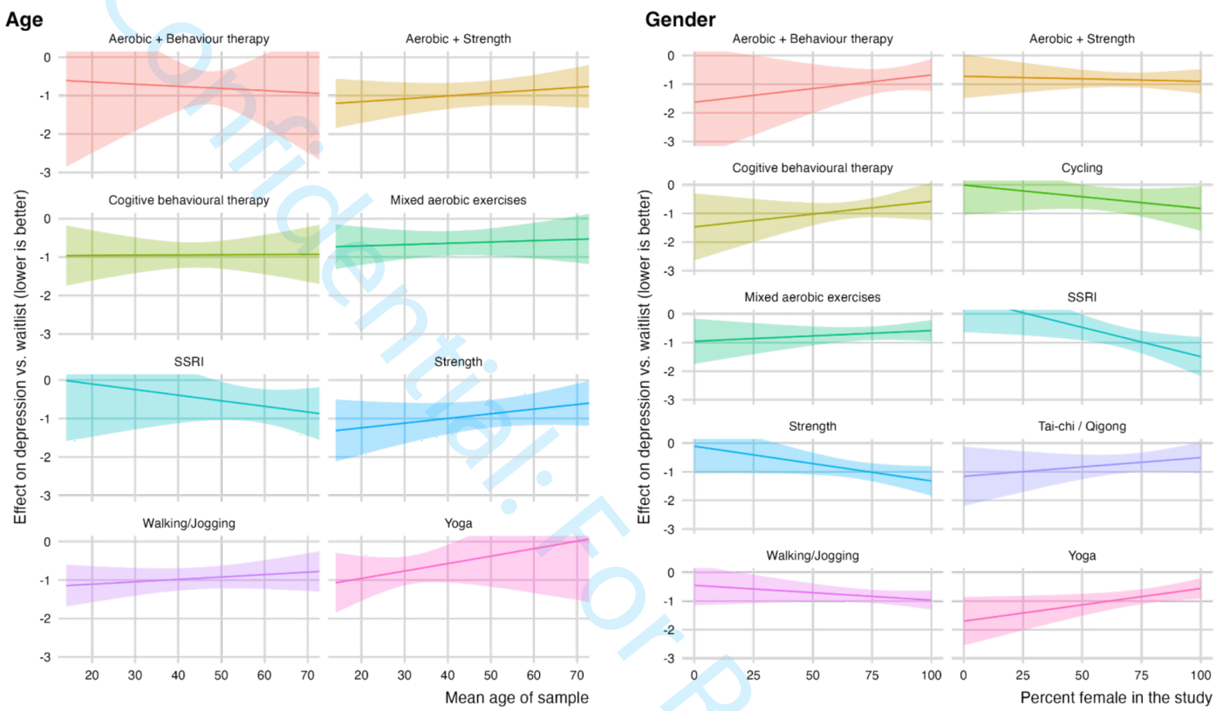
Figure 3. Predicted Effects Compared Against Usual Care, with 95% Credibility Intervals



The optimal modality appears to be moderated by age and gender. Compared with models that only included exercise modality (R^2 = 0·63), R^2 was higher for models that included interactions with gender (R^2 = 0·69) and age (R^2 = 0·69). There was no substantial increase in R^2 for models including baseline depression (R^2 = 0·64) or comorbidities (R^2 = 0·64; see OSF S8).

