



## Systematic Review

# Effectiveness of different exercise modalities in Heart Failure with preserved Ejection Fraction. A systematic review with network meta-analysis



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## ABSTRACT

**Aims:** The study aimed to compare the effectiveness of various exercise modalities in improving exercise performance, echocardiographic parameters and quality of life in patients with heart failure with preserved ejection fraction.

**Methods:** A systematic review over 7 databases was conducted up to May 2024. Randomised controlled trials analysing the efficacy of any exercise modality in isolation were included. For each variable, a Frequentist and Bayesian Network Meta-Analysis were conducted. Mean differences between groups with 95% confidence and credible intervals were calculated for each outcome. Quality of the evidence was assessed with GRADE, being very low for every outcome.

**Results:** 12 RCTs were included, providing data from 602 patients. The Frequentist model showed effectiveness for: CT on peak VO<sub>2</sub>, VO<sub>2</sub> at ventilatory threshold (VT) and E/é ratio; high-intensity interval training (HIIT) on peak VO<sub>2</sub>, VE/VCO<sub>2</sub> slope, cardiopulmonary exercise testing (CPET) time and E/é; inspiratory muscle training (IMT) on peak VO<sub>2</sub>, VE/VCO<sub>2</sub> slope, RER and 6-minute walking test (6MWT); moderate-intensity aerobic training (MIAT) on peak VO<sub>2</sub>, CPET time, peak power output (PPO), 6MWT and E/é ratio; and Tai Chi on peak VO<sub>2</sub>. The Bayesian model only supports these findings for CT on peak VO<sub>2</sub>; IMT on peak VO<sub>2</sub>; MIAT on CPET time, PPO, and 6MWT; and Tai Chi on peak VO<sub>2</sub>.

**Conclusions:** Considering both models, the evidence, albeit of very low quality, supports the effectiveness of various exercise modalities except HIIT in exercise capacity parameters (peak VO<sub>2</sub>, CPET time, PPO and 6MWT). There is an effect over VO<sub>2</sub> at VT, VE/VCO<sub>2</sub> slope, RER, LVEF, E/é and MLHFQ, but only supported by the Frequentist model.

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## Abbreviations

A late mitral wave  
E early mitral wave  
CERT Consensus on exercise reporting template  
CI Confidence interval  
CPET Cardiopulmonary exercise testing  
CrI Credible interval

FITT Frequency, intensity, time, type.  
GRADE Grading recommendations Assessment, Development, and Evaluation.  
HFpEF Heart failure with preserved ejection fraction  
HIIT High-intensity interval training  
HRR Heart rate reserve  
IMT Inspiratory muscle training  
KCCQ Kansas City cardiomyopathy questionnaire

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LAD	Left atrial diameter
LVEF	Left ventricle ejection fraction
LVMI	Left ventricle mass index
LVVI	Left ventricle volume index
MeSH	Medical subject headings
MIAT	Moderate intensity aerobic training
MLHFQ	Minnesota living with heart failure questionnaire
NMA	Network Meta-Analysis
QoL	Quality of life
PPO	Peak power output
RCT	Randomized controlled trial
RER	Respiratory exchange ratio
RoB	Risk of Bias
SF-36	short-form 36 health survey
MD	Mean difference
UC	Usual care
VT	Ventilatory threshold
VE/VCO <sub>2</sub>	CO <sub>2</sub> equivalent
6MWT	6-minute walking test

## Introduction

Heart failure (HF) is a clinical syndrome characterised by high morbidity and mortality, with a median incidence of 3.20 cases per 1000 person-years and a prevalence of 1–2% of adults in Europe.<sup>1–3</sup> HF also significantly impairs physical function and quality of life, with an annual healthcare costs reaching \$284.17 billion globally.<sup>4</sup> Traditionally it has been classified by left ventricle ejection fraction (LVEF), with worse pharmacological response in patients with >50% LVEF.<sup>5</sup> However, differences have also been observed in mortality, sex, cardiac remodelling and systemic biomarkers.<sup>6</sup>

With an ageing population, HF with preserved ejection fraction (HFpEF) has become the most common type of HF, and its incidence is expected to increase. Its typical multimorbid nature and lack of established pharmacological treatments present significant challenges for healthcare systems.<sup>5</sup> Current clinical Practice Guidelines,<sup>5,7</sup> recommend focusing on comorbidity management in patients with HFpEF. Among non-pharmacological interventions, exercise programmes effectively control cardiovascular risk factors and key comorbidities such as obesity, diabetes, obstructive pulmonary disease, anaemia,<sup>5,7,8</sup> and atrial fibrillation,<sup>9,10</sup> making them a valuable adjunctive option.

Previous reviews,<sup>11–13</sup> have analysed the comparative effectivity of different exercise modalities on HFpEF, showing positive results especially for peak VO<sub>2</sub>, which is correlated with fewer recurrent hospitalisations.<sup>14</sup> However, some exercise modalities studied were not included in the assessment of effectiveness across all exercise performance, echocardiographic parameters, and quality of life (QoL) variables. In addition, they all included studies in which the baseline LVEF mean with its standard deviation exceeded the 50% threshold, which could imply a selection bias, affecting the implementation of the results.

In light of the prognostic differences among phenotypes, the studied interventions, and the growing body of scientific literature, we conducted a network meta-analysis (NMA). The objective was to analyse the effectiveness of different exercise modalities on exercise performance, echocardiographic parameters and quality of life in HFpEF patients. An additional objective was to compare the exercise modalities to analyse which ones were superior for each outcome.

## Methods

This systematic review followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Protocols (PRISMA-P) extension for network meta-analyses,<sup>15</sup> and the Cochrane Handbook for Systematic Reviews of Interventions.<sup>16</sup> The protocol of this review was registered in PROSPERO. Literature search, studies selection, data extraction, the risk of bias and quality of the evidence assessment were conducted

by two independent authors and discrepancies were solved by a third author.

## Data sources and search strategy

Two authors independently searched in PubMed, SCOPUS, Web of Science, EMBASE, CINAHL Complete, Physiotherapy Evidence Database May 2024. Gray literature search was limited to OpenGray database and snowball technique. The search strategy and keywords used are shown in **Supplementary material A**. The study duplicates were managed using Covidence (<https://www.covidence.org>) and Rayyan (<https://www.rayyan.ai/>) software.

To complete the search, the reference lists of previous studies, abstracts and documents were all analysed. All the searches were conducted following the PICOS framework:

- Population: patients HFpEF.
- Intervention: any exercise modality.
- Comparators: any comparator, as it could be used for the network.
- Outcomes: peak VO<sub>2</sub>, VO<sub>2</sub> at ventilatory threshold (VT), peak power output (PPO), cardiopulmonary exercise testing (CPET) time, peak heart rate (HR), respiratory exchange ratio (RER), CO<sub>2</sub> equivalent (VE/VCO<sub>2</sub>) slope, and 6-minute walking test (6MWT). early mitral wave (E), late mitral wave (A), E/A ratio, early diastolic velocity of the mitral annulus (e'), E/e' ratio, LVEF, left ventricular volume index (LVVI), left ventricular mass index (LVMI), left atrial volume index (LAVI), left atrial diameter (LAD), stroke volume, cardiac output, flow-mediated dilatation, and global longitudinal strain (GLS). Minnesota Living with Heart Failure Questionnaire (MLHFQ), Kansas City Cardiomyopathy Questionnaire (KCCQ), Short-Form 36 Health Survey (SF-36).

