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**Effects of Different Exercise Modalities and Dose–Response Relationships on Depressive Symptoms Among Adults with Chronic Heart Failure: A Model-Based Bayesian Network Meta-Analysis**

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**ADMINISTRATIVE INFORMATION****Support** - 2025 University-level Teaching Research Project of Wuhan Sport University (Project No. 2025252).**Review Stage at time of this submission** - Completed but not published.**Conflicts of interest** - None declared.**INPLASY registration number:** INPLASY2026100128**Amendments** - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 30 October 2026 and was last updated on 30 October 2026.**INTRODUCTION**

**Review question / Objective** This review addresses two linked questions. First, among adults with chronic heart failure, do aerobic exercise, high-intensity interval training, mixed aerobic–resistance or graded rehabilitation, mind–body exercise and resistance exercise differ from usual care, and from one another, in reducing depressive symptoms? Second, within each modality and across modalities combined, how does the magnitude of improvement vary with prescribed weekly exercise volume, and which dose is associated with the largest predicted improvement?

**Objectives:** to estimate modality-specific effects against usual care and between modalities; to rank the five modalities together with usual care; to fit modality-specific and pooled dose–response functions over the observed dose range and locate candidate doses; to compare modalities at a common dose; and to grade the certainty of every network comparison.

**Framework (PICOS):** adults with chronic heart failure; the five exercise modalities, with weekly volume coded in MET-min/week; usual care, no additional prescribed exercise, or another modality; change in depressive symptom scores; randomised controlled trials.

**Rationale** Heart failure affects more than 50 million people worldwide, and about one fifth of patients have clinically meaningful depressive symptoms, which predict death, hospitalisation and poorer self-care. Exercise is central to cardiac rehabilitation and is recommended for functional capacity, exercise tolerance and quality of life, yet depressive symptoms are seldom the explicit target when a programme is prescribed.

Meta-analyses in this population have estimated average effects of exercise or physical activity on depression and have examined programme features through subgroup analysis. Two questions remain open: whether modalities differ in their effect, and how much weekly exercise is required. Existing syntheses treat modality and volume as

separate dimensions, and the single dose–response synthesis in heart failure addressed quality of life rather than mood. Weekly volume integrates intensity, session length and frequency, and therefore offers a common scale for comparing heterogeneous prescriptions.

Model-based network meta-analysis links doses within a hierarchical model, borrows strength across sparse dose nodes, and estimates smooth dose–response curves while retaining randomised comparisons. Applying this framework to depressive symptoms in chronic heart failure should show whether the choice of modality or the amount of exercise matters more, and where on the dose range the largest improvement is predicted, informing both rehabilitation prescription and the design of future dose-comparing trials.

**Condition being studied** Chronic heart failure is a syndrome in which structural or functional cardiac abnormality impairs ventricular filling or ejection, producing breathlessness, fatigue, fluid retention and reduced exercise tolerance. It is grouped by left ventricular ejection fraction into reduced (<40%), mildly reduced (40–49%) and preserved (≥50%) phenotypes, and graded by NYHA functional class. It is common in older adults, frequently accompanied by multimorbidity, and associated with high rates of hospital admission, death and impaired health-related quality of life.

Depression is among its most frequent comorbidities: pooled prevalence of clinically significant depressive symptoms is about 21%, and the two conditions share neurohormonal, inflammatory and behavioural pathways. Depressive symptoms reduce adherence to treatment and self-care, amplify symptom burden and worsen prognosis, yet they are often under-recognised during cardiology follow-up. This review concerns adults with chronic heart failure of any ejection-fraction phenotype, with or without a formal depressive disorder at baseline, and takes depressive symptom scores as the outcome.

## METHODS

**Search strategy** Searches were run in six bibliographic databases, each from inception to 31 August 2026: PubMed/MEDLINE, Embase (Embase.com), Web of Science Core Collection, the Cochrane Central Register of Controlled Trials (CENTRAL), the China National Knowledge Infrastructure (CNKI) and Wanfang Data. No language, date or study-design filter was applied, and no dose-specific terms were required at the search stage.

Three concept blocks were combined with AND: heart failure; exercise, physical activity or cardiac

rehabilitation; and depression, anxiety or related psychological outcomes. Within each block, controlled vocabulary and free-text terms were combined with OR. Anxiety and mood terms were included in the psychological block to maximise sensitivity, while eligibility and synthesis were restricted to depressive symptoms.