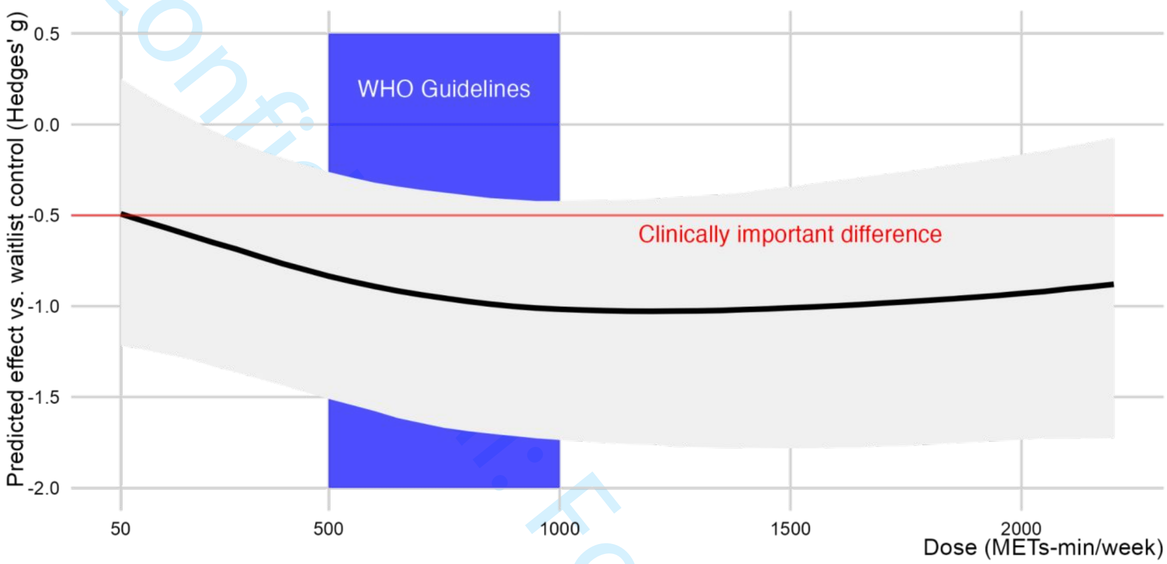
As shown in Figure 4, there appeared to be larger effects for women than men for strength training, cycling, and SSRIs. There appeared to be larger effects for men than women when prescribing yoga and cognitive behaviour therapy. Yoga and strength training appeared more effective for younger participants than older people. SSRIs appeared more effective when prescribed to older participants than younger people. There is substantial uncertainty for some estimates, because some modalities were not well studied in some demographics (e.g., yoga for older adults).

Figure 4. Effects of Interventions (with 95% Credible Intervals) by Gender and Age



Across modalities, there was a modest dose-response curve for the amount of exercise prescribed per week (Figure 5). Prescriptions meeting or exceeding the WHO guidelines for physical activity tended to be more effective than lower doses, with diminishing marginal returns beyond the recommended level (150–300 minutes of moderate-intensity or 75–150 minutes of vigorous-intensity; 500–1000 MET-minutes/week). Interventions lasting between 10 and 20 weeks appeared to have the strongest effects, with considerable uncertainty as most studies lasted less than 20 weeks (see [OSF, S9](#)).

Figure 5. Dose-response Curve Across Exercise Modalities, Versus Waitlist Control



We found no behaviour change techniques that significantly moderated overall effects. We also did not find that effect sizes were predicted by the level of participant autonomy described in the method. In exploratory metaCART analyses using only studies on walking or running, we found the largest effect sizes (g = -1·85, 95% CI [-2·16, -1·53,]) from the 31 studies that involved the participant exercising *with* the researcher (i.e., 'Behavioural practice'), as long as researchers did not also gradually increase the challenge (i.e., *without* 'Graded tasks'). Effects were smaller for the 14 studies that provided prescriptions for participants to do on their own (g = -1·21, 95% CI [-1·67, -0·75], or the six that used graded tasks (g = -1·14, 95% CI[-1·83, -0·44]).

Risk of Bias Across Studies

There was modest evidence of some publication bias but not enough to nullify effects. Comparing exercise vs. control, the bias-corrected estimate of effects (g = -0·65) was only slightly smaller than an uncorrected estimate (g = -0·73). Funnel plots showed pooled effects remained significant when only including non-significant studies (OSF, S10). As a result, no amount of publication bias would be sufficient to nullify effects.