## Study selection and exclusion criteria

The inclusion criteria were as follows: (1) Randomised Controlled Trials (RCTs) published in scientific journals; (2) including patients with HFpEF, defined as having a mean left ventricular ejection fraction (LVEF)  $\geq$  50%, with standard deviation not crossing this threshold in either the intervention or control group; (3) included at least one treatment group receiving any kind of exercise; (4) compared to other interventions or usual care (UC); (5) studies that provided statistical data on the outcome variables described above.

The exclusion criteria were: (1) inadequate study design, (2) other pathologies, (3) absence of an exercise group, (4) studies including interventions with no voluntary actions such as functional electrical stimulation, (5) studies in which the treatment arm was not exercised in isolation.

## Data extraction

Microsoft Excel was used for data collection. The following data were collected from the included studies: (1) general characteristics. (2) Characteristics of participants from each group. (3) Characteristics of the intervention. (4) Characteristics of the comparison group. (5) Data for each variable of interest: type of variable assessed, instrument used to measure it, point in time of the assessment, quantitative data for each outcome extracted in means and standard deviations (SD). When a study reported interquartile ranges and medians, these were converted into means and SD.<sup>17</sup> When no information was provided in an article, we contacted the authors via e-mail. The Consensus on Exercise Reporting Template (CERT) was used to summarise the characteristics of the exercise interventions.<sup>18</sup> The assessment process for CERT is described in **Supplementary material B**. When a study provided repeated measurements over time, only assessments at the end of the intervention were included in the analysis.

### Risk of bias and quality of evidence

Risk of bias of the RCTs was assessed using the Cochrane Collaboration tool for assessing the risk of bias (RoB 2).<sup>19</sup> The degree of concordance between both assessors in the RoB 2 was evaluated with Gwet's AC2 coefficient.<sup>20</sup>

Meanwhile, quality of the evidence was assessed following the Grading recommendations Assessment, Development, and Evaluation (GRADE) tool and its checklist adaptation to NMA.<sup>21</sup>

The assessment process for the use of both instruments is described in **Supplementary Material C and D**.

### Statistical analysis

To enhance robustness and address sensitivity of the results, two NMA were performed for each variable following a Frequentist and a Bayesian approach in RStudio (RStudio, PBC, Boston, MA, USA), employing R version 4.1.1. The "netmeta" package was used for the Frequentist approach (<https://CRAN.R-project.org/package=netmeta>) and the "gemtc" for the Bayesian model (<https://CRAN.R-project.org/package=gemtc>), following the guide developed by Harrer et al.<sup>22</sup> Exercise modalities were categorised as combined training (CT) (aerobic training plus resistance training), high-intensity aerobic training (HIIT), inspiratory muscle training (IMT), moderate-intensity aerobic training (MIAT) and Tai Chi. Direct comparisons between exercise modalities were represented with a network graph in which the nodes represented the type of intervention. For each treatment comparison, the effect size was calculated in mean differences (MD) plus their 95% confidence intervals (CI) or credible intervals (CrI). Statistical significance threshold was set at  $p < 0.05$ . A modality was considered supported when both models estimate pointed the same direction and their 95% CIs and CrIs did not cross the null value. For each NMA were presented using forest plots to illustrate differences between each exercise modality and usual care (UC).

Further explanation on transitivity, consistency, publication bias, meta-regression, treatment ranking and sensitivity analyses are described in **Supplementary Material E**.

### Results

A total of 12 studies were included in the quantitative analysis.<sup>23-34</sup> The selection process is summarised in the PRISMA flow diagram in **Supplementary material F**.

The included studies were carried out between 2011 and 2021, reporting data on 602 patients, with a mean age of 64.23 years, of whom 397 were women (65.94%). The type of exercise interventions found were HIIT,<sup>23,26,31</sup> IMT,<sup>32,33</sup> MIAT,<sup>23-26,28,30,31</sup> CT<sup>27,29,34</sup> and Tai Chi.<sup>34</sup> The weekly frequency of the treatment was 3 days for HIIT, 2-5 days for MIAT, 2-7 days for CT, 7 days for IMT, and 2 days for Tai Chi. Other characteristics of the included articles are summarised in **Table 1**.

With respect to exercise reporting, CERT complementation ranged between 26 and 74%. Only one study reported >60% (13 items) of the checklist. **Fig. 1** shows the compliance for each item per individual study.

### Risk of bias and quality of evidence

**Supplementary material G** shows the assessment for risk of bias. No studies were classified as low risk, only 1 study was classified as some concerns, and 11 studies were rated as high risk of bias. The concordance between revisers was good (AC2=0.86).

GRADE assessment showed very low quality for the efficacy of every intervention when compared to UC across all the NMA outcomes. Furthermore, when comparing the efficacy of each intervention respect to the others, the quality of evidence was also very low across the studied variables (**Supplementary material H**).

### Exercise performance variables

Compared to UC: CT showed an effect on peak VO<sub>2</sub>, but only in the Frequentist model for VO<sub>2</sub> at VT; IMT showed an effect on peak VO<sub>2</sub>, but only in the Frequentist model for VE/VCO<sub>2</sub> slope, RER and 6MWT; MIAT showed an effect on peak CPET time, PPO, and 6MWT, but only in the Frequentist approach for peak VO<sub>2</sub>. Tai Chi showed an effect on peak VO<sub>2</sub>. HIIT only reached statistical significance in the Frequentist model for peak VO<sub>2</sub>, VE/VCO<sub>2</sub> slope and CPET. No intervention reached had a significant effect on peak HR. According to the rank table, CT was most probable first-line treatment for VO<sub>2</sub> at VT (P-score=0.77) and PPO (P-score=0.75), HIIT was the most probable first-line treatment for CPET time (P-score=0.81), IMT was the most probable first-line treatment for VE/VCO<sub>2</sub> slope (P-score=0.99), RER (P-score=0.96) and 6MWT (P-score=0.80), and Tai Chi was the most probable first-line treatment for VO<sub>2</sub> peak (P-score=0.92). Regarding between-intervention comparisons, HIIT was superior to IMT for VE/VCO<sub>2</sub> slope. Only the Frequentist model supported that: for peak VO<sub>2</sub> CT was superior to MIAT and to HIIT, and Tai Chi was superior to MIAT. For VE/VCO<sub>2</sub> slope, MIAT was superior to IMT. Finally, IMT was superior to MIAT for RER. **Table 2** shows the effect estimates across all comparisons. **Fig. 2** shows the forest plot for each exercise modality on peak VO<sub>2</sub>. Forest plots for the rest of variables can be found in **Supplementary material I**.

Heterogeneity was found for peak VO<sub>2</sub>, VO<sub>2</sub> at VT, HR peak, and especially for 6MWT. Meanwhile, heterogeneity was lower for RER, PPO and VE/VCO<sub>2</sub>. Inconsistency was not significant for peak VO<sub>2</sub> and VE/VCO<sub>2</sub> and could not be calculated for the rest of the variables (**Supplementary material J**). Net and node-splitting functions revealed no inconsistency for VO<sub>2</sub> peak and the VE/VCO<sub>2</sub> slope; for the remaining variables, inconsistency could not be assessed due to the absence of loops. (**Supplementary material K**).

The leverage versus residual deviance plots indicated good model fit for all variables, except for VO<sub>2</sub> peak, where one study (16) was identified as contributing to a poorer model fit (**Supplementary material L**). Sensitivity analysis for peak VO<sub>2</sub> showed that, when compared to UC: CT, HIIT, IMT, MIAT and Tai Chi were still effective (**Supplementary material M**). Heterogeneity significantly decreased and inconsistency remained non-significant (**Supplementary material J**).

Meta-regression for assessing if age, sex differences or weeks of treatment could influence the magnitude of the estimates was non-significant for peak VO<sub>2</sub>.