Representative PubMed strategy:

#1 ("Heart Failure"[Mesh] OR "heart failure"[tiab] OR "cardiac failure"[tiab] OR "congestive heart failure"[tiab] OR CHF[tiab] OR HFrfEF[tiab] OR HFmrEF[tiab] OR HFpEF[tiab])

#2 ("Exercise"[Mesh] OR "Exercise Therapy"[Mesh] OR "Cardiac Rehabilitation"[Mesh] OR "Motor Activity"[Mesh] OR exercis\*[tiab] OR "physical activity"[tiab] OR training[tiab] OR aerobic[tiab] OR "resistance training"[tiab] OR "interval training"[tiab] OR HIIT[tiab] OR walking[tiab] OR telerehabilitation[tiab] OR yoga[tiab] OR "tai chi"[tiab] OR qigong[tiab] OR baduanjin[tiab] OR hydrotherapy[tiab])

#3 ("Depression"[Mesh] OR "Depressive Disorder"[Mesh] OR "Anxiety"[Mesh] OR depress\*[tiab] OR anxi\*[tiab] OR psycholog\*[tiab] OR "mental health"[tiab] OR mood[tiab] OR BDI[tiab] OR HADS[tiab] OR PHQ-9[tiab] OR CES-D[tiab] OR "Geriatric Depression Scale"[tiab] OR HAM-D[tiab] OR SDS[tiab])

#4 #1 AND #2 AND #3

Equivalent blocks were translated for Embase (subject headings with :ti,ab,kw), Web of Science (TS=), CENTRAL (MeSH with :ti,ab,kw), CNKI (SU=) and Wanfang (主题), including Chinese terms for heart failure, exercise modes such as tai chi, qigong, baduanjin and hydrotherapy, and depression or mood. Records were exported to NoteExpress 4.3.0, deduplicated, and screened. Reporting follows PRISMA-S; complete database-specific strings and per-database yields are given in Supplementary Table 2 of the review.

**Participant or population** Adults aged 18 years or older with a diagnosis of chronic heart failure, irrespective of ejection fraction (reduced, mildly reduced or preserved), NYHA class, aetiology, treatment setting (centre-based, home-based or hybrid) or baseline depression status (diagnosed disorder, elevated screening score, or an unselected sample). Trials restricted to acute decompensation, inpatient stabilisation only, ventricular assist device recipients or transplant candidates were not eligible.

**Intervention** Any structured exercise programme whose predominant training mode could be classified as aerobic exercise, high-intensity interval training, mixed aerobic–resistance training or explicitly prescribed graded rehabilitation, mind–

body exercise (for example tai chi, qigong, baduanjin or yoga), or resistance exercise including water-based resistance work. Warm-up and cool-down were assigned to the predominant mode. Programmes had to report intensity, session duration and weekly frequency well enough to compute prescribed volume as MET-min/week (MET value  $\times$  minutes per session  $\times$  sessions per week), using the Adult and Older Adult Compendia of Physical Activities; staged prescriptions were weighted by the number of weeks at each stage. Exercise had to be the primary intervention rather than an adjunct to another co-intervention.

**Comparator** Usual care, no additional prescribed exercise, or an alternative exercise modality from the five categories. Comparators could therefore be inactive (usual care, wait-list, or an attention control without structured exercise) or active (another eligible modality). Co-interventions were permitted only when delivered equally to both arms. Trials in which the control arm received a structured exercise programme that could not be separated from the experimental programme were excluded.

**Study designs to be included** Randomised controlled trials (parallel-group, crossover or cluster-randomised) that compared an eligible exercise programme with an eligible comparator and reported depressive symptom scores before and after intervention. Only randomised designs were eligible because risk of bias was assessed with RoB 2.

**Eligibility criteria** Inclusion: adults aged 18 years or older with chronic heart failure; a structured exercise programme assignable to one of the five modalities; a comparator of usual care, no additional prescribed exercise or another eligible modality; depressive symptoms measured with a validated scale at baseline and after intervention, with data allowing a between-group standardised mean change to be calculated; randomised design. Multiple reports of one trial were treated as a report family.

Exclusion: paediatric or acute heart failure populations; exercise as a minor component of a broader intervention, or used only as a comparator; no depressive symptom outcome (anxiety-only or quality-of-life-only reports); non-randomised studies, reviews, protocols, editorials and animal studies; reports lacking usable numerical data and recoverable statistics; duplicate or supplementary reports adding no new data.