Discussion

Summary of Evidence

Exercise demonstrates strong effects on depression, either alone or in combination with other established treatments like cognitive behaviour therapy. In isolation, the most effective exercise modalities were dancing, strength training, and walking/jogging. While walking/jogging appeared equally effective across demographics, strength training and dance appeared more effective for women than men, and in younger rather than older people. Exercise tended to be more effective when prescribed at or above the World Health Organisation guidelines, but appeared equally effective for people of different comorbidities or baseline levels of depression. As a result, treatment guidelines for depression are right to include exercise prescriptions, and may consider emphasising these modalities.

Our analyses provide different conclusions compared with a recent overview of systematic reviews assessing exercise for depression.[15] For example, while they found all modalities were equally effective,[15] we found that some modalities had strong effect sizes compared with others. We put this down to the higher resolution available in a network meta-analysis, compared with an overview of reviews.[16] Where an overview of reviews is constrained by the moderators available within existing reviews, we could separate the effects of specific doses and exercise modalities. Rather than being beholden to dichotomous moderation effects for exercise dose (e.g., <150 minutes / week vs. > 150 minutes / week),[15] we could model nonlinear effects using the dose of each individual study. Similarly, rather than grouping stretching, yoga and other mind–body modalities (e.g., Qigong),[15] we could analyse the effects of these interventions separately, revealing yoga and Qigong to be far more effective than stretching. Network meta-analyses revealed the same phenomena with psychotherapy: researchers once concluded there was a dodo verdict (‘Everybody has won, and all must have prizes’)[39] until network meta-analyses showed some interventions were robustly more effective than others.[6,18] While we agree with consensus statements that professionals should account for patients’ values, preferences, and constraints,[40] those professionals could emphasise dance, walking/jogging, and strength training as the options that work well, on average.

Health professionals treating depression could universally prescribe walking/running, because it requires few costs, no equipment, and works well across demographics. In exploratory analyses, we found that walking/running is more effective when done with the health practitioner, but without breaking large goals into intermediate ones. However, on the whole, we did not find that autonomy or behaviour change techniques meaningfully moderated the effect sizes from exercise interventions. This may be due to a number of factors. It may be that the modality explains most of the variance between effects, such that behaviour change techniques (e.g., presence or absence of feedback) did not provide a meaningful contribution. Some forms of exercise likely contain therapeutic benefits beyond just energy expenditure. For example, they may promote mindfulness (e.g., yoga), be more social (e.g., dance), be more likely to be conducted in green spaces (e.g., walking), or be more conducive to acute adaptations that may increase self-efficacy (e.g., strength).[40] These characteristics of the modality may be more influential than the behaviour change techniques layered on top. Alternatively, researchers may not have reported behaviour change techniques clearly or transparently enough for them to explain meaningful variance (e.g., researchers may have provided feedback without reporting so in the methods). As a result, our review could not provide confident recommendations for promoting adherence. Adherence is a challenge in treating depression with psychotherapy and pharmacotherapy as well.[41,42] As a result, exploring strategies to increase adherence may be a priority for future research across all treatments for depression.

The evidence here appeared robust to publication bias, but may be subject to a range of experimental biases. In particular, researchers seldom blinded participants and personnel delivering the intervention to the study’s hypotheses. Blinding for exercise interventions may be harder than for medications; however, future studies could attempt to blind participants and personnel to the study’s hypotheses to avoid expectancy effects.[43]

Our review found some interesting moderators by age and gender, but these were at the study level, rather than individual level. That is, rather than being able to determine whether women *within* a strength intervention benefit more than men, we could only conclude that studies with more women showed larger effects than studies with fewer women. These studies may have been tailored toward women, so effects may be subject to confounding, as both gender and intervention may have changed. Future reviews should consider individual patient meta-analyses to allow for more detailed assessments of participant-level moderators. Similarly, autonomy provided to participants did not moderate effects, but participants may have self-selected into trials with exercise modalities they enjoy. The participant's perceived autonomy is likely determined by a range of factors not described in the method, so reviews relying upon individual reports of the motivational climate are likely to be more reliable.[44] Finally, for many modalities, the evidence is made up of many small trials (e.g., the median *n* for walking/jogging arms was 17). In addition to reducing risks from bias, primary research may benefit from deconstruction designs or larger, head-to-head analyses of exercise modalities to better identify what works best for whom.