Comparison-adjusted funnel plot and Egger test suggested there is no publication bias. (**Supplementary material N**).

### Echocardiographic variables

When compared to UC, only the Frequentist model supported: CT showed an effect on E/é ratio, HIIT showed an effect on E/é, IMT showed an effect on LVEF, MIAT showed an effect on E/é ratio. Tai Chi did not show any effect across the studied outcomes. None of the interventions reached statistical significance for LAVI, A, E, é and E/A. According to the rank table, HIIT was the most probable first-line treatment for LVEF (P-score=0.83) and LAVI (P-score=0.71), and Tai Chi was the most probable first-line treatment for E/é. Additionally, only the Frequentist model supported that: for LVEF, HIIT was superior to IMT and IMT was superior to MIAT and Tai Chi. **Table 2** shows the effect across all comparisons. Forest plots for the outcomes can be found in **Supplementary material I**.

Heterogeneity was identified for é, LAVI and E. Meanwhile, heterogeneity was lower for LVEF, E/A ratio, E/é ratio and A. Inconsistency was found for é; however, Q value significantly decreased after assuming a full design-by-treatment interaction random effects model. Inconsistency was non-significant for LAVI and E/é, but was not calculated for E, LVED, E/A and A (**Supplementary material J**). The net and node splitting showed no inconsistency for LAVI, E/é ratio and é, while for the rest of the variables they were not performed as there were no loops

**Table 1**  
Characteristics of the included studies.

Study	Country	Exclusion criteria	Sample size (woman)	Age	Comorbidities, BMI and NYHA class	FITT	Monitoring	Outcome	Test	Time-point assessment
Angadi et al. 2015	USA	Unstable angina, myocardial infarction in the past 4 weeks, uncompensated HF, NYHA class IV, complex arrhythmias, medical conditions that precluded treadmill walking, symptomatic aortic stenosis, acute pulmonary embolus, acute myocarditis, medication non-compliance	<b>IG 1:</b> 9 (1) <b>IG2:</b> 6 (2)	<b>IG 1:</b> 69 (6.1) <b>IG 2:</b> 71.5 (11.7)	Diabetes, Joint diseases <b>IG1 BMI:</b> 29.8 (5.1) <b>IG2 BMI:</b> 29.3 (2.8) NYHA: II-III (% NR)	<b>IG1:</b> 3 days/week 80–85% peak HR 14–22 min HIIT <b>IG 2:</b> 3 days/week 60–70% peak HR 15–30 min. MIAT	Peak HR	Peak VO <sub>2</sub> , VO <sub>2</sub> at VT, Peak RER, VE/VCO <sub>2</sub> slope, peak HR, CPET time LVEF, LAVI, E, A, E/A, E/e', e' medial	CPET Treadmill Echocardiography	4 weeks
Ayad SW al. 2021	Egypt	Haemodynamically significant valvular disease, acute coronary syndrome, end stage HF, several renal dysfunction, severe COPD or asthma, cognitive decline, non-ambulatory conditions and orthopaedic problems interfering with exercise and life expectancy <12 months	<b>IG:</b> 30 (19) <b>CG:</b> 30 (17)	<b>IG:</b> 57.47 (6.10) <b>CG:</b> 58.50 (6.31)	Diabetes, Hypertension, smoking. <b>IG BMI:</b> 33.89 (5.17) <b>CG BMI:</b> 34.48 (5.35) <b>IG NYHA:</b> II: 14 (46.7%) III: 16 (53.3%) <b>CG NYHA:</b> II: 16 (53.3%) III: 14 (46.7%)	<b>IG:</b> 2–3 days/week 40–70% HRR 15–60 min MIAT <b>CG:</b> UC	HRR	Meters A mitral, E mitral, E/A, e' medial, E/e', LAD, LAVI, LVEF QoL	6MWT Echocardiography MLHFQ	12 weeks
Brubaker et al. 2020	USA	Not being 60 years old, segmental wall motion abnormalities and nonsignificant ischemic or valvular disease, pulmonary disease or anaemia that could explain the patient's symptoms.	<b>IG 1:</b> 58 (44) <b>CG 2:</b> 58 (50)	<b>IG 1:</b> 70.3 (6.7) <b>CG 2:</b> 69.2 (6.2)	Diabetes <b>IG BMI:</b> 31.1 (5.9) <b>CG BMI:</b> 32.5 (6.6) <b>IG NYHA:</b> II: 32 (55%) III: 26 (45%) <b>CG NYHA:</b> II: 33 (57%) III: 25 (43)	<b>IG:</b> 3 days/week 40–50% HRR- 60% HRR 60 min MIAT <b>CG:</b> UC	HRR	Peak VO <sub>2</sub> , VO <sub>2</sub> at VT, peak workload meters QoL	CPET cycle ergometer 6MWT MLHFQ	16 weeks
Donelli da Silveira et al. 2020	Brasil	Unstable ventricular arrhythmias, unstable angina, moderate-severe valvular heart disease, anaemia, cognitive limitations, medication non-compliance and limitations to walk.	<b>IG1:</b> 10 (7) <b>IG2:</b> 9 (5)	<b>IG1:</b> 60 (10) <b>IG2:</b> 60 (9)	Atrial fibrillation, coronary artery disease, chronic kidney disease, dyslipemia, smoking. BMI: <b>IG1:</b> 34 (6%) <b>IG2:</b> 33 (5%) <b>IG1 NYHA:</b> II: 8 (89%) III: 1 (11%) <b>IG2 NYHA:</b> II: 8 (80%) III: 2 (20%)	<b>IG1:</b> 3 days/week 85–95% HR peak 38 min/session HIIT <b>IG2:</b> 3 days/week 60–70% HR peak 47 min/session MIAT	Peak HR and Borg	VO <sub>2</sub> peak, VE/VCO <sub>2</sub> , HR peak, peak RER A, E, E/A, E/e', e', LAD, LAVI, LVEF	CPET Treadmill Echocardiography	12 weeks
Edelmann et al. 2011	Germany	Hemodynamically relevant valvular disorders, pulmonary disease, current angina pectoris, untreated coronary artery stenosis >50%, previous myocardial infarction, anaemia, relevant musculoskeletal disease, resting SBP	<b>IG:</b> 46 (24) <b>CG:</b> 20 (12)	<b>IG:</b> 64 (8) <b>CG:</b> 65 (6)	Overweight, diabetes mellitus, hypertension, hyperlipidaemia, smoking BMI: <b>IG1:</b> 31 (5) <b>CG:</b> 31 (6) <b>IG NYHA:</b> II: 35 (80%) III 9 (20%) <b>CG NYHA:</b>	<b>IG:</b> 2–3 days/week 50–70% HR associated to VO <sub>2</sub> peak (MIAT)/ 60–70% 1RM (RT) 20–40 min (MIAT)	HR associated to peak VO <sub>2</sub>	VO <sub>2</sub> peak, peak workload, VO <sub>2</sub> at VT, CPET time Meters E/e', emedial, LAVI, LVEF QoL	CPET cycle ergometer 6MWT Echocardiography MLHFQ, SF-36	12 weeks

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Table 1 (continued)