**Information sources** Six bibliographic databases: PubMed/MEDLINE, Embase, Web of Science Core Collection, Cochrane CENTRAL, CNKI and Wanfang Data, each searched from inception to 31 August 2026. No trial registries, regulatory repositories, conference proceedings or grey literature were searched, and no citation-tracking records entered the screening flow, so the PRISMA flow counts derive solely from these six sources. Full strings and per-database yields are reported in Supplementary Table 2.

**Main outcome(s)** Depressive symptoms measured with validated self-report or clinician-rated scales (for example HADS-D, BDI-II, PHQ-9, SDS, CES-D, GDS or the SCL-90 depression subscale) and analysed as the change from baseline to the post-intervention assessment. Treatment effects were expressed as Hedges  $g$ , with negative values indicating greater improvement with exercise than with the comparator. Where several scales or time points were reported, the scale and time point used in the main analysis were documented per report in the supplementary tables.

**Quality assessment / Risk of bias analysis** Risk of bias was assessed with Cochrane RoB 2 across five domains: randomisation process, deviations from intended interventions, missing outcome data, measurement of the outcome, and selection of the reported result. Judgements were made for the scale and time point that contributed to the main analysis. Two reviewers assessed each report independently, resolving disagreements by discussion and involving a third reviewer when required. Domain and overall judgements were tabulated and displayed graphically. Certainty of evidence for each network comparison was rated with GRADE for network meta-analysis, considering risk of bias, inconsistency, indirectness, imprecision and publication bias.

**Strategy of data synthesis** Treatment effects were expressed as Hedges  $g$  with a small-sample correction, standardised within each report by a common change-score standard deviation, and the complete within-report variance-covariance matrix was retained so that shared control arms and shared standardisation were preserved.

Modality effects were estimated in a Bayesian random-effects network meta-analysis with a normal likelihood and identity link, using usual care as reference, Normal(0,100<sup>2</sup>) priors for relative effects and a half-normal(0,1<sup>2</sup>) prior for the common between-study standard deviation. Posterior medians, 95% credible intervals and SUCRA values were reported; transitivity was examined across age, duration, ejection fraction

and population characteristics, and direct and indirect evidence were compared for separable comparisons.

Dose-response was modelled with model-based network meta-analysis. Prescribed weekly volume (MET-min/week) was mapped to the nearest node among 250, 500, 750, 1250, 1750, 2250, 2750, 3250 and 3750, with usual care coded as zero. Natural cubic splines with one internal knot and two coefficients per modality, under  $\text{Normal}(0, 2.5^2)$  coefficient priors, described modality-specific curves, and a shared-function model produced an exploratory overall curve. Each curve was summarised by its posterior mean minimum, the draw-wise interval of that minimum and the predicted effect at the candidate dose.

Models were fitted in MBNMAdose 0.5.1 through rjags and JAGS 4.3.2, with three chains, 20,000 iterations, 10,000 burn-in and thinning of 10. Convergence was checked with rank-normalised R-hat, effective sample size and Monte Carlo error; fit was checked with joint posterior predictive distributions retaining the within-report covariance.

**Subgroup analysis** Formal subgroup meta-analyses by participant or programme characteristics were not undertaken, because most dose nodes were informed by few reports. Heterogeneity was explored through study-level meta-regression on mean age, intervention duration and left ventricular ejection fraction, each entered separately with a common slope for active-versus-usual-care comparisons. Exploratory strata by mean age (<60 vs ≥60 years) were described without inferential testing. In addition, modalities were ranked at a common dose of 750 MET-min/week across the four modalities with overlapping support, which provides a dose-standardised comparison. These analyses are ecological and cannot establish patient-level effect modification.

**Sensitivity analysis** Nine scenarios examined the robustness of the modality estimates: within-person correlations of 0.25 and 0.75 for imputing change-score standard deviations; restriction to arms with at least 15 participants; conservative handling of potentially overlapping report families; restriction to programmes of four weeks or longer; exclusion of effects larger than  $|g| = 2$ ; a combined restriction set; restriction to a subset of reports; and use of raw or paired-change inputs. Dose models were refitted under alternative spline specifications and coefficient priors, and with a uniform resting metabolic basis for MET assignment. In each scenario, convergence and fit were re-checked, and the direction of effect,

interval width and location of dose minima were compared with the main analysis.

**Country(ies) involved** China. Authors are based at Wuhan Sport University and Wuchang University of Technology (Wuhan), and at Hunan University of Chinese Medicine and Central South University (Changsha).

**Keywords** heart failure; depressive symptoms; dose-response; Bayesian network meta-analysis; cardiac rehabilitation.

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