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Exercise-based cardiac rehabilitation for adults with heart failure (Review)

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Exercise-based cardiac rehabilitation for adults with heart failure.
Cochrane Database of Systematic Reviews 2024, Issue 3. Art. No.: CD003331.
DOI: 10.1002/14651858.CD003331.pub6.

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[Intervention Review]

Exercise-based cardiac rehabilitation for adults with heart failure

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Editorial group: Cochrane Heart Group.
Publication status and date: New search for studies and content updated (no change to conclusions), published in Issue 3, 2024.

Citation: Molloy C, Long L, Mordi IR, Bridges C, Sagar VA, Davies EJ, Coats AJS, Dalal H, Rees K, Singh SJ, Taylor RS. Exercise-based cardiac rehabilitation for adults with heart failure. *Cochrane Database of Systematic Reviews* 2024, Issue 3. Art. No.: CD003331. DOI: 10.1002/14651858.CD003331.pub6.

ABSTRACT

Background

People with heart failure experience substantial disease burden that includes low exercise tolerance, poor health-related quality of life (HRQoL), increased risk of mortality and hospital admission, and high healthcare costs. The previous 2018 Cochrane review reported that exercise-based cardiac rehabilitation (ExCR) compared to no exercise control shows improvement in HRQoL and hospital admission amongst people with heart failure, as well as possible reduction in mortality over the longer term, and that these reductions appear to be consistent across patient and programme characteristics. Limitations noted by the authors of this previous Cochrane review include the following: (1) most trials were undertaken in patients with heart failure with reduced (< 45%) ejection fraction (HFrEF), and women, older people, and those with heart failure with preserved (≥ 45%) ejection fraction (HFpEF) were under-represented; and (2) most trials were undertaken in a hospital or centre-based setting.

Objectives

To assess the effects of ExCR on mortality, hospital admission, and health-related quality of life of adults with heart failure.

Search methods

We searched CENTRAL, MEDLINE, Embase, CINAHL, PsycINFO and Web of Science without language restriction on 13 December 2021. We also checked the bibliographies of included studies, identified relevant systematic reviews, and two clinical trials registers.

Selection criteria

We included randomised controlled trials (RCTs) that compared ExCR interventions (either exercise only or exercise as part of a comprehensive cardiac rehabilitation) with a follow-up of six months or longer versus a no-exercise control (e.g. usual medical care). The study population comprised adults (≥ 18 years) with heart failure - either HFrEF or HFpEF.

Data collection and analysis

We used standard Cochrane methods. Our primary outcomes were all-cause mortality, mortality due to heart failure, all-cause hospital admissions, heart failure-related hospital admissions, and HRQoL. Secondary outcomes were costs and cost-effectiveness. We used GRADE to assess the certainty of the evidence.

Main results

We included 60 trials (8728 participants) with a median of six months' follow-up. For this latest update, we identified 16 new trials (2945 new participants), in addition to the previously identified 44 trials (5783 existing participants). Although the existing evidence base predominantly includes patients with HFrEF, with New York Heart Association (NYHA) classes II and III receiving centre-based ExCR programmes, a growing body of trials includes patients with HFpEF with ExCR undertaken in a home-based setting. All included trials employed a usual care comparator with a formal no-exercise intervention as well as a wide range of active comparators, such as education, psychological intervention, or medical management. The overall risk of bias in the included trials was low or unclear, and we mostly downgraded the certainty of evidence of outcomes upon GRADE assessment.

There was no evidence of a difference in the short term (up to 12 months' follow-up) in the pooled risk of all-cause mortality when comparing ExCR versus usual care (risk ratio (RR) 0.93, 95% confidence interval (CI) 0.71 to 1.21; absolute effects 5.0% versus 5.8%; 34 trials, 36 comparisons, 3941 participants; low-certainty evidence). Only a few trials reported information on whether participants died due to heart failure. Participation in ExCR versus usual care likely reduced the risk of all-cause hospital admissions (RR 0.69, 95% CI 0.56 to 0.86; absolute effects 15.9% versus 23.8%; 23 trials, 24 comparisons, 2283 participants; moderate-certainty evidence) and heart failure-related hospital admissions (RR 0.82, 95% CI 0.49 to 1.35; absolute effects 5.6% versus 6.4%; 10 trials; 10 comparisons, 911 participants; moderate-certainty evidence) in the short term. Participation in ExCR likely improved short-term HRQoL as measured by the Minnesota Living with Heart Failure (MLWHF) questionnaire (lower scores indicate better HRQoL and a difference of 5 points or more indicates clinical importance; mean difference (MD) −7.39 points, 95% CI −10.30 to −4.77; 21 trials, 22 comparisons, 2699 participants; moderate-certainty evidence). When pooling HRQoL data measured by any questionnaire/scale, we found that ExCR may improve HRQoL in the short term, but the evidence is very uncertain (33 trials, 37 comparisons, 4769 participants; standardised mean difference (SMD) −0.52, 95% CI −0.70 to −0.34; very-low certainty evidence).

ExCR effects appeared to be consistent across different models of ExCR delivery: centre- versus home-based, exercise dose, exercise only versus comprehensive programmes, and aerobic training alone versus aerobic plus resistance programmes.

Authors' conclusions

This updated Cochrane review provides additional randomised evidence (16 trials) to support the conclusions of the previous 2018 version of the review. Compared to no exercise control, whilst there was no evidence of a difference in all-cause mortality in people with heart failure, ExCR participation likely reduces the risk of all-cause hospital admissions and heart failure-related hospital admissions, and may result in important improvements in HRQoL. Importantly, this updated review provides additional evidence supporting the use of alternative modes of ExCR delivery, including home-based and digitally-supported programmes. Future ExCR trials need to focus on the recruitment of traditionally less represented heart failure patient groups including older patients, women, and those with HFpEF.

PLAIN LANGUAGE SUMMARY

What are the benefits and risks of exercise-based cardiac rehabilitation for heart failure?

Key messages

- Compared to no exercise, there was no evidence of a difference in deaths from any cause in patients with heart failure. Participating in exercise-based cardiac rehabilitation likely reduces the risk of hospital admissions from any cause and heart failure-related hospital admissions, and likely results in important improvements in health-related quality of life assessed by the 'Minnesota Living with Heart Failure' questionnaire.

- Importantly, this updated review provides additional evidence supporting the use of alternative modes of exercise-based cardiac rehabilitation delivery, including home-based and digitally-supported programmes.

- Future studies should recruit people not usually represented in studies, such as older patients and women with heart failure, and people with preserved ejection fraction heart failure.

What is heart failure?

Heart failure is when your heart can't pump blood around your body as well as it should. People with heart failure experience fatigue and shortness of breath. This makes doing everyday activities difficult and can affect people's quality of life. People with heart failure are at increased risk of hospital admission and death.

What is cardiac rehabilitation?

Cardiac rehabilitation aims to help people recover from heart problems, including heart failure. Cardiac rehabilitation programmes can involve exercise training and may also provide education on lifestyle and risk factor management, plus counselling and psychological support.

What did we want to find out?

We wanted to find out if exercise-based rehabilitation was better than no exercise to improve:

- deaths

- hospital admission

- health-related quality of life

What did we do?

We searched for studies that assessed the effects of exercise-based cardiac rehabilitation in people with heart failure. We compared and summarised the results of relevant studies and rated our confidence in the evidence based on factors such as study methods and sizes.

What did we find?

We found 60 studies that involved 8728 people with heart failure. The studies were conducted in countries around the world. About 40% of the people came from 2 large studies. All studies lasted for around 6 months or longer.

Participation in exercise-based cardiac rehabilitation:

• likely reduces the risk of hospital admissions from any cause and due to heart failure up to 12 months from the start of the study;
• probably makes little to no difference in the risk of death from any cause;
• likely improves health-related quality of life as measured by the Minnesota Living with Heart Failure questionnaire.

The effects of exercise-based cardiac rehabilitation appear to be consistent:

• whether they are delivered in a hospital or medical centre, or are home-based;
• regardless of the amount of exercise or whether the programme also includes other components such as education or counselling;
• regardless of the type of training (just aerobic or aerobic plus resistance training).

What are the limitations of the evidence?

Our confidence in the evidence is limited because not all the studies used robust methods. Further studies are needed to assess the impact of alternative models of exercise-based rehabilitation relative to traditional centre-based programmes, especially home-based and digitally supported programmes. Future studies need to consider the generalisability of trial populations (women, older people, and people with heart failure with preserved ejection fraction remain under-represented in trial populations), the application of interventions to enhance long-term maintenance of exercise training and outcome, and costs.

How up to date is this evidence?

This review updates our previous 2018 review. The evidence is up to date to December 2021.