Study	Country	Exclusion criteria	Sample size (woman)	Age	Comorbidities, BMI and NYHA class	FITT	Monitoring	Outcome	Test	Time-point assessment
		>150 mmHg or DPB >100 mmHg, clinically relevant arrhythmia.			II: 19 (95%) III: 1(5%)	Combined CG: UC				
Kitzman et al. 2013	USA	Hyperlipidaemia, smoking, peripheral artery disease and significant ischemic or valvular disease, pulmonary disease or anaemia that could explain the patient symptoms.	IG: 32 (23) CG: 31 (25)	IG: 70 (7) CG: 70 (7)	Diabetes, hypertension, smoking. BMI: IG: 32.2 (6.7) CG: 32.0 (6.6) IG NYHA: II: 15 (47%) III: 17 (53%) CG NYHA: II: 17 (55) III: 14 (45)	IG1: 3 days/week 40–70% HRR, 10–40 min MIAT CG: UC	HRR	VO2 peak, peak HR, peak RER, VO2 at VT, VE/VCO2 slope, peak workload, exercise time meters A, E, E/A, LVEF	CPET cycle ergometer 6MWT Echocardiography MLHFQ	16 weeks
Liu et al. 2021	China	Contraindications to exercise training, severely impaired liver and kidney function, musculoskeletal disease affecting exercise training, language barrier, emotional disorders	IG: 17 (5) CG: 20 (8)	IG: 64.95 (7.64) CG: 67.95 (4.65)	Diabetes, hypertension, coronary heart disease, atrial fibrillation. BMI: IG: 25.73 (3.52) CG: 24.46 (3.87) NYHA II-III NR	IG: 5–7 days/week (MIAT)/ 3–4 days/week (RT) VT1 (MIAT) 30–40 min (MIAT)/ 15–20 min (RT) Combined CG: UC	HR associated to VT and Borg	VO2 peak, VO2 at VT Meters QoL	CPET cycle ergometer 6MWT	12 weeks
Maldonado-Martín et al. 2017	USA	Hyperlipidaemia, smoking, peripheral artery disease and significant ischemic or valvular disease, pulmonary disease or anaemia that could explain the patient symptoms.	IG: 23 CG: 24	IG1: 70.04 IG2: 66	NR	IG: 3 days/week 50–70% VO2 peak, 40 min, MIAT CG: UC	HR and Borg	VO2 peak, VO2 at VT, VE/VCO2, peak HR, peak workload, exercise time meters	CPET cycle ergometer 6MWT	16 weeks
Mueller et al. 2021	Germany	Significant valvular or coronary disease, uncontrolled hypertension or arrhythmias or primary cardiomyopathies that could explain HF symptoms, significant pulmonary disease (GOLD II-IV), any condition interfering with exercise interventions.	IG1: 53 (41) IG2: 58 (35) CG: 60 (41)	IG1: 70 (7) IG2: 70 (8) CG: 69 (10)	Atrial fibrillation, coronary artery disease, diabetes, hypertension, hyperlipemia, peripheral artery disease, sleep apnoea syndrome, smoking. BMI: IG1: 30.0 (5.7) IG2: 31.1 (6.2) CG: 29.0 (4.7) IG1 NYHA: II: 44 (76%) III: 14 (24%) IG2 NYHA: II: 44 (76) III: 14 (24%) CG NYHA: II: 42 (70%) 18 (30%)	IG1: 3days/week /80–90% HRR 38 min/session HIIT IG2: 5 days/week 35–50% HRR 40 min/session MIAT CG: UC	HRR and BORG	VO2 peak, VE/VCO2 émedial, E/e', LAVI NT-proBNP QoL	CPET Echocardiography	12 weeks
Palau et al. 2014	Spain	NYHA class <II, inability to perform exercise testing, unstable angina, myocardial infarction or cardiac surgery in the past 3 months, chronic metabolic, orthopaedic, infectious or previous pulmonary	IG1: 14 (7) CG: 12 (6)	IG1: 68 (13.17) CG: 74.44 (3.35)	Atrial fibrillation, diabetes, dyslipemia, hypertension BMI: IG: 34.3 (28.2–38) CG: 30 (26–32) IG NYHA: II: 5 (36%) III-IV: 9 (64%) CG NYHA:	IG: 7 days/week, twice a day 25/30% MIP 20 min/session IMT CG: UC	NR	VO2 peak, VO2 at VT, VE/VCO2, peak HR, peak RER Meters émedial, E/e', LVEF; LAVI QoL NTproBNP	CPET cycle ergometer 6MWT Echocardiography MLHFQ	12 weeks

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Table 1 (continued)

Study	Country	Exclusion criteria	Sample size (woman)	Age	Comorbidities, BMI and NYHA class	FITT	Monitoring	Outcome	Test	Time-point assessment
		disease, treatments with chemotherapy, hormones or steroids, reduced maximal inspiratory mouth pressure according to age and sex, acute decompensation of HF, life expectancy < 1-year, actual smokers.			II: 3 (25%) III-IV: 9 (75%)					
Palau et al. 2019	Spain	NYHA class < II, inability to perform exercise testing, significant primary moderate-to-severe valve disease, unstable angina, myocardial infarction or cardiac surgery in the previous 3 months, uncontrolled arrhythmias or uncontrolled blood pressure during CPET, significant primary pulmonary disease, life expectancy <1 year	IG: 13 (8) CG: 13 (9)	IG: 75 (10) CG: 75 (9)	Atrial fibrillation, coronary heart disease, diabetes dyslipemia, hypertension, smoker. BMI: IG: 30.5 (4.3) CG: 34.8 (5.4) NYHA class III: IG: 5 (38.5%) CG: 3 (20%)	IG: 7 days/week, twice a day 25–30% 1 RM 20 min/session IMT CG: UC	NR	VO2 peak, VE/VCO2 slope E/e', LAVI NT-proBNP QoL	CPET Echocardiography MLHFQ	12 weeks
Yeh et al. 2012	USA	NYHA class IV, unstable angina, myocardial infarction or major cardiac surgery in the past 3 months, cardiac arrest in the past 6 months, significant valvular or pericardial disease accounting for signs and symptoms of HF, severe COPD on bronchodilators or chronic lung disease with cor pulmonale, pulmonary hypertension, atrial fibrillation as the dominant rhythm, severe vascular disease or musculoskeletal precluding a walk test, inability to perform a bicycle ergometry, mitral annular calcification, cognitive dysfunction, current participation in cardiac rehabilitation or regular practice of Tai-Chi.	IG1: 8 (4) IG2: 8 (4)	IG1: 63 (11) IG2: 68 (11)	Anxiety, arrhythmia, arthritis, asthma, cancer, coronary artery disease, depression, high cholesterol, renal disease BMI: IG1: 34 (14) IG2: 32 (10) IG1 NYHA: I: 2 (25) II: 5 (63) III: 1 (12) IG2 NYHA: I: 1 (12) II: 4 (50) III: 3 (38)	IG1: 5 days/week intensity NR 60 min Combined IG2: 2 days/week 60 min Intensity NR Tai Chi	NR	VO2 peak, peak HR, peak RER, meters E/A, E/e', LAD, LVEF 6MWT QoL	CPET cycle ergometer 6MWT Echocardiography MLHFQ	12 weeks

Data expressed as means (standard deviations), medians (interquartile range) or absolute (relative frequencies). late mitral flow, CG: control group, COPD: chronic obstructive pulmonary disease, CPET: cardiopulmonary exercise testing, DBP: diastolic blood pressure, E: early mitral flow, e': early diastolic velocity of the mitral annulus, FITT: frequency/intensity/time/type, HR: Heart rate, HRR: heart rate reserve, HIIT: high intensity interval training, IG: intervention group, IMT: inspiratory muscle training, LAVI: left atrial volume index, LVEF: left ventricle ejection fraction, MIAT: moderate intensity aerobic training, min: minutes, MLHFQ: Minnesota living with heart failure questionnaire, NR: not reported, QoL: quality of life, RER: respiratory exchange ratio, RT: resistance training, SBP: systolic blood pressure, VE: minute ventilation, VCO2: carbon dioxide production, VO2 peak: peak oxygen uptake, VT1: oxygen uptake at first ventilatory threshold, 6MWT: 6-minute walking test.