Conclusions

Depression imposes a significant global burden. Exercise appears to be an effective treatment. Some interventions with very few costs, side-effects, or pragmatic barriers, like walking and running, are effective across people with different demographics, depression severity, and comorbidities. Exercise can be as effective as other established treatments (cognitive behaviour therapy, selective serotonin reuptake inhibitors), while also attenuating risks to physical health associated with depression.[3] Therefore, exercise should be considered alongside those therapies as a first-line treatment for depression.

Funding

We received no funding for this review and declare no competing interests.

Author Contributions

MN led the project and drafted the manuscript. MN, TS, PT, MM, BdPC, PP, SB, and CL drafted the initial study protocol. MN, TS, PT, BdPC, DvdH, JS, MM, RV, HA, and BV conducted screening, extraction, and risk of bias assessment. MN, JS, and JM coded methods for Behaviour Change Techniques. MN and DGG conducted statistical analyses. PP, SB, and CL provided supervision and mentorship. All authors reviewed and approved the final manuscript.

References

1 World Health Organisation. Depression. 2020. https://www.who.int/news-room/fact-sheets/detail/depression (accessed March 12, 2020).

2 Birkjær M, Kaats M, Rubio A. Wellbeing adjusted life years: A universal metric to quantify the happiness return on investment. Happiness Research Institute, 2020 https://www.happinessresearchinstitute.com/waly-report.

3 Rugulies R. Depression as a predictor for coronary heart disease. a review and meta-analysis. *Am J Prev Med* 2002; **23**: 51–61.

4 Jacobson NC, Newman MG. Anxiety and depression as bidirectional risk factors for one another: A meta-analysis of longitudinal studies. *Psychol Bull* 2017; **143**: 1155–200.

5 Pinquart M, Duberstein PR. Depression and cancer mortality: a meta-analysis. *Psychol Med* 2010; **40**: 1797–810.

6 Cuijpers P, Noma H, Karyotaki E, Vinkers CH, Cipriani A, Furukawa TA. A network meta-analysis of the effects of psychotherapies, pharmacotherapies and their combination in the treatment of adult depression. *World Psychiatry* 2020; **19**: 92–107.

7 Cuijpers P, Quero S, Noma H, *et al.* Psychotherapies for depression: a network meta-analysis covering efficacy, acceptability and long-term outcomes of all main treatment types. *World Psychiatry* 2021; **20**: 283–93.

8 Strawbridge R, Carter B, Marwood L, *et al.* Augmentation therapies for treatment-resistant depression: systematic review and meta-analysis. *Br J Psychiatry* 2019; **214**: 42–51.

9 Hu MX, Turner D, Generaal E, *et al.* Exercise interventions for the prevention of depression: a systematic review of meta-analyses. *BMC Public Health* 2020; **20**: 1255.

10 Rimer J, Dwan K, Lawlor DA, *et al.* Exercise for depression. *Cochrane Database Syst Rev* 2012; **7**. https://www.scopus.com/inward/record.uri?eid=2-s2.0-84866461883&partnerID=40&md5=017f47a207b41fc4d2fddb12b69e6ba2.

11 National Collaborating Centre for Mental Health (UK). Depression: The Treatment and Management of Depression in Adults (Updated Edition). Leicester (UK): British Psychological Society https://www.ncbi.nlm.nih.gov/pubmed/22132433.