SUMMARY OF FINDINGS

Summary of findings 1. Exercise-based cardiac rehabilitation compared to usual care for adults with heart failure (short-term)

Exercise-based cardiac rehabilitation compared to usual care for heart failure (short-term; up to 12 months of follow-up)

Patient or population: adults with heart failure
Setting: centre-based, home-based, and hybrid settings
Intervention: exercise-based cardiac rehabilitation
Comparator: usual care (formal no-exercise intervention with other active interventions e.g. education, psychological intervention, medical management)

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No. of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with usual care	Risk with exercise interventions				
All-cause mortality Range: 6-12 months	58 per 1000	50 per 1000	RR 0.93 (0.71 to 1.21)	3941 (34 RCTs, 36 comparisons)	⊕⊕⊖⊖ Low[a,b]	ExCR may result in little to no difference in all-cause mortality in the short term (up to 12 months). One study had no events in either the exercise arm or the control arm. Sensitivity analysis from studies at low risk of bias show no difference in statistical conclusion (RR 1.26, 95% CI 0.86 to 1.85; I^2 = 79%; 1443 participants, 8 RCTs). We downgraded evidence due to risk of bias and imprecision.
All-cause hospital admissions Range: 6-12 months	238 per 1000	159 per 1000	RR 0.69 (0.56 to 0.86)	2283 (23 RCTs, 24 comparisons)	⊕⊕⊕⊖ Moderate[c]	ExCR likely reduces all-cause hospital admissions in the short term (up to 12 months). Sensitivity analysis shows that studies at low risk of bias had a similar effect estimate to the overall effect estimate (RR 0.78, 95% CI 0.58 to 1.04; I^2 =24%; 874 participants, 6 RCTs). We downgraded evidence due to risk of bias.
HF-related hospital admissions Range: 6-12 months	64 per 1000	56 per 1000	RR 0.82 (0.49 to 1.35)	911 participants (10 RCTs, 10 comparisons)	⊕⊕⊕⊖ Moderate[d]	ExCR probably reduces HF-related hospital admissions. Sensitivity analysis from studies at low risk of bias had a similar effect estimate to the overall effect esti-

						mate (RR 0.72, 95% CI 0.25 to 2.02; I^2 = 14%; 742 participants, 4 RCTs). We downgraded evidence due to suspected publication bias.
HRQoL (MLWHF only) Range: 6-12 months Lower MLWHF scores indicate better HRQoL and difference of 5 points or more indicates clinical importance.	Mean score in the control group ranged from −3.3 to 61.0	MD 7.39 lower (10.30 lower to 4.47 lower)	-	2699 (21 RCTs, 22 comparisons)	⊕⊕⊕⊖ Moderate[e]	ExCR likely improves HRQoL in the short term (up to 12 months) as measured by the MLWHF questionnaire. The effect size incorporates a clinically meaningful improvement in overall MLWHF score (i.e. ≥ 5 points). Sensitivity analysis from studies at low risk of bias demonstrates a reduced benefit (MD 3.32 lower, 95% CI 8.20 lower to 1.57 higher; I^2 = 82%; 947 participants, 7 RCTs). We downgraded evidence due to inconsistency.
HRQoL (all measurement scales) Range: 6-12 months Lower SMD scores indicate higher levels of HRQoL in ExCR than control group	Mean score in the control group ranged from −81 to 71.4	SMD 0.52 lower (0.70 lower to 0.34 lower)	-	4769 (33 RCTs, 37 comparisons)	⊕⊖⊖⊖ Very low[a,f,g]	ExCR may improve HRQoL (based on all measurement scales) in the short term (up to 12 months) but the evidence is very uncertain. Sensitivity analysis from studies at low risk of bias suggest ExCR improves HRQoL in the short term (SMD 0.28 lower, 95% CI 0.51 lower to 0.04 lower; I^2 = 85%; 2495 participants, 9 RCTs). This suggests a small clinical improvement. We downgraded evidence due to risk of bias, inconsistency, and publication bias.

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the __relative effect__ of the intervention (and its 95% CI).

CI: confidence interval; **ExCR:** exercise-based cardiac rehabilitation; **HF:** heart failure; **HRQoL:** health-related quality of life; **MD:** mean difference; **MLWHF:** Minnesota Living With Heart Failure questionnaire; **RCT:** randomised controlled trial; **RR:** risk ratio; **SMD:** standardised mean difference.

GRADE Working Group grades of evidence.
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

[a]Plausible bias likely to seriously alter the results, concerns with random sequence generation and allocation concealment; downgraded by one level due to risk of bias.
[b]Number of events fewer than 300 (n = 212; Ryan 2016); downgraded by one level due to imprecision
[c]Plausible bias likely to seriously alter the results, concerns with random sequence generation, allocation concealment, and blinding; downgraded by one level due to risk of bias.
[d]Egger's test P = 0.015; downgraded by one level due to suspected publication bias.
[e]I^2 = 82% and Chi^2 P < 0.00001; downgraded by one level due to inconsistency.
[f]I^2 = 85% and Chi^2 P < 0.00001; downgraded by two levels due to inconsistency.
[g]Egger's test P = 0.002; downgraded by one level due to publication bias.

BACKGROUND

Description of the condition

An estimated 64.3 million people are living with heart failure worldwide (Conrad 2018). In high-income countries, the prevalence of known heart failure is generally estimated at 1% to 2% of the general adult population (GBD 2017). Survival after heart failure diagnosis has improved, but prognosis remains poor; 30% to 40% of patients die within one year of diagnosis (Conrad 2018; GBD 2017). Patients living with heart failure experience marked reductions in their exercise capacity, which has detrimental effects on their activities of daily living and health-related quality of life (HRQoL) (Braunwald 2015; Calvert 2007). The economic burden of heart failure on healthcare systems is considerable. Unplanned hospital admissions are a key driver of the cost of heart failure (Conrad 2018). Due to population growth, ageing, and the increasing prevalence of comorbidities, the absolute number of hospital admissions for heart failure is expected to increase considerably in the future, perhaps by as much as 50% in the next 25 years (Savarese 2017).

Heart failure has three main subcategories:

- heart failure with impaired left ventricular contraction, which results in a reduced ejection fraction, typically less than 40%, known as heart failure with reduced ejection fraction (HFrEF; ACCF/AHA 2013);
- heart failure with preserved ejection fraction (HFpEF), with an ejection fraction above 50% (Dunley 2017; Lam 2011);
- heart failure with mildly reduced ejection fraction (HFmrEF), with an ejection fraction between 40% and 50% (AHA/ACC/HFSA 2022).

Whilst epidemiological data show that approximately half of all people with heart failure have HFpEF (Dunley 2017), only more recent trials of drug and medical device therapies have recruited this patient subgroup. Although drug therapy and device therapy have helped to improve outcomes in HFrEF, the prognosis in HFpEF largely remains unchanged (Gajjela 2021). More recently, the sodium-glucose cotransport-2 inhibitors (SGLT2i) have emerged as promising therapies that alter the natural course of HFpEF, or that lower mortality (Anker 2021; Holland 2011; Komajda 2017).

Description of the intervention

The British Association for Cardiovascular Prevention and Rehabilitation (BACPR) defines cardiac rehabilitation as: "the coordinated sum of activities required to influence favourably the underlying cause of cardiovascular disease, as well as to provide the best possible physical, mental and social conditions, so that the patients may, by their own efforts, preserve or resume optimal functioning in their community and, through improved health behaviour, slow or reverse progression of disease" (BACPR 2017). This definition emphasises that whilst the central component of cardiac rehabilitation is exercise training (Piepoli 1998; Piepoli 2015), cardiac rehabilitation programmes should be comprehensive and should provide education on lifestyle and risk factor management plus counselling and psychological support (Corra 2005; Cowie 2019).

Based on current evidence on clinical outcomes and costs, national and international guidelines on the management of heart failure, including those of the American College of Cardiology/American Heart Association, the European Society of Cardiology, and the National Institute for Health and Care Excellence (NICE) in the UK, recommend exercise-based cardiac rehabilitation (ExCR) as an effective and safe intervention (AHA/ACC/HFSA 2022; ESC 2021; NICE 2018). However, surveys in the USA and Europe have shown that the current uptake of ExCR for heart failure remains suboptimal, with only 5% to 20% of heart failure patients receiving rehabilitation (Bjarnason-Wehrens 2010; Pandey 2021). To improve access to and uptake of ExCR for heart failure, there have been calls for alternative models to centre-based ExCR, including home-based and technology-based provisions (Dalal 2021).

How the intervention might work

Exercise-based cardiac rehabilitation (ExCR) is understood to benefit patients with heart failure through a variety of mechanisms. First, for people whose heart failure is due to ischaemic heart disease, exercise training improves myocardial perfusion by alleviating endothelial dysfunction, thereby dilating coronary vessels, and by stimulating new vessel formation by way of intermittent ischaemia (ExTraMatch 2004). Indeed, Belardinelli and colleagues have demonstrated that aerobic training improves myocardial contractility and diastolic filling (Belardinelli 1998). In addition, a meta-analysis by Haykowsky and associates shows the benefits of exercise training for cardiac remodelling, as measured by ejection fraction, end-diastolic volume, and end-systolic volume (Haykowsky 2007). Regardless of the cause, heart failure is characterised by important neurohormonal and musculoskeletal abnormalities. Exercise training may reduce adrenergic tone and increase vagal tone, as suggested by an assessment of variability in heart rate. Skeletal muscle dysfunction and wasting may also respond to exercise training (ExTraMatch 2004). Regular physical activity in people with heart failure has been shown to stimulate vasodilation in the skeletal muscle vasculature (Hambrecht 1998).