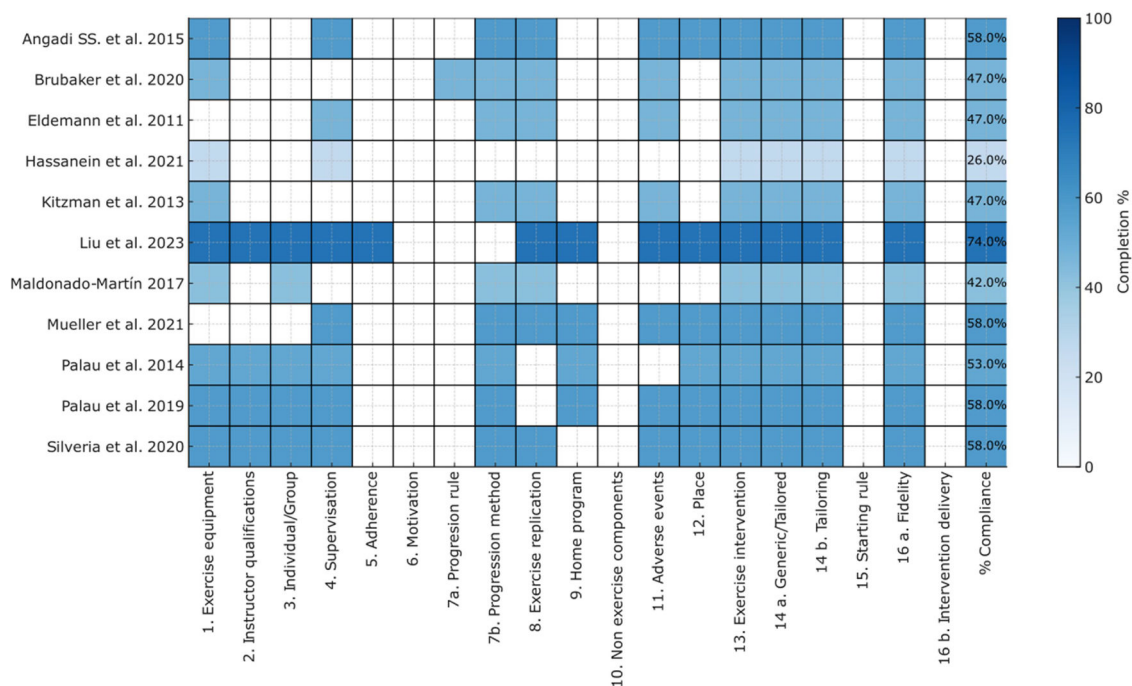


Fig. 1. CERT evaluation for each study. Colored cells represent reported items. Darker colored cells represent a higher percentage of CERT completion.

**(Supplementary material K).**

Leverage versus residual deviance plots showed good model fit for all the variables, so sensitivity analysis was not performed (Supplementary material L). Meta-regression for assessing if age, sex differences or weeks of treatment could influence the magnitude of the estimates was non-significant for LAVI and E/é. Comparisons adjusted funnel plots and Egger tests suggested there is no publication bias (Supplementary material N).

*Quality of life*

When compared to UC, MIAT was the only intervention that showed an effect on MLHFQ, but only in the Frequentist approach (Supplementary material I). Heterogeneity was detected and inconsistency was not calculated (Supplementary material J). Net and node splitting were not performed as there were no loops in the Network (Supplementary material K). There were no significant differences in the effect estimates between interventions (Table 2).

Leverage versus residual deviance plot showed good model fit for MLHFQ, so sensitivity analysis was not performed (Supplementary material L).

Comparisons adjusted funnel plot and Egger test suggest no publication bias (Supplementary material N).

**Discussion**

Our results align with previous research for the study of peak VO2, as we found the effectiveness of CT,<sup>11,12</sup> HIIT,<sup>11-13</sup> MIAT,<sup>11,12</sup> and IMT.<sup>12</sup> Contrary to Gomes-Neto,<sup>12</sup> we observed an effect of Tai Chi on this outcome, possibly due to the inclusion of only one study meeting the LVEF ≥ 50% criterion, resulting in low precision of the observed estimate.<sup>29</sup> For CPET time and PPO, we found MIAT to be effective, consistent with the findings of the only previous NMA that addressed these variables.<sup>11</sup> Conversely, we did not observe any effect on peak HR, nor HIIT across the outcomes. This could be due to our inclusion criteria, different studies and more comparators included in this NMA. For 6MWT, our results coincide with Cavero-Redondo.<sup>11</sup> for the

effectiveness of MIAT, with the novel finding of an effect on IMT on this outcome. Regarding RER, our NMA is the first to obtain an effect of IMT. Only one previous systematic review addressed this outcome, finding no differences when comparing HIIT to MIAT, which is also in line with our findings.<sup>35</sup>

Concerning the echocardiographic variables, our findings are in line with Cavero-Redondo.<sup>11</sup> for the effectiveness of HIIT on E/é ratio and the absence of statistical significance on E/A; however we did not find any effect on é. Surprisingly, we found a negative effect for IMT on LVEF. As only one study reported information for this exercise modality, this should be further studied in future trials.<sup>32</sup> Regarding LAVI, this is the first time an NMA has analysed it. Although we did not find a significant effect, consistent with a previous RS comparing HIIT and MIAT,<sup>35</sup> there is a tendency for HIIT to reduce LAVI; future investigations may corroborate or refute this. The lack of an observed effect on é, E and A, may be attributed to differences in the included studies, low statistical power to detect differences, or the absence of it. The better results for the exercise performance variables in contrast to the echocardiographic parameters could be explained as myocardial muscle has a limited capacity for improvement when compared to skeletal muscle,<sup>36</sup> furthermore, it seems that improvements in exercise performance are driven primarily by peripheral (arteriovenous O2 difference) rather than central adaptations.<sup>37,38</sup> Longer interventions may be required to achieve better results for these outcomes.

Regarding QoL, our results contrast with those of Walters,<sup>13</sup> as we found MIAT but not HIIT to be effective on MLHFQ. The more conservative nature of our findings compared to previous reviews may be attributed to: (1) the inclusion of only studies where the intervention was exercise in isolation, (2) the exclusion of articles involving HF patients with LVEF < 50%, and (3) the exclusion of duplicate studies with the same NCT, retaining only the most recent one, (19) thus lowering the precision of the effect estimates and not reaching statistical significance.

Regarding transitivity assumption, we did not find age, sex or duration of the intervention to influence on some estimates. In addition, patients' characteristics and exclusion criteria were similarly distributed across studies (Table 1), except for one study reporting lower BMI,<sup>29</sup> other including patients with cancer.<sup>34</sup> and two including patients with

**Table 2**  
Effect estimates for every possible treatment comparison.

Peak VO2					6MWT							
CT				-2.20 (-7.79, 3.39)	6.20 (3.90, 8.49)	CT			-44.10 (-251.49, 163.29)	46.28 (-14.62, 107.19)		
									-43.21 (-264.64, 180.03)	46.43 (-41.54, 134.34)		
3.49 (0.17, 6.82)	HIIT		1.04 (-1.29, 3.37)		1.30 (-2.06, 4.66)	-70.39 (-200.55, 59.77)	IMT			116.67 (1.64, 231.69)		
3.67 (-1.55, 7.48)					1.30 (-2.10, 4.80)	-70.33 (-239.29, 98.32)				116.65 (-29.01, 260.86)		
2.30 (-1.05, 5.65)	IMT				3.90 (1.46, 6.34)	-17.61 (-91.42, 56.19)	MIAT			63.89 (22.21, 105.58)		
2.39 (-2.55, 6.37)								52.77 (-69.58, 175.12)			63.87 (3.30, 127.37)	
4.12 (1.41, 6.83)		0.63 (-1.58, 2.83)	1.82 (-1.01, 4.65)	MIAT		2.18 (0.72, 3.64)		26.29 (-218.57, 271.14)	-26.49 (-246.62, 193.65)	Tai-Chi		
4.28 (0.03, 7.54)		0.58 (-2.03, 3.69)	1.85 (-1.87, 5.68)						27.20 (-250.31, 304.48)		-26.71 (-271.30, 220.45)	
-2.20 (-7.79, 3.39)		-5.69 (-12.20, 0.81)	-4.50 (-11.01, 2.01)	TAICHI				46.28 (-14.62, 107.19)	116.67 (1.64, 231.7)	63.9 (22.21, 105.59)	90.38 (-125.77, 306.54)	UC
-2.17 (-8.40, 3.99)		-5.78 (-13.05, 2.30)	-4.54 (-11.97, 3.34)						46.55 (-41.53, 134.34)	116.99 (-29.01, 260.85)	63.15 (3.30, 127.37)	
6.20 (3.90, 8.49)		2.70 (0.30, 5.11)	3.90 (1.46, 6.34)	2.08 (0.63, 3.52)	8.40 (2.36, 14.44)	UC						
6.33 (2.56, 8.94)		2.62 (-0.31, 5.97)	3.90 (0.74, 7.05)	2.08 (-0.07, 4.00)	8.42 (1.20, 15.16)							
VO2 at VT					CPET time							
CT					4.05 (1.64, 6.46)	CT			-66.00 (-344.91, 212.91)	85.00 (-45.50, 215.50)		
0.55 (-5.28, 6.39)	HIIT		1.40 (-2.77, 5.57)			-121.19 (-347.84, 105.45)	HIIT					
0.59 (-7.41, 8.80)								-121.67 (-427.29, 190.02)				
1.02 (-3.15, 5.20)	IMT				3.03 (-0.38, 6.44)	-40.19 (-184.97, 104.59)	MIAT			125.19 (62.49, 187.90)		
0.59 (-5.55, 6.91)								81.00 (-93.37, 255.37)				
1.95 (-2.13, 6.03)		1.40 (-2.77, 5.57)	0.93 (-3.81, 5.67)	MIAT	2.10 (-1.19, 5.39)	-66.00 (-344.91, 212.91)		55.19 (-304.19, 414.58)	-25.81 (-340.05, 288.44)	Tai-Chi		
1.04 (-5.13, 7.32)		0.44 (-4.66, 5.53)	0.47 (-6.74, 7.58)				-64.17 (-373.75, 242.14)		57.03 (-381.84, 489.59)		-24.16 (-403.03, 353.96)	
4.05 (1.64, 6.46)		3.50 (-1.82, 8.82)	3.03 (-0.38, 6.44)	2.10 (-1.19, 5.39)	UC	85.00 (-45.50, 215.50)		206.19 (20.89, 391.50)	125.19 (62.49, 187.90)	151.00 (-156.93, 458.93)	UC	
2.18 (-1.40, 5.84)		1.58 (-5.66, 8.76)	1.58 (-3.49, 6.69)	1.14 (-3.94, 6.21)			84.00 (-102.43, 267.54)		205.53 (-38.87, 449.67)	124.99 (7.28, 239.15)		148.44 (-211.92, 512.57)

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Table 2 (continued)

VE/VCO2 slope				RER			
HIIT		1.66 (-0.78, 4.10)	2.40 (-0.61, 5.41)	HIIT		0.02 (-0.06, 0.10)	
			2.40 (6.8, 12.0)				
7.08 (2.69, 11.48)	IMT		-4.29 (-7.94, -0.64)	-0.11 (-0.25, 0.04)	IMT		0.15 (0.05, 0.25)
7.36 (1.18, 14.31)				-0.10 (-0.33, 0.14)			
1.56 (-0.79, 3.91)	-5.52 (-9.44, -1.60)	MIAT	1.29 (-0.16, 2.74)	0.02 (-0.06, 0.10)	0.13 (0.01, 0.24)	MIAT	0.02 (-0.04, 0.09)
1.75 (-1.82, 5.71)	-5.60 (-11.58, 0.09)				0.01 (-0.09, 0.15)		0.12 (-0.08, 0.32)
2.79 (0.35, 5.24)	-4.29 (-7.94, -0.64)	1.23 (-0.19, 2.66)	UC	0.04 (-0.06, 0.14)	0.15 (0.05, 0.25)	0.02 (-0.04, 0.09)	UC
2.82 (-1.28, 7.11)	-4.56 (-9.83, 0.30)	1.08 (-2.24, 3.97)			0.04 (-0.12, 0.22)	0.14 (-0.02, 0.32)	
Peak HR				PPO			
HIIT		-4.34 (-23.20, 14.51)			CT		18.00 (-3.67, 39.67)
-18.70 (-51.41, 14.02)	IMT			12.67 (-10.80, 36.14)	1.70 (-19.98, 23.39)	MIAT	16.30 (15.57, 17.03)
-18.44 (-52.17, 14.58)							1.67 (-27.87, 31.28)
-4.34 (-23.20, 14.51)	14.35 (-12.38, 41.09)	MIAT		-1.68 (-14.50, 11.13)	18.00 (-3.67, 39.67)	16.30 (15.57, 17.03)	UC
-4.29 (-23.16, 14.57)	14.19 (-12.84, 41.75)					18.01 (-9.39, 45.51)	
-6.03 (-28.82, 16.77)	12.67 (-10.80, 36.14)		-1.68 (-14.50, 11.13)	UC			
-5.79 (-29.19, 17.09)	12.65 (-11.24, 36.31)		-1.47 (-15.14, 11.68)				
E/A ratio				E			
HIIT		-0.18 (-0.40, 0.04)		HIIT		-8.83 (-29.24, 11.57)	
		-0.20 (-0.63, 0.18)					
-0.18 (-0.41, 0.04)	MIAT		-0.02 (-0.23, 0.18)	-8.83 (-29.24, 11.58)	MIAT		-3.10 (-20.64; 14.43)
-0.19 (-0.63, 0.19)				-0.02 (-0.36, 0.32)		-9.73 (-26.99, 9.34)	
-0.21 (-0.51, 0.1)	-0.02 (-0.23, 0.18)	UC		-11.94 (-38.84, 14.97)	-3.10 (-20.64, 14.43)	UC	
-0.22 (-0.78, 0.29)	-0.02 (-0.37, 0.32)				-12.31 (-36.02, 12.22)		-2.68 (-18.95, 12.88)

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Table 2 (continued)

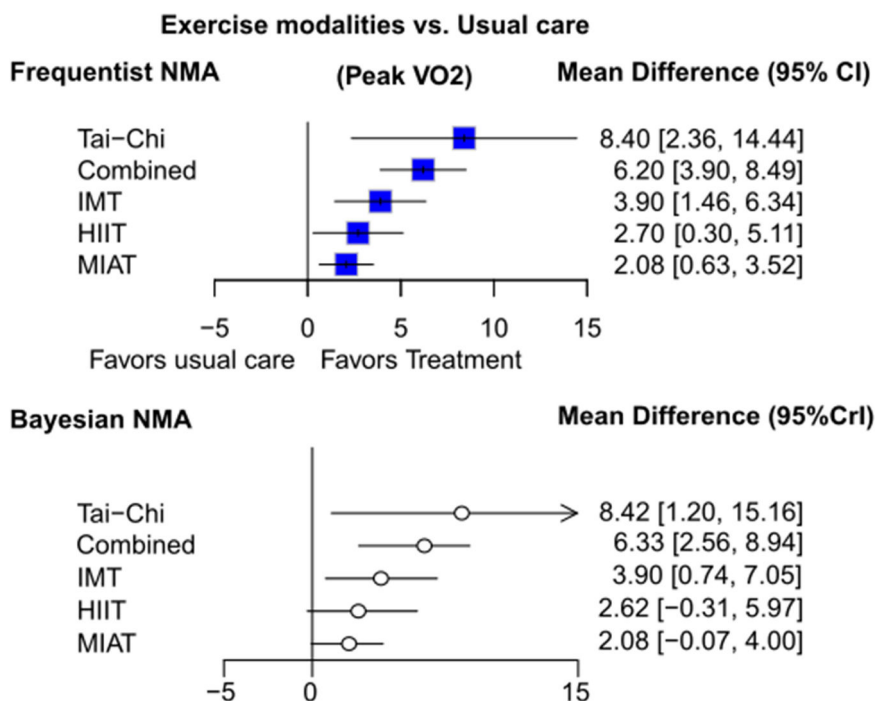
E/é ratio					LAVI					
CT				1.00 (-3.50, 5.50)	-3.60 (-5.60, -1.59)	CT				-4.30 (-12.83; 4.23)
-1.60 (-4.35, 1.15)	HIIT		-0.34 (-1.81, 1.12)		-1.30 (-3.74, 1.14)	0.50 (-10.75; 11.75)	HIIT		-1.77 (-8.36; 4.81)	-3.20 (-12.44; 6.04)
-1.41 (-6.82, 4.21)					-1.3 (-7.4, 4.8)	1.03 (-17.53, 20.04)				-3.30 (-23.00, 16.00)
-3.22 (-8.02, 1.59)	-1.62 (-6.37, 3.14)	IMT			-0.38 (-4.75, 3.98)	-4.51 (-17.24; 8.21)	-5.01 (-16.96; 6.94)	IMT		0.21 (-9.23; 9.66)
-3.14 (-9.53, 3.59)	-1.74 (-7.71, 4.47)						-4.54 (-23.45, 15.12)		-5.52 (-22.14, 11.69)	
-1.76 (-4.32, 0.79)	-0.16 (-1.59, 1.26)	1.45 (-3.20, 6.10)	MIAT		-1.86 (-3.48, -0.24)	-0.66 (-10.94; 9.62)	-1.16 (-7.46; 5.13)	3.85 (-7.20; 14.90)	MIAT	-3.78 (-9.65; 2.10)
-1.81 (-7.19, 3.26)	-0.37 (-3.24, 1.94)	1.32 (-4.77, 6.94)					-0.35 (-18.74, 16.71)	-1.41 (-11.21, 6.78)		4.01 (-12.64, 18.86)
1.00 (-3.50, 5.50)	2.60 (-2.67, 7.87)	4.22 (-2.37, 10.80)	2.76 (-2.41, 7.94)	TAICHI		-4.30 (-12.83; 4.23)	-4.80 (-12.12; 2.52)	0.21 (-9.23; 9.66)	-3.64 (-9.37; 2.10)	UC
0.98 (-4.71, 6.71)	2.42 (-5.57, 10.25)	4.16 (-4.65, 12.70)	2.82 (-4.75, 10.67)				-4.30 (-19.00, 10.41)	-5.37 (-17.30, 6.30)	0.16 (-12.28, 12.23)	
-3.60 (-5.61, -1.59)	-2.00 (-3.89, -0.11)	-0.38 (-4.75, 3.98)	-1.84 (-3.42, -0.25)	-4.60 (-9.53, 0.33)	UC					
-3.60 (-7.85, 0.69)	-2.18 (-5.70, 1.20)	-0.43 (-5.63, 4.48)	-1.79 (-4.65, 1.40)	-4.61 (-11.75, 2.52)						
MLHFQ					A					
CT				-0.10 (-24.87, 24.67)	-4.00 (-21.04, 13.04)	HIIT	-3.95 (-17.03, 9.12)			
8.28 (-13.76, 30.33)	IMT				-12.28 (-26.25, 1.69)		-3.95 (-17.03, 9.13)	MIAT		0.08 (-12.79, 12.95)
8.49 (-21.19, 38.04)							-4.52 (-16.21, 9.13)			
6.89 (-12.95, 26.72)	-1.4 (-18.66, 15.87)	MIAT			-10.88 (-21.02; -0.74)	-3.87 (-22.22, 14.49)	0.08 (-12.79, 12.96)		UC	
6.95 (-20.53, 35.40)	-1.57 (-25.12, 22.49)						-4.26 (-21.21, 14.08)	0.11 (-12.28, 12.57)		
-0.1 (-24.87, 24.67)	-8.38 (-41.54, 24.77)	-6.99 (-38.72, 24.75)	Tai-Chi							
-0.09 (-29.48, 29.11)	-8.58 (-50.55, 32.87)	-7.00 (-48.21, 32.70)								
-4 (-21.05, 13.05)	-12.28 (-26.26, 1.69)	-10.89 (-21.03, -0.74)		-3.9 (-33.97, 26.17)	UC					
-3.89 (-27.36, 19.60)	-12.39 (-30.41, 5.69)	-10.77 (-26.56, 4.25)		-3.82 (-41.18, 34.16)						

(continued on next page)

Table 2 (continued)

LVEF						é					
				2.00 (-5.90, 9.90)	-1.00 (-4.93, 2.93)						0.80 (-0.23, 1.83)
CT				-1.99 (-11.99, 8.07)	-1.03 (-8.72, 6.64)	CT					
-2.46 (-8.11, 3.19)			1.35 (-1.96, 4.66)			0.78 (-0.52, 2.09)				-0.32 (-0.97, 0.34)	0.28 (-0.74, 1.30)
-2.52 (-13.56, 8.33)	HIIT		1.42 (-4.24, 7.24)			0.73 (-1.08, 2.56)	HIIT				0.28 (-1.1, 1.6)
8.16 (-0.51, 16.83)	10.62 (1.89, 19.35)				-9.16 (-16.89, -1.43)	0.93 (-0.94, 2.80)	0.15 (-1.61, 1.90)				-0.13 (-1.70, 1.44)
8.08 (-4.41, 20.61)	10.61 (-1.79, 23.29)	IMT				0.91 (-1.41, 3.27)	0.18 (-1.95, 2.36)				
2 (-5.9, 9.9)	1.35 (-1.96, 4.66)	-9.27 (-17.35, -1.19)			0.11 (-2.25, 2.47)	0.45 (-0.77, 1.68)	-0.33 (-0.97, 0.31)	-0.48 (-2.18, 1.23)			0.21 (-0.49, 0.91)
-1.13 (-10.34, 8.12)	1.39 (-4.24, 7.24)	-9.18 (-20.47, 1.88)	MIAT		0.09 (-5.14, 5.32)	0.46 (-1.26, 2.20)	-0.26 (-1.14, 0.57)	-0.45 (-2.55, 1.61)	MIAT		
2.00 (-5.90, 9.90)	4.46 (-5.25, 14.17)	-6.16 (-17.89, 5.57)	0.35 (-0.33, 1.02)			0.80 (-0.23, 1.83)	0.02 (-0.79, 0.82)	-0.13 (-1.70, 1.44)	0.35 (-0.33, 1.02)		UC
2.01 (-8.07, 11.99)	4.51 (-10.06, 19.18)	-6.04 (-22.31, 9.82)	0.33 (-0.63, 1.31)			0.79 (-0.65, 2.23)	0.06 (-1.07, 1.18)	-0.12 (-2.00, 1.71)	0.33 (-0.63, 1.31)		
-1.00 (-4.93, 2.93)	1.46 (-2.60, 5.52)	-9.16 (-16.89, -1.43)	0.11 (-2.25, 2.47)	-3.00 (-11.82, 5.82)							
-1.01 (-8.72, 6.64)	1.52 (-6.18, 9.37)	-9.12 (-19.10, 0.85)	0.13 (-5.14, 5.32)	-3.01 (-15.70, 9.47)							

The upper part of each table contains the effect estimate for direct comparisons, the lower part contains the effect estimate from the Network-Meta-Analysis. For each comparison, the upper cell presents the Frequentist estimate and the lower cell the Bayesian estimate. Green cells represent statistical significance for that specific comparison. A: late mitral flow, CT: combined training, CPET: cardiopulmonary exercise testing, E: early mitral flow, é: early diastolic velocity of the mitral annulus, HR: Heart rate, HIIT: high intensity interval training, IMT: inspiratory muscle training, LAVI: left atrial volume index, LVEF: left ventricle ejection fraction, MIAT: moderate intensity aerobic training, MLHFQ: Minnesota living with heart failure questionnaire, RER: respiratory exchange ratio, RT: resistance training, VE: minute ventilation, VCO2: carbon dioxide production, VO2 peak: peak oxygen uptake, VT1: oxygen uptake at first ventilatory threshold, 6MWT: 6-minute walking test.



**Fig. 2.** Frequentist and Bayesian Forest plots for peak VO<sub>2</sub>. Upper Forest plot represents Frequentist NMA, lower Forest represents Bayesian NMA. HIIT: high-intensity aerobic training, IMT: inspiratory muscle training, MIAT: moderate-intensity aerobic training.

NYHA class IV.<sup>32,33</sup> Furthermore, for several comparisons we could not perform inconsistency tests to assess incoherence, or there was substantial heterogeneity (**Supplementary material J**). Thus, we decided to downgrade for indirectness and inconsistency in some of the comparisons.<sup>21,39,40</sup>

Current guidelines<sup>5,7</sup> recommend exercise to improve exercise capacity, functional status, QoL and reduce hospitalisations with a grade IA recommendation for HF patients in general, although there are no exact recommendations regarding which kind of exercise modality is the best for HFpEF.<sup>41</sup> The main finding of this NMA was the effectiveness of CT, IMT, MIAT, and Tai Chi, particularly in improving exercise performance, as its impairment is a hallmark of this population. Our findings support the implementation of MIAT in clinical practice, as it appears to have the greatest overall impact across the evaluated outcomes, while incorporating resistance training yields superior improvements in peak VO<sub>2</sub> (Table 2). From a practical point of view, progressing from lower to higher intensities could have an impact across the continuum of metabolic adaptations such as mitochondrial oxidative function.<sup>42-45</sup> and neurohormonal effects.<sup>46,47</sup> Adding IMT seems plausible to further improve these results.

To our knowledge, this is the first review to present results from both models on the comparative effectiveness of all exercise interventions in isolation across the spectrum of exercise capacity, echocardiography and QoL. Notably, this is the first NMA providing information about the effect of CT on VO<sub>2</sub> at VT, HIIT on VE/VCO<sub>2</sub> slope, IMT on 6MWT, RER and LVEF, MIAT on MLHFQ and Tai Chi for peak VO<sub>2</sub>. Our findings offer a guide for selecting specific exercise interventions to target each parameter in HFpEF. Additionally, this review presents a characterisation of the FITT and exercise monitoring parameters summarised in the in Table 1, which are also relevant for clinicians. Another insight is that exercise interventions in RCTs including HFpEF patients are moderately reported according to CERT, hence limiting the replicability of the interventions. This underscores the need for scientific journals to mandate more detailed reporting of exercise interventions in future RCTs, particularly for the less frequently reported items outlined in Fig. 1.

Although our findings have clinical relevance, they are not without

limitations. First, the quality of the evidence was very low for all the outcomes evaluated, partially due to the high risk of bias for almost all the included studies. Second, the heterogeneity observed in some of the estimates limits the applicability of the findings. Third, the low number of studies included in the NMA impacts the precision of the results, reduces the power for some analyses, and prevents the testing of overall consistency within the networks. Fourth, we were only able to perform meta-regressions for a limited number of variables. Although no significant effects modifiers were identified, it may have impacted the transitivity assumption. Fifth, the large number of variables analysed for exercise performance and echocardiography parameters implies more likelihood of false positives, which is why we highly recommend taking into account the convergence of both approaches. Sixth, in one study we had to estimate the mean and SD.<sup>32</sup> Seventh, although we intended to minimise the presence of patients with an EF < 50% in the analysis, we cannot assume their absence because we didn't have individual data.

**Conclusions**

Considering both approaches very low quality of the evidence indicates an effect of CT, IMT, and Tai Chi on peak VO<sub>2</sub>, as well as an impact of MIAT on other exercise performance parameters. Furthermore, CT is superior to MIAT on peak VO<sub>2</sub>, and HIIT is superior to IMT on VE/VCO<sub>2</sub> slope. Only the Frequentist model showed an effect for CT, HIIT and MIAT on exercise performance and echocardiography parameters, and an effect of MIAT on quality of life. Only the Frequentist model supported the superiority of CT over HIIT for peak VO<sub>2</sub> and Tai Chi over MIAT; for VE/VCO<sub>2</sub> slope, MIAT is superior to IMT, and for RER IMT is superior to MIAT. Future RCTs should aim to improve methodological quality and include bigger sample sizes (especially for HIIT and Tai-Chi) to enhance precision and overall quality of the evidence.

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## Supplementary material

Supplementary material A. Search strategy in the bibliographical search.

Supplementary material B. Consensus on Exercise Reporting Template description.

Supplementary material C. Risk of bias assessment description.

Supplementary material D. Grading recommendations Assessment, Development, and Evaluation (GRADE) tool assessment description.

Supplementary material E. Sensitivity analysis, meta-regression and publication bias analyses.

Supplementary material F. PRISMA flow diagram of the bibliographical search.

Supplementary material G. Risk of bias assessment.

Supplementary material H. GRADE assessment for each Network Meta-Analysis.

Supplementary material I. Frequentist and Bayesian Forest plots for each Network Meta-Analysis.

Supplementary material J. Heterogeneity and Inconsistency for each Network Meta-Analysis

Supplementary material K. Network graph for various Network Meta-Analysis

Supplementary material L. Leverage versus residual deviance plots for each Network Meta-Analysis.

Supplementary material M. Sensitivity analysis for peak VO<sub>2</sub>.

Supplementary material N. Comparison adjusted funnel plots for each Network Meta-Analysis.

## Authors' Contributions

Concept and design (AICV, JMHJ), acquisition (JMHJ, IJFA), analysis or interpretation of the data (JMHJ, IVJFA, CGC), drafting of the manuscript (JMHJ, AICV, IJFA, CGC), critical revision of the manuscript (IJFA, AICV), statistical analysis (JMHJ), and supervision (AICV).

## Declaration of competing interest

The authors declare no competing interest

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## Supplementary materials

Supplementary material associated with this article can be found, in the online version, at [doi:10.1016/j.bjpt.2026.101596](https://doi.org/10.1016/j.bjpt.2026.101596).

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