12 Malhi GS, Bell E, Bassett D, *et al.* The 2020 Royal Australian and New Zealand College of Psychiatrists clinical practice guidelines for mood disorders. *Aust N Z J Psychiatry* 2021; **55**: 7–117.

13 American Psychiatric Association. Practice Guideline for the Treatment of Patients with Major Depressive Disorder, Third Edition. Washington, DC: American Psychiatric Association, 2010 https://psychiatryonline.org/pb/assets/raw/sitewide/practice_guidelines/guidelines/mdd-1410197717630.pdf.

14 NICE. Depression in adults: treatment and management. The National Institute for Health and Care Excellence. 2022. https://www.nice.org.uk/guidance/ng222/resources (accessed March 13, 2023).

15 Singh B, Olds T, Curtis R, *et al.* Effectiveness of physical activity interventions for improving depression, anxiety and distress: an overview of systematic reviews. *Br J Sports Med* 2023; published online Feb 16. DOI:10.1136/bjsports-2022-106195.

16 Chaimani A, Caldwell DM, Li T, Higgins JPT, Salanti G. Undertaking network meta-analyses. In: Higgins JPT, Thomas J, Chandler J, *et al.*, eds. Cochrane Handbook for Systematic Reviews of Interventions. Cochrane, 2022. www.training.cochrane.org/handbook.

17 Cipriani A, Furukawa TA, Salanti G, *et al.* Comparative efficacy and acceptability of 21 antidepressant drugs for the acute treatment of adults with major depressive disorder: a systematic review and network meta-analysis. *Lancet* 2018; **391**: 1357–66.

18 Barth J, Munder T, Gerger H, *et al.* Comparative efficacy of seven psychotherapeutic interventions for patients with depression: a network meta-analysis. *PLoS Med* 2013; **10**: e1001454.

19 Gallardo-Gómez D, Del Pozo-Cruz J, Noetel M, Álvarez-Barbosa F, Alfonso-Rosa RM, Del Pozo Cruz B. Optimal dose and type of exercise to improve cognitive function in older adults: A systematic review and bayesian model-based network meta-analysis of RCTs. *Ageing Res Rev* 2022; **76**: 101591.

20 Owen PJ, Miller CT, Mundell NL, *et al.* Which specific modes of exercise training are most effective for treating low back pain? Network meta-analysis. *Br J Sports Med* 2019; published online Oct 30. DOI:10.1136/bjsports-2019-100886.

21 Naci H, Salcher-Konrad M, Dias S, *et al.* How does exercise treatment compare with antihypertensive medications? A network meta-analysis of 391 randomised controlled trials assessing exercise and medication effects on systolic blood pressure. *Br J Sports Med* 2019; **53**: 859–69.

22 Glowacki K, Duncan MJ, Gainforth H, Faulkner G. Barriers and facilitators to physical activity and exercise among adults with depression: A scoping review. *Ment Health Phys Act* 2017; **13**: 108–19.

23 Michie S, Richardson M, Johnston M, *et al.* The behavior change technique taxonomy (v1) of 93 hierarchically clustered techniques: building an international consensus for the reporting of behavior change interventions. *Ann Behav Med* 2013; **46**: 81–95.

24 Hutton B, Salanti G, Caldwell DM, *et al.* The PRISMA Extension Statement for Reporting of Systematic Reviews Incorporating Network Meta-analyses of Health Care Interventions: Checklist and Explanations. *Ann Intern Med* 2015; **162**: 777–84.

25 Cooney GM, Dwan K, Greig CA, *et al.* Exercise for depression. *Cochrane Database Syst Rev* 2013; published online Sept 12. DOI:10.1002/14651858.CD004366.pub6.

26 Caspersen CJ, Powell KE, Christenson GM. Physical activity, exercise, and physical fitness: definitions and distinctions for health-related research. *Public Health Rep* 1985; **100**: 126–31.

27 American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders (DSM-5). American Psychiatric Pub, 2013 DOI:10.1176/appi.books.9780890425596.

28 Veritas Health Innovation. Covidence systematic review software. Melbourne, Australia, 2023 www.covidence.org.

29 Ainsworth BE, Haskell WL, Herrmann SD, *et al.* 2011 Compendium of Physical Activities: a second update of codes and MET values. *Med Sci Sports Exerc* 2011; **43**: 1575–81.

30 Higgins JPT, Altman DG, Gøtzsche PC, *et al.* The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. *BMJ* 2011; **343**: d5928.

31 Lin L, Zhang J, Hodges JS, Chu H. Performing Arm-Based Network Meta-Analysis in R with the pcnetmeta Package. *J Stat Softw* 2017; **80**. DOI:10.18637/jss.v080.i05.

32 Dias S, Welton NJ, Sutton AJ, Ades AE. NICE DSU technical support document 2: a generalised linear modelling framework for pairwise and network meta-analysis of randomised controlled trials. In: National Institute for Health and Care Excellence (NICE), ed. NICE Decision Support Unit Technical Support Documents. London: Citeseer, 2011. https://www.ncbi.nlm.nih.gov/books/NBK310366/.

33 R Core Team. R: A language and environment for statistical computing. Vienna, Austria: R Foundation for

Statistical Computing, 2022 https://www.R-project.org/.

34 Bürkner P-C. brms: An R Package for Bayesian Multilevel Models Using Stan. *J Stat Softw* 2017; **80**: 1–28.

35 Hengartner MP, Plöderl M. Estimates of the minimal important difference to evaluate the clinical significance of antidepressants in the acute treatment of moderate-to-severe depression. *BMJ Evid Based Med* 2022; **27**: 69–73.

36 Mathur MB, VanderWeele TJ. Sensitivity analysis for publication bias in meta-analyses. *J R Stat Soc Ser C Appl Stat* 2020; **69**: 1091–119.

37 Harrer M, Cuijpers P, Furukawa TA, Ebert DD. Doing meta-analysis with R: A hands-on guide. Chapman and Hall, 2021 DOI:10.1201/9781003107347.

38 Li X, Dusseldorp E, Su X, Meulman JJ. Multiple moderator meta-analysis using the R-package Meta-CART. *Behav Res Methods* 2020; **52**: 2657–73.

39 Hunsley J, Di Giulio G. Dodo bird, phoenix, or urban legend? *The Scientific Review of Mental Health Practice* 2002; **1**: 11–22.

40 Vella SA, Aidman E, Teychenne M, *et al.* Optimising the effects of physical activity on mental health and wellbeing: A joint consensus statement from Sports Medicine Australia and the Australian Psychological Society. *J Sci Med Sport* 2023; published online Jan 8. DOI:10.1016/j.jsams.2023.01.001.

41 González de León B, Del Pino-Sedeño T, Serrano-Pérez P, Rodríguez Álvarez C, Bejarano-Quisoboni D, Trujillo-Martín MM. Effectiveness of interventions to improve medication adherence in adults with depressive disorders: a meta-analysis. *BMC Psychiatry* 2022; **22**: 487.

42 Kazantzis N, Whittington C, Zelencich L, Kyrios M, Norton PJ, Hofmann SG. Quantity and Quality of Homework Compliance: A Meta-Analysis of Relations With Outcome in Cognitive Behavior Therapy. *Behav Ther* 2016; **47**: 755–72.

43 Hecksteden A, Faude O, Meyer T, Donath L. How to Construct, Conduct and Analyze an Exercise Training Study? *Front Physiol* 2018; **9**: 1007.

44 Gillison FB, Rouse P, Standage M, Sebire SJ, Ryan RM. A meta-analysis of techniques to promote motivation for health behaviour change from a self-determination theory perspective. *Health Psychol Rev* 2019; **13**: 110–30.