Why it is important to do this review

This is the fourth update of a Cochrane review first published in 2004. The first review version in 2004 concluded that exercise training improved short-term (up to one-year follow-up) exercise capacity compared with no exercise control (Rees 2004). However, only one of the 29 included randomised controlled trials (RCTs) was formally powered for hospitalisation and mortality. Few trials at that time assessed HRQoL. Accepting the evidence for improvement in short-term exercise capacity, the first updated version, published in 2010, focused on trials providing follow-up of six months or longer that reported clinical events (mortality, hospitalisation) or HRQoL (Davies 2010). The 2010 review of 19 RCTs (3647 participants) showed no difference between exercise and control in either short-term or long-term all-cause mortality, a reduction in heart failure-related hospitalisations (risk ratio (RR) 0.72, 95% confidence interval (CI) 0.52 to 0.99), and improvement in patient-reported HRQoL (standardised mean difference (SMD) 20.63, 95% CI 20.37 to 20.80) with exercise therapy. Most of the trials included in the 2010 review included men with New York Heart Association (NYHA) class II to III disease. None of these trials included people with HFpEF, and programmes were delivered only in a centre-based setting.

The second update, published in 2014, included 33 RCTs (4740 participants) and presented findings consistent with the 2010 update and concluded that ExCR reduced the risk of hospital

admission due to heart failure and led to improvements in HRQoL compared with no exercise (Taylor 2014). The third update published in 2019 included 44 RCTs (5783 participants) presented findings consistent with the 2014 review (Long 2019).

Participation in ExCR is consistently a class I recommendation by national and international guidelines for the management of adults with heart failure (AHA/ACC/HFSA 2022; ESC 2021). However, global access and uptake of ExCR remains poor, a situation that has worsened with the COVID-19 pandemic. The availability of evidence-based alternative modes of ExCR delivery is urgently needed to improve future access. To continue to promote international access and uptake of cardiac rehabilitation for heart failure, the current evidence base must be updated to reflect recent trials that are increasingly testing alternative models to centre-based cardiac rehabilitation, such as home- and technology-based programmes or hybrid programmes that combine centre and home-based elements (Dalal 2021).

OBJECTIVES

To assess the effects of ExCR on mortality, hospital admission, and HRQoL of adults with heart failure.

METHODS

Criteria for considering studies for this review

Types of studies

We included RCTs of any design that provided follow-up for at least six months post randomisation. We chose this follow-up as it is likely to reflect changes in event outcomes as well as the focus of policymakers. We excluded quasi-randomised trials (e.g. trials that allocated patients according to the day of the week).

Types of participants

We included adults aged 18 years or older with heart failure. We excluded trials that focused on participants who had received ExCR as previous participant exposure to the intervention may confound the interpretation of trials. However, if the trial population consisted primarily of new ExCR patients who predominantly had heart failure, we included the trial. To be included, the trial population with heart failure must account for more than 50% of the total number of participants.

Types of interventions

We included exercise-based interventions given alone or as a component of comprehensive cardiac rehabilitation (defined as programmes with components such as health education and psychological interventions, in addition to exercise interventions). The control group must not have received exercise training but may have received active intervention (i.e. education, psychological intervention) or usual medical care alone.

Types of outcome measures

Outcomes did not form the basis for trial exclusion. When reported, we extracted outcome results at two time points: up to and including 12 months' follow-up ('short-term'), and longer than 12 months' follow-up ('long-term'). The longest follow-up was included in each time point analysis to assess treatment effects.

Primary outcomes

- All-cause mortality
- Heart failure mortality
- Number of participants who experienced an all-cause hospital admission
- Number of participants who experienced a heart failure-related hospital admission
- HRQoL assessed by a validated outcome measure (e.g. 36-item Short Form (SF-36), Minnesota Living with Heart Failure (MLWHF) questionnaire)

These event outcomes reflect both potential efficacy and potential adverse effects.

Secondary outcomes

- Costs and cost-effectiveness

Search methods for identification of studies

Electronic searches

For this fourth update, we reran searches in the following databases on 13 December 2021 (search strategies presented in Appendix 1).

- Cochrane Central register of Controlled Trials (CENTRAL; 2021, Issue 12) in the Cochrane Library
- Epub Ahead of Print, In-Process & Other Non-Indexed Citations, MEDLINE Daily, and MEDLINE (Ovid, 1946 to 10 December 2021).
- Embase (Ovid, 1980 to 2021 week 49).
- Cumulative Index to Nursing and Allied Health Literature (CINAHL) (EBSCO, 1937 to 13 December 2021).
- PsycINFO (Ovid, 1806 to December week 5 2021).
- Web of Science - SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH (Thomson Reuters, 1900 to 13 December 2021)

We used an RCT filter for MEDLINE, and we applied to our Embase search terms recommended in the *Cochrane Handbook for Systematic Reviews of Interventions* (Lefebvre 2022). We applied adaptations of this filter to CINAHL, and PsycINFO. We imposed no restrictions on language of publication.

We also conducted a search of two trials registers on 13 December 2021:

- World Health Organization International (WHO) International Clinical Trials Registry Platform (ICTRP) (trialsearch.who.int/).
- ClinicalTrials.gov (www.clinicaltrials.gov/).

For the original review (Rees 2004), and the first update (Davies 2010), we searched CENTRAL in the Cochrane Library (2001, Issue 1; 2007, Issue 1), MEDLINE, Embase and CINAHL (1984 to January 2008). The search strategy developed in 2008 for the second review update included broader terms (Taylor 2014), as this search was part of a wider review project that sought to identify evidence for cardiac rehabilitation that included an update of this review and a review on exercise-based rehabilitation for coronary heart disease (Heran 2011), as well as a review on home-based versus centre-based cardiac rehabilitation (Taylor 2010). For the third update (Long 2019), we updated the search from the previous version, and we searched CENTRAL in the Cochrane Library (2013, Issue 1), MEDLINE (Ovid, 30 January 2013 week 4) and MEDLINE In-

Process (Ovid, 5 February 2013), Embase (Ovid, January 2013 week 5), CINAHL (EBSCOhost, 5 February 2013) and PsycINFO (Ovid, 30 January 2013 week 5). We made a small addition to this January 2013 search strategy to reflect more recent use of the terms 'HFpEF' and 'HFrEF'.

Searching other resources

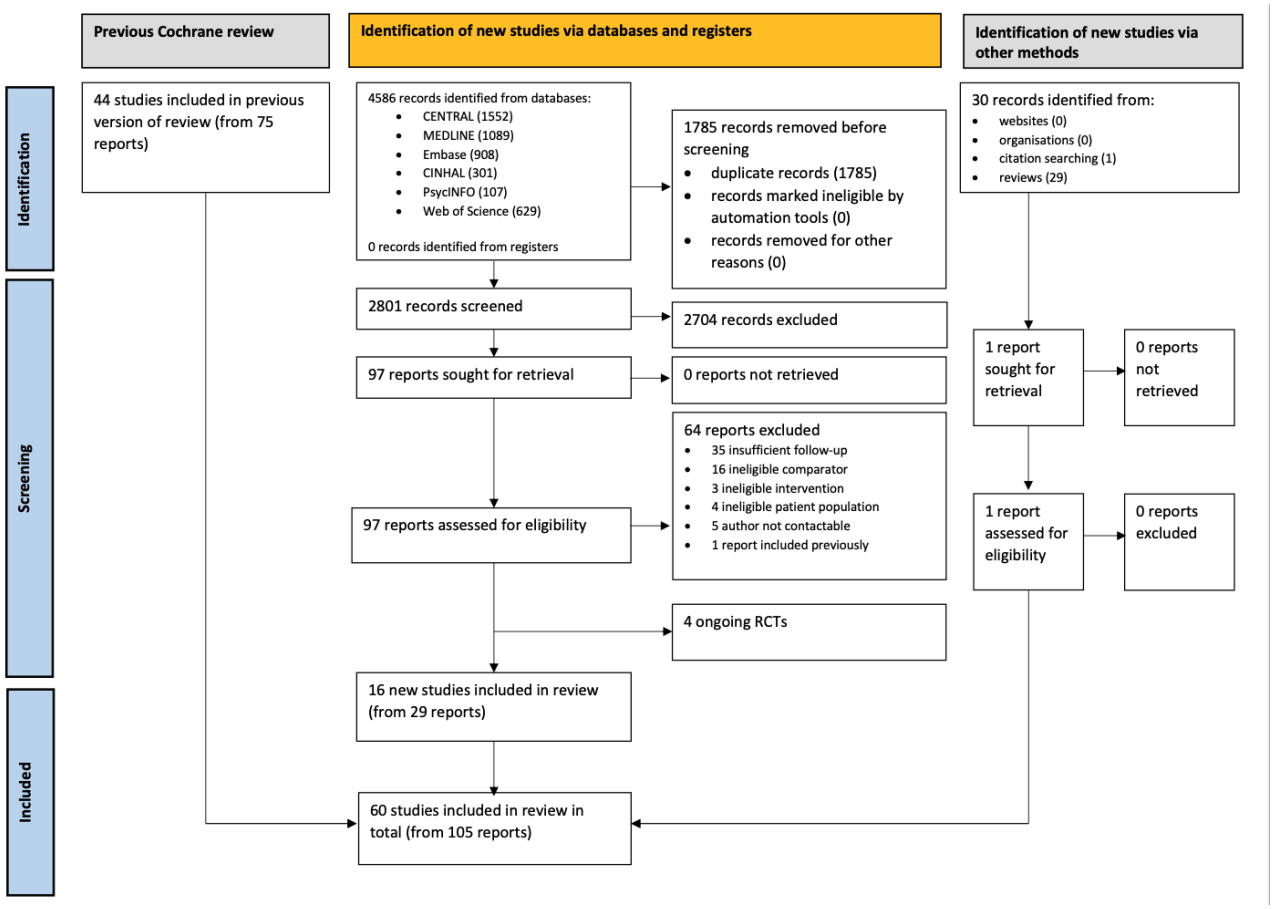
We handsearched the reference lists of all eligible trials and conducted forward citation searching of all primary trials and reviews (systematic or narrative reviews) for additional references not identified by electronic searches. We contacted experts in the field for unpublished and ongoing trials, and we contacted trial authors for additional information when necessary. We also examined any relevant retraction statements and errata for included trials.

Data collection and analysis

Selection of studies

Two review authors (CM, IM) independently screened references identified by the search strategy by reviewing titles and abstracts and discarded clearly irrelevant trials. To be selected, abstracts had to clearly identify the trial design, an appropriate population, and relevant components of the intervention, as described above. We obtained the full-text reports of all potentially relevant trials, and two review authors independently assessed them for eligibility based on the defined inclusion criteria. We resolved disagreements by discussion with a third review author (RST). We recorded the selection process in sufficient detail to produce a PRISMA flow diagram (Moher 2009; Figure 1).

Figure 1.



Data extraction and management

We extracted relevant data regarding inclusion criteria (trial design; participants; interventions including type of exercise, frequency, duration, intensity, and modality; comparisons; and outcomes) and risk of bias (randomisation, blinding, attrition, and control). Two review authors (CM, IM) independently extracted data using a standardised data extraction form that had been piloted on at least one of the trials included in the review. We resolved disagreements by discussion with a third review author (RST). We contacted trial authors when necessary to seek clarification on issues of reporting or to obtain further outcome details. We have detailed excluded trials and reasons for their exclusion in the Characteristics of excluded studies.

We extracted the following trial characteristics.

- Methods: trial design, total duration of trial, number of trial centres and locations, trial setting, withdrawals, and trial dates
- Participants: number, mean age, age range, gender, severity of condition, diagnostic criteria, inclusion criteria, and exclusion criteria
- Interventions: intervention, comparison, and co-interventions

- Outcomes: primary and secondary outcomes and time points reported
- Notes: trial funding and notable conflicts of interest of trial authors, when reported

One review author transferred data into Review Manager Web (RevMan Web), and another review author double-checked that data were entered correctly by checking trial characteristics for accuracy against the trial report.

Assessment of risk of bias in included studies

We used the RoB 1 tool to assess the risk of bias in included studies against the following domains (Higgins 2011):

- random sequence generation;
- allocation concealment;
- blinding of outcome assessment (it is not possible to blind participants or personnel in rehabilitation trials);
- incomplete outcome data;
- selective reporting.

As per our previous review version (Long 2019), we assessed three additional risk of bias domains:

- whether trial groups were balanced at baseline (small trials although randomised may be subject to chance imbalances);
- whether intervention and control groups received comparable care (apart from the exercise component of the intervention, as this may confound between-group comparisons); and
- analysis by intention to treat (as stated in each trial).

Two of these criteria (groups balanced at baseline and groups receiving comparable treatment), agreed upon in advance by the review authors, have not been validated but have been used to assess risk of bias in several of our previous Cochrane reviews on ExCR (Long 2019; Taylor 2010; Taylor 2014). Our judgements on these additional criteria are as follows.

Groups balanced at baseline

- Low risk of bias: characteristics of participants in the intervention and control groups at baseline are reported to be comparable or can be judged to be comparable (e.g. baseline data reported in Table 1) in terms of likely main prognostic factors.
- Unclear risk of bias: whether characteristics of participants in the intervention and control groups are balanced at baseline is not reported, and reported information is inadequate for assessment (e.g. no Table 1).
- High risk of bias: evidence shows substantive imbalance in the baseline characteristics of intervention and control groups with regard to likely major prognostic factors.

Groups received comparable treatment (except exercise)

- Low risk of bias: all co-interventions were delivered equally across intervention and control groups.
- Unclear risk of bias: information was insufficient to assess whether co-interventions were delivered equally across groups.
- High risk of bias: co-interventions were not delivered equally across intervention and control groups.

Intention-to-treat analysis

- Low risk of bias: the trial reports that trial authors conducted intention-to-treat analyses, and it includes all the principles of such an analysis (e.g. keeping participants in the intervention groups to which they were randomised, regardless of the intervention they actually received; measuring outcome data on all or most participants (i.e. > 80% of those randomised); imputing all missing data in the analysis via appropriate methods (e.g. multiple imputation)).
- Uncertain risk of bias: it is unclear whether trial authors performed an intention-to-treat analysis.
- High risk of bias: the trial does not include an intention-to-treat analysis, or trial authors reported substantive loss of outcome data (e.g. > 20%) and performed analyses according to imputation methods known to create bias, such as last observation carried forward.

Two review authors (CM, IM) assessed the risk of bias in eligible trials, and a third review author (RST) verified the decision. We conducted a sensitivity analysis and stratified results by risk of bias at the trial level (presence of low risk of bias for random sequence generation and allocation concealment). We graded each potential source of bias as high, low, or unclear, and we provided a quote from the trial report together with a justification for our judgement in the risk of bias table. We summarised the risk-of-bias judgements across different trials for each of the domains listed. When information on risk of bias was related to unpublished data or correspondence with a trial author, we noted this in the risk of bias table.

When considering treatment effects, we took into account the risk of bias in trials that contributed to those outcomes.

Measures of treatment effect

We processed data in accordance with the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2022). We expressed dichotomous outcomes as risk ratios (RRs) and 95% confidence intervals (CIs) for each trial. For continuous variables, we compared net changes (i.e. exercise group minus control group to obtain differences) and calculated the mean difference (MD) or the standardised mean difference (SMD) and 95% CI for each trial. We calculated SMDs when all trials assessed the same outcome but measured it in a variety of ways (e.g. different HRQoL measures). For each trial, we sought the mean change (and standard deviation (SD)) in outcomes between baseline and follow-up for both exercise and control groups, and, when not available, we instead used the absolute mean (and SD) outcome at follow-up for both groups. When trials reported more than one HRQoL outcome subscale or more than one HRQoL measure, we prioritised inclusion of data in the meta-analysis in the following manner: (1) the overall or total HRQoL score; and (2) if not available, the first HRQoL subscale reported. We tabulated all reported HRQoL outcomes for all measures and all subscales at all follow-up times included for each. When necessary, we reversed the scores of HRQoL measures so that a negative between-group difference consistently reflected improvement in HRQoL in favour of exercise-based cardiac rehabilitation (ExCR). We considered treatment effects for HRQoL in terms of clinically meaningful differences (e.g. we considered a 5-point difference on the MLWHF questionnaire as clinically meaningful; Rector 1992).

Unit of analysis issues

For trials with more than one relevant intervention arm included in the same analysis, we divided the number randomised in the control group by the number of intervention arms to obtain the denominator for data analysis. In accordance with the *Cochrane Handbook for Systematic Reviews of Intervention* (Higgins 2022). If we had included data from cross-over trials, we would have included both periods of any cross-over trials identified, assuming that (1) there had been a washout period considered long enough to reduce carry-over, (2) no irreversible events such as mortality had occurred, and (3) appropriate statistical approaches had been used. If we had included cluster trials, we would have considered whether the reported data analysis had appropriately taken account of the aggregate nature of the data.

Dealing with missing data

We contacted trial authors or trial sponsors to verify key trial characteristics and to obtain missing numerical outcome data when possible (e.g. when we identified a trial as abstract only). When this was not possible, and when missing data were not thought to introduce serious bias, we explored the impact of including such trials on the overall assessment of results by performing a sensitivity analysis. We did not numerically analyse the effect of missing outcome data.

Assessment of heterogeneity

We explored heterogeneity among included trials qualitatively by comparing their characteristics, and quantitatively, using the Chi^2 test for heterogeneity (Deeks 2022), and the I^2 statistic (Higgins 2003).

Assessment of reporting biases

We used funnel plots and Egger tests to assess potential small-trial effects and publication bias for outcomes with an adequate number (≥ 10) of trials (Egger 1997; Page 2022).

Data synthesis

We processed data in accordance with the *Cochrane Handbook for Systematic Reviews of Interventions* (Deeks 2022), and we undertook meta-analyses when these were meaningful (i.e. when treatments, participants, and the underlying clinical question were similar enough for pooling to make sense). We pooled data from each trial using a random-effects model, which provided a more conservative statistical comparison of the difference between intervention and control, because a confidence interval around a random-effects estimate is wider than a confidence interval around a fixed-effect estimate. We completed data synthesis and analysis using Review Manager Web online software (RevMan Web).

Subgroup analysis and investigation of heterogeneity

We explored potential heterogeneity in ExCR via two approaches: (1) within-trial subgroup analyses (supported by subgroup × intervention/control interaction terms), and (2) between-trial analyses via meta-regression. We used meta-regression to examine the association between effects of exercise on all-cause mortality, all-cause hospitalisation, and HRQoL (MLWHF or other measures) up to 12 months, as these three outcomes were reported by the greatest number of trials. The meta-regression included the following specific trial co-variates.

- Type of rehabilitation (exercise only versus comprehensive)
- Setting (hospital only, home only, hybrid)
- Type of exercise (aerobic training alone or aerobic plus resistance training)
- Dose of aerobic exercise (calculated as overall number of weeks of training × mean number of sessions per week × mean duration of sessions in minutes)
- Overall risk of bias ('low', i.e. absence of bias in allocation concealment and sequence generation)
- Single centre versus multicentre
- Publication date
- Latest follow-up duration
- Continent (North America versus Europe versus other)
- Sample size

We added year of publication as an additional trial-level factor (pre- versus post-2000) to assess the potential effect of a change in the standard of usual care over time, that is, to reflect when beta blockers, angiotensin-receptor blockers, and angiotensin-converting enzyme inhibitors became established therapies for heart failure (Shekelle 2003). Given the relatively small ratio of trials to co-variates, we limited meta-regression to univariate analysis (Deeks 2022). Due to the risks of multiple testing, we used a conservative cut-off of $P \leq 0.01$ for interpretation of meta-regression results.

Sensitivity analysis

We compared the results of meta-analysis including all trials versus meta-analysis including only those trials judged to have overall low risk of bias (low risk of allocation concealment and sequence generation).

Summary of findings and assessment of the certainty of the evidence

Two review authors (CM, LL) independently employed GRADE to interpret trial results (Ryan 2016; Schünemann 2022). We used the five GRADE considerations (trial limitations, consistency of effect, imprecision, indirectness, and publication bias) to assess the certainty of a body of evidence as it related to trials that contributed data to the meta-analyses and narrative summaries for prespecified outcomes. We resolved any discrepancies in judgement through discussion or by consulting a third author (RST). One review author (CM/LL) used RevMan Web to create a summary of findings table that included the following prespecified outcomes: all-cause mortality; all-cause hospital admissions; heart failure hospital admissions; and HRQoL.

RESULTS

Description of studies

We have presented the details of trials included in this review in the Characteristics of included studies, and reasons for exclusion in the Characteristics of excluded studies. We have detailed the status of ongoing trials in the Characteristics of ongoing studies.

Results of the search

The electronic search for this update yielded a total of 4586 titles and abstracts. We identified one additional trial through backward-

and-forward searching of the reference lists of eligible publications (Andryukhin 2010).

After deduplication, we found that 2795 trials were eligible for screening. Following screening, we formally evaluated 95 reports for inclusion or exclusion by retrieving the full-text publications. We excluded a total of 62 full-text reports (see Characteristics of excluded studies). In this update, we newly included a total of 16 RCTs (29 reports), bringing the total of included studies to 60 (105 reports). See Characteristics of included studies. We also identified four ongoing studies (Characteristics of ongoing studies). We have summarised the trial selection process in the PRISMA flow diagram (Moher 2009; Figure 1).

Included studies

The previous versions of this Cochrane review contributed a total of 44 trials (8 in Rees 2004, 11 in Davies 2010, 14 in Taylor 2014, and 11 in Long 2019) to this latest update. As part of the 2010 review, several trials included in the 2004 review were excluded, as their follow-up was less than six months, or trial authors reported only exercise capacity outcomes. For this update, we identified 16 new trials investigating 155 comparisons in patients with heart failure (Andryukhin 2010; Gary 2019; Hagglund 2018; Hasanpour-Dehkordi 2020; Hieda 2021; Jaarsma 2020; Kitzman 2021; Liu 2018; Lugo 2018; Mueller 2021; Peng 2018; Ricca-Mallada 2017; Ryu 2018; Santa-Clara 2019; TELEREH-HF 2020; Wang 2021). Hasanpour-Dehkordi 2020 and Mueller 2021 both provided two comparisons.

The 60 included trials (105 publications) randomised 8728 participants predominantly with HFrEF and NYHA classes II and III heart failure. Nine trials included an (undefined) proportion of people with HFpEF (Andryukhin 2010; Antonicelli 2016; Davidson 2010; Gary 2010; Jaarsma 2020; Lang 2018; Nilsson 2008; Reeves 2017; Wall 2010). This update included two new trials that included people with HFpEF. Most trials were small, single-centre trials. Two large trials contributed ~40% (3181 participants) of all included participants (HF ACTION 2009; TELEREH-HF 2020).

The mean age of participants across the included trials ranged from 51 to 81 years. The included trials recruited predominantly men (median 78%); however, the newly included trials included women more frequently. Only 10 trials reported on ethnicity. Nine trials reported follow-up in excess of 12 months (Andryukhin 2010; Austin 2005; Belardinelli 1999; Belardinelli 2012; Cowie 2014; HF ACTION 2009; Jónsdóttir 2006; Mueller 2007; TELEREH-HF 2020). Six trials included more than one exercise intervention arm, and each contributed two separate comparative arms for the purpose of the meta-analysis (Cowie 2014; Gary 2010; Hasanpour-Dehkordi 2020; Kaltsatou 2014; Klocek 2005; Mueller 2021).

All trials evaluated an aerobic intervention, and 21 trials (22 comparisons) also included resistance training (Andryukhin 2010; Austin 2005; Chen 2018; DANREHAB 2008; Davidson 2010; Dracup 2007; Hagglund 2018; Hieda 2021; Jolly 2009; Jónsdóttir 2006; Kaltsatou 2014; Kitzman 2021; Koukouvou 2004; McKelvie 2002; Norman 2012; Peng 2018; Pozehl 2008; Reeves 2017; TELEREH-HF 2020; Witham 2005; Witham 2012).

Included trials most commonly delivered exercise training in an exclusively centre-based setting or in a centre-based setting in combination with some home exercise sessions. Sixteen trials (18 comparisons) were conducted in a home-based setting (Andryukhin 2010; Cowie 2014; Dalal 2018; Dracup 2007; Du 2018; Gary 2010; Gary 2019; Jaarsma 2020; Jolly 2009; Kaltsatou 2014; Lang 2018; Passino 2006; Peng 2018; Ryu 2018; TELEREH-HF 2020; Wall 2010).

The dose of exercise training ranged widely across trials, with session duration of 8 to 120 minutes, one to seven sessions per week, intensity of 40% to 80% maximal heart rate to 50% to 85% maximal oxygen uptake (VO_2 max) to Borg rating 11 to 18, over a period of eight to 120 weeks. In addition to exercise training, 18 trials included other ('comprehensive rehabilitation') elements that consisted of educational and psychological interventions (Andryukhin 2010; Bocalini 2008; Chen 2018; Dalal 2018; DANREHAB 2008; Davidson 2010; Gary 2010; Gary 2019; Jolly 2009; Jónsdóttir 2006; Lang 2018; Liu 2018; Lugo 2018; Mueller 2007; Myers 2000; Nilsson 2008; Pozehl 2008; Witham 2012).

All included trials employed a usual-care control group with a formal no-exercise training intervention together with a wide range of active interventions, such as education, psychological intervention, and medical care.

All but 21 trials reported their funding sources (Belardinelli 1999; Bocalini 2008; Chen 2018; Davidson 2010; Giallauria 2008; Giannuzzi 2003; Gielen 2003; Gottlieb 1999; Hagglund 2018; Hambrecht 1995; Jónsdóttir 2006; Klocek 2005; Koukouvou 2004; Liu 2018; McKelvie 2002; Mehani 2013; Nilsson 2008; Passino 2006; Peng 2018; Ryu 2018; Wang 2021). Two trials were funded by the pharmaceutical industry (HF ACTION 2009; Keteyian 1996).

We have provided details of the trials included in this review in Characteristics of included studies.

Excluded studies

We excluded a substantive number of titles and abstracts. Common reasons for exclusion were active comparator, non-RCT design, and follow-up duration of less than six months. We presented reasons for excluding 62 full-text articles (reporting 61 studies) in Characteristics of excluded studies.

Ongoing studies

Four trials were still ongoing when we completed this update (Bobenko 2019; Koifman 2014; Vetrovsky 2017; Zuazagoitia 2010). See Characteristics of ongoing studies.

Risk of bias in included studies

The overall risk of bias in included trials was generally low or unclear. The level of reporting improved in more recent trials (Figure 2; Figure 3). Trial authors reported particularly poorly the details of random sequence generation and allocation concealment of random allocation sequence and blinding.

Figure 2. Risk of bias graph: review authors' judgements about each risk-of-bias domain presented as percentages across all included studies.

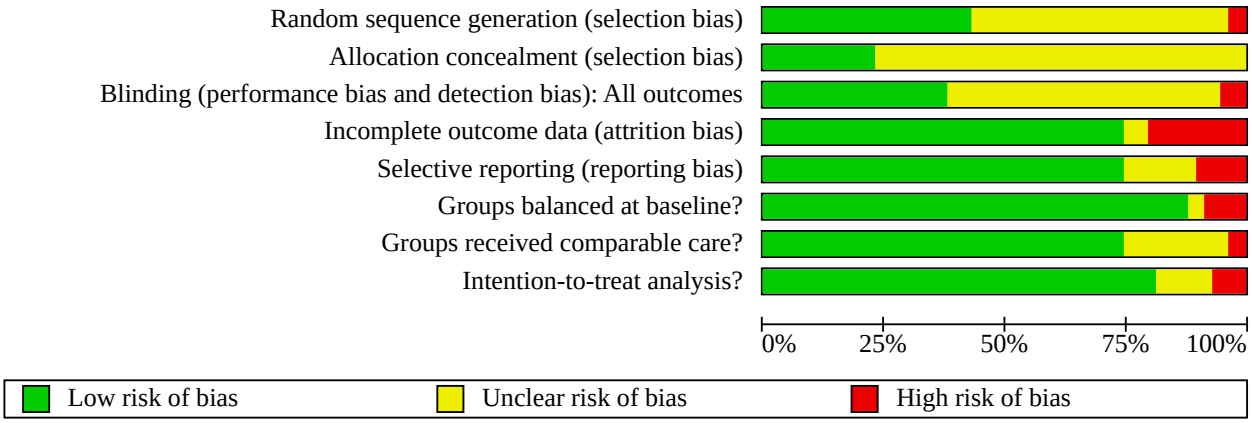


Figure 3. Risk of bias summary: review authors' judgements about each risk-of-bias domain for each included study.

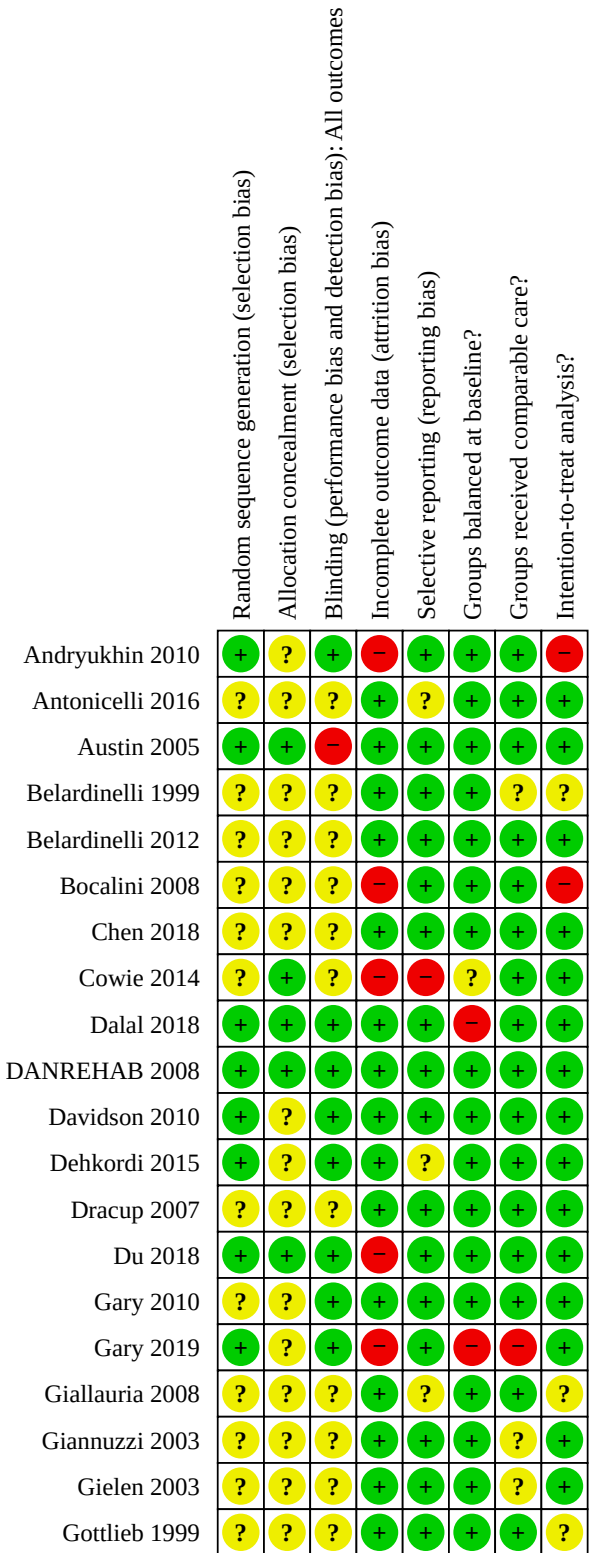


Figure 3. (Continued)

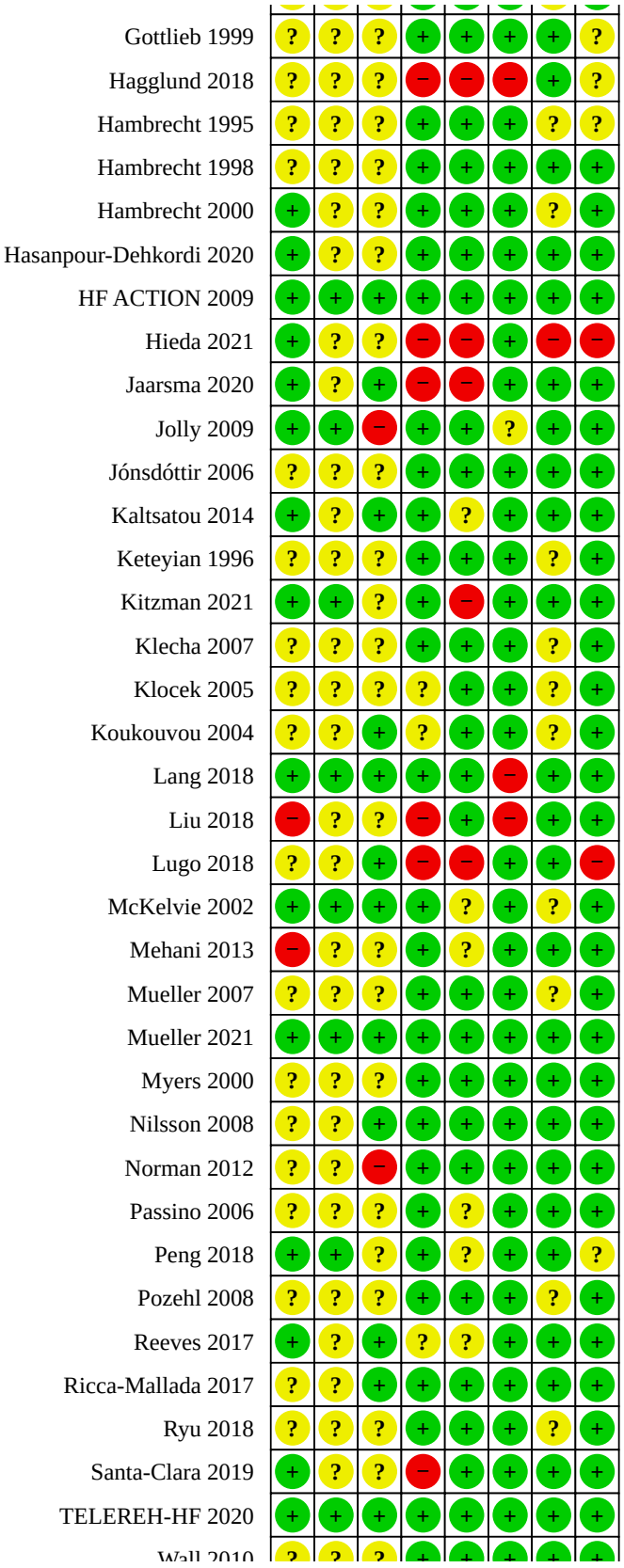
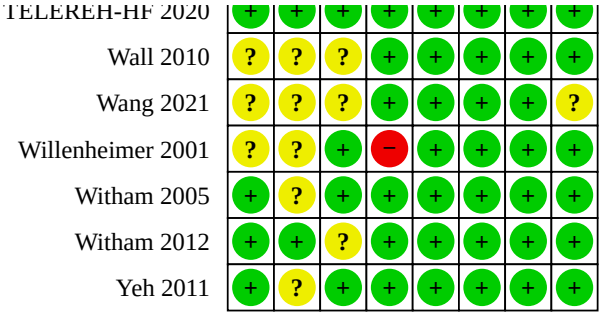


Figure 3. (Continued)



Allocation

We judged Austin 2005, Dalal 2018, DANREHAB 2008, Du 2018, HF ACTION 2009, Jolly 2009, Kitzman 2021, Lang 2018, McKelvie 2002, Peng 2018, TELEREH-HF 2020, and Witham 2012 to be at low risk of bias for allocation concealment and sequence generation.

Random sequence generation

All trials randomly allocated participants to trial conditions. We deemed that 32 trials had unclear risk of bias and 26 trials had low risk of bias in the method used to generate randomisation sequence. We judged two trials to have a high risk of bias (Liu 2018; Mehani 2013).

Allocation concealment

We deemed that 47 trials had unclear risk of bias and 13 trials had low risk of bias in the methods used to conceal participant allocation. We did not judge any trials to have a high risk of bias for allocation concealment.

Blinding

Given the nature of an exercise intervention, it is not possible to blind participants, carers or personnel. We deemed that 34 trials had unclear risk of bias and 23 trials had low risk of bias in the methods used to attempt to blind participants/carers. We judged three trials to be at high risk of bias for blinding of outcome assessment (Austin 2005; Jolly 2009; Norman 2012).

Incomplete outcome data

When reported, losses to follow-up and rates of dropout were relatively high, ranging from 5% to 40% across trials. We judged 48 trials to be at low risk of bias, which we defined as less than a 20% dropout rate for each arm of the trial. We judged 12 trials to be at high risk of bias (Andryukhin 2010; Bocalini 2008; Cowie 2014; Du 2018; Gary 2019; Hagglund 2018; Hieda 2021; Jaarsma 2020; Liu 2018; Lugo 2018; Santa-Clara 2019; Willenheimer 2001). Eight of these 12 trials are new to this review in this update.

Andryukhin 2010 provided data at follow-up for only 35 of 50 (70%) participants for HRQoL outcomes. Bocalini 2008 provided data at follow-up for only 42 of 53 (79%) participants. Cowie 2019 provided follow-up data for only 46 of 60 participants (77%). Du 2018 had a high dropout rate in the intervention group (24%) compared to the control group (14%), and provided no explanation for differences between the two groups. Gary 2019 provided data at follow-up for only 14/24 (58%) participants in the ExCR-only group. Hagglund 2018 reported outcome data for only 12 of 20 (60%) participants randomised at six months' follow-up. Hieda 2021 provided data for only 31 out of the 56 (55%) randomised participants at final follow-up. Jaarsma 2020 reported 234 of 305 (77%) of intervention, and 230 of 300 (76%) of control provided outcomes for primary analysis at 12 months. Liu 2018 reported 53 of 70 (76%) of participants randomised to no exercise control, and 63 of 71 (89%) participants randomised to exercise intervention for primary analysis at 12 months. Lugo 2018 provided data as follows: exercise 15 of 23 (65%); control 16 of 26 (62%) reported complete outcome data at six months. Santa-Clara 2019 provided data at follow up for 20 of 34 (59%) of exercise intervention group, and 17 of 29 (58%) of control group. Willenheimer 2001 reported outcome data for only 43 of 54 participants (80%) randomised at 10 months' follow-up. We undertook no imputation or sensitivity analysis to assess effects of loss to follow-up in that trial, and its authors stated that participants available at 10 months' follow-up are representative.

Selective reporting

We judged the risk of selective reporting to be unclear in eight trials (Antonicelli 2016; Dehkordi 2015; Giallauria 2008; Kaltsatou 2014; McKelvie 2002; Mehani 2013; Passino 2006; Peng 2018). We judged six trials to be at high risk of bias for selective reporting (Cowie 2014; Hagglund 2018; Hieda 2021; Jaarsma 2020; Kitzman 2021; Lugo 2018). The 46 other included trials were at low risk of bias.

Other potential sources of bias

Groups balanced at baseline

Of the 60 included studies, we assessed 53 to be at low risk of bias in terms of baseline imbalance. Seven trials provided objective evidence of imbalance in baseline characteristics. Five were deemed to be at high risk of bias (Dalal 2018; Gary 2019; Hagglund 2018; Lang 2018; Liu 2018). Two were deemed to be at an unclear risk of bias (Cowie 2014; Jolly 2009).

Groups received comparable care

Because some trials did not report co-intervention details for both exercise and control groups, they may be prone to performance bias. Two were deemed to be at high risk of bias (Gary 2019; Hieda 2021). Thirteen were deemed to be at an unclear risk of bias (Belardinelli 1999; Giannuzzi 2003; Gielen 2003; Hambrecht 1995; Hambrecht 2000; Keteyian 1996; Klecha 2007; Klocek 2005; Koukouvou 2004; McKelvie 2002; Mueller 2007; Pozehl 2008; Ryu 2018). We assessed the remaining 45 studies to be at low risk of bias.

Intention-to-treat analysis

Most trials performed an intention-to-treat analysis, comparing exercise and control group outcomes according to the initial random allocation. Four trials did not perform an intention-to-treat analysis, and as such we judged them to be at high risk of bias (Andryukhin 2010; Bocalini 2008; Hieda 2021; Lugo 2018).

Effects of interventions

See: **Summary of findings 1** Exercise-based cardiac rehabilitation compared to usual care for adults with heart failure (short-term)

All-cause mortality

Short-term (up to 12 months) follow-up

A total of 34 trials (36 comparisons; 3941 participants) reported all-cause mortality at up to 12 months' follow-up. Six trials reported no deaths in either the ExCR or the control arm (Dehkordi 2015; Gielen 2003; Kaltsatou 2014; Klecha 2007; Lang 2018; Reeves 2017).

There was no evidence of a difference between the ExCR and control interventions with regards to their impact on all-cause mortality, with 100 deaths out of 2013 participants (5.0%) in the ExCR group versus 112 deaths out of 1928 participants (5.8%) in the control group (RR 0.93, 95% CI 0.71 to 1.21; heterogeneity: P = 0.95, I^2 = 0%; Analysis 1.1). The test for overall effect was P = 0.58. We assessed the evidence to be of low certainty using GRADE because of concerns about risk of bias (random sequence generation and allocation concealment) and concerns about imprecision (small number of events at < 300). See Summary of findings 1.

Long-term (more than 12 months) follow-up

Andryukhin 2010, Austin 2005, Belardinelli 1999, HF ACTION 2009, Jónsdóttir 2006, Mueller 2007 and TELEREH-HF 2020 reported mortality at 18, 60, 26, 30, 28, 74, and 26 months, respectively. Although not reported in their original publication, we obtained mortality data at 10 years from Belardinelli 2012 by contacting the trial authors.

There was evidence of a reduction in all-cause mortality when pooled across the longest follow-up point of the eight trials, with 300 deaths out of 1887 participants (15.9%) in the ExCR group versus 334 deaths out of 1893 participants (17.6%) in the control group (RR 0.87, 95% CI 0.72 to 1.04; heterogeneity: P = 0.31, I^2 = 16%; Analysis 1.2). The test for overall effect was P = 0.12. HF ACTION 2009 dominated this effect estimate. We assessed the evidence to be of high certainty.

Heart failure mortality

Few trials reported information on whether participants died due to heart failure. In this latest update, only one trial reported heart failure-specific mortality with one death due to heart failure in the high-intensity interval training arm and no heart failure-specific deaths in either the moderate continuous training or control arms (Mueller 2021).

All-cause hospital admissions

Short-term (up to 12 months) follow-up

ExCR likely reduced all-cause hospital admissions at up to 12 months' follow-up, with 182 admissions out of 1148 participants (15.9%) in the ExCR group versus 270 admissions out of 1135 participants (23.8%) in the control group (RR 0.69, 95% CI 0.56 to 0.86; heterogeneity: P = 0.14, I^2 = 24%; 23 trials, 24 comparisons, 2283 participants; Analysis 1.3). The test for overall effect was P = 0.0010. Ryu 2018 provided two relevant comparisons. Using GRADE, we assessed the evidence to be of moderate certainty because of concerns about risk of bias (random sequence generation, allocation concealment, and blinding). See Summary of findings 1.

Long-term (more than 12 months) follow-up

ExCR likely resulted in a reduction in all-cause hospital admissions in the long term, with 1004 admissions out of 1757 participants (57.1%) in the ExCR group versus 1079 admissions out of 1752 participants (61.4%) in the control group (RR 0.84, 95% CI 0.70 to 1.01; heterogeneity: P = 0.01, I^2 = 61%; 7 trials, 8 comparisons, 3509 participants; Analysis 1.4). The test for overall effect was P = 0.06. We judged the evidence to be of moderate certainty because of concerns about inconsistency.

Heart failure-related hospital admissions

Short-term (up to 12 months) follow-up

There was some evidence that ExCR likely reduced the risk of heart failure-specific hospital admissions in the short term, with 26 admissions out of 457 participants (5.6%) in the ExCR group versus 36 admissions out of 554 participants (6.4%) in the control group (RR 0.82, 95% CI 0.49 to 1.35; heterogeneity: P = 0.41, I^2 = 4%; 10 trials, 10 comparisons, 911 participants; Analysis 1.5). The test for overall effect was P = 0.43. Using GRADE, we assessed the evidence to be of moderate certainty because of concerns about risk of bias (random sequence generation, allocation concealment, and blinding). See Summary of findings 1.

Long-term (more than 12 months) follow-up

There was some evidence that ExCR reduced the risk of heart failure-specific hospital admissions in the long term, with 131 admissions out of 558 participants (23.5%) in the ExCR group versus 140 admissions out of 540 participants (25.9%) in the control group (RR 0.74, 95% CI 0.50 to 1.08; heterogeneity: P = 0.15, I^2 = 38%; 5 trials, 6 comparisons, 1098 participants; Analysis 1.6). The test for overall effect was P = 0.12.

Health-related quality of life

Of the 60 included trials, 39 trials reported a validated HRQoL measure (Table 1). Most trials reported disease-specific quality of life using the MLWHF questionnaire; although the large HF ACTION 2009 trial used the Kansas City Cardiomyopathy Questionnaire. Trial authors also assessed generic HRQoL using the EuroQoL Group Quality of Life Questionnaire based on 5 dimensions (EQ-5D), the SF-36, the Psychological General Wellbeing index (PGWB), the Patient's Global Assessment of Quality of Life (PGAQoL), and Spritzer's Quality of Life Index (QLI). Gottlieb 1999 reported HRQoL values at follow-up for the ExCR group but not for the control group. Of the 106 comparisons, 40 (38%) reported statistical superiority in one or more HRQoL domains following ExCR compared with control. Sixty-three comparisons (59%) reported no difference. Three comparisons (3%) reported a lower HRQoL domain score with ExCR than with control.

Short-term (up to 12 months) follow-up, MLWHF only

Lower MLWHF questionnaire scores indicate better patient HRQoL. We found evidence of high levels of statistical heterogeneity in

the ExCR-control difference in MLWHF scores at follow-up across trials. Pooled data showed ExCR likely led to a clinically important improvement in HRQoL (MD −7.39, 95% CI −10.30 to −4.47; heterogeneity: P < 0.00001, I^2 = 82%; 21 trials, 22 comparisons, 2699 participants; Analysis 1.7). The test for overall effect was P < 0.00001. We assessed the evidence to be of moderate certainty because of inconsistency, with considerable heterogeneity. See Summary of findings 1.

Short-term (up to 12 months) follow-up, all HRQoL measurement scales

Pooling across all trials, regardless of the HRQoL scale used, showed uncertain evidence of a small effect size of improvement with ExCR (SMD −0.52, 95% CI −0.70 to −0.34; heterogeneity: P < 0.00001, I^2 = 86%; 33 trials, 37 comparisons, 4769 participants; Analysis 1.8). The test for overall effect was P < 0.00001. As advised in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011), we excluded McKelvie 2002 from this SMD analysis as it reported the difference in HRQoL between baseline and follow-up, while all other included trials were based on final HRQoL outcome scores. We assessed this evidence to be of very low certainty because of concerns about risk of bias (random sequence generation and allocation concealment), inconsistency with considerable heterogeneity, and suspected publication bias. See Summary of findings 1.

Long-term (more than 12 months) follow-up, MLWHF only

There was evidence of improvement in MLWHF with ExCR compared with control (MD −9.49, 95% CI −17.48 to −1.50; heterogeneity: P = 0.03, I^2 = 73%; 3 trials, 3 comparisons, 329 participants; Analysis 1.9). The test for overall effect was P = 0.02. The evidence was of very low certainty because of concerns about risk of bias (random sequence generation, allocation concealment), inconsistency with considerable heterogeneity, and imprecision due to small numbers of participants (< 400). No long-term data assessed by other HRQoL scales were available.

Costs and cost-effectiveness

Seven included trials reported economic data, with three undertaking a full cost-effectiveness analysis (Dalal 2018; Georgiou 2001; HF ACTION 2009), and four reporting costs (Cowie 2014; Dalal 2018; Lang 2018; Witham 2012; Table 2). Based on data reported in Belardinelli 1999, Georgiou 2001 estimated an additional mean healthcare cost in the ExCR group compared with the control group of USD 3227 per person. Researchers calculated this cost by subtracting the averted hospitalisation cost (USD 1336 per person) from the cost of exercise training and wages lost due to exercise training -(estimated at USD 4563 per person). Based on exponential survival modelling to 15.5 years, the estimated increment in life expectancy with exercise was 1.82 years per person compared with control, and the incremental cost-effectiveness ratio was USD 1773 per life-year saved. The HF ACTION 2009 group estimated a mean gain in quality-adjusted life-years (QALYs) of 0.03 at an additional mean cost of USD 1161 per person at 2.5 years' follow-up (HF ACTION 2009). Although they did not report an incremental cost-effectiveness ratio, trial authors stated that there was an 89.9% probability that ExCR was more cost-effective than usual care at a maximum willingness-to-pay threshold of USD 50,000. The REACH-HF group estimated a mean gain in QALYs of 0.23, at an additional cost of GBP 1721 per QALY saved with ExCR (Dalal 2018). They estimated that there was a 78% probability that the REACH-HF ExCR intervention was more cost-effective than usual care, at the willingness-to-pay threshold of GBP 20,000 per QALY. Witham 2012 reported that mean costs in the exercise group were lower (by GBP 477.85 per person) than in the control group at six months' follow-up. This cost difference was primarily the result of a reduction in the days of hospital admission in the exercise group compared with the control group. No clear between-group differences in costs or outcomes were observed across these three trials. Cowie 2014 reported that ExCR programmes incurred similar costs, whether delivered in the patient's home (GBP 196.53 per patient) or in a supervised hospital setting (GBP 221.58 per patient).

Meta-regression

We examined predictors of all-cause mortality, all-cause hospital admissions, heart failure-related hospital admissions, HRQoL by MLWHF only, and HRQoL by all scales (follow-up of 12 months or less) using univariate meta-regression. There was evidence of association (at P < 0.05) between outcomes and trial-level covariates in terms of risk of bias, publication date, and location of trial (continent; Table 3).

Within-trial subgroup analyses

Several trial authors reported that they had undertaken subgroup analyses. However, most of these analyses were not based on a formal subgroup interaction test with the intervention effect but instead on a cross-sectional association between particular participant characteristics and outcomes, for example, association between participant age at baseline and mortality, regardless of exercise or control group allocation (Austin 2005; Belardinelli 1999; Belardinelli 2012; Davidson 2010; Klocek 2005). Two trials reported subgroup analyses although the statistical methods that they used were unclear (Pozehl 2008; Yeh 2011).

Four trials carried out prespecified subgroup analyses (Dalal 2018; HF ACTION 2009; Jaarsma 2020; TELEREH-HF 2020; Table 4). The HF ACTION 2009 authors reported no evidence of differences in intervention effects as assessed for either the primary outcome (all-cause mortality or hospital admissions) or HRQoL (Kansas City Cardiomyopathy Questionnaire overall score) across several participant-defined subgroups. The HF ACTION 2009 group also undertook a large post hoc observational analysis of people assigned to exercise training (Keteyian 2012). This analysis shows that the volume of exercise undertaken by participants was associated with the risk for clinical events, and moderate levels (3 to 7 metabolic equivalent (MET) hours per week) of exercise were needed to derive clinical benefit. Dalal 2018 found no evidence of subgroup treatment interaction. TELEREH-HF 2020 only found evidence of an interaction with regards to site. Jaarsma 2020 found no evidence of an interaction in a multitude of subgroups, except the subgroup of those premorbid with stroke, which worsened treatment effect.

Sensitivity analyses

We undertook the following sensitivity analyses by restricting to data from studies at low risk of bias. For all-cause mortality at short-term follow-up, we found no evidence of a difference (RR 1.26, 95% CI 0.86 to 1.85; I^2 = 79%; 8 trials, 1443 participants). For all-cause hospitalisation at short-term follow-up, we observed a similar effect estimate to the overall effect estimate of the main analysis (RR 0.78, 95% CI 0.58 to 1.04; I^2 = 24%; 6 trials, 874 participants). This was also true for heart failure-related hospitalisation at short-

term follow-up, where a similar effect estimate to that of the overall analysis was noted (RR 0.72, 95% CI 0.25 to 2.02; I^2 = 14%; 4 trials, 742 participants). For HRQoL measured by MLWHF at short-term follow-up, sensitivity analysis of studies at low risk of bias showed a reduced benefit (MD −3.32, 95% CI −8.20 to 1.57; I^2 = 82%; 7 trials, 947 participants); however, for HRQoL by all scales at short-term follow-up, pooled data from studies at low risk of bias suggest ExCR improved HRQoL in the short term (SMD −0.28, 95% CI −0.51 to −0.04; I^2 = 85%; 9 trials, 2495 participants). This suggests a small clinical improvement.

Small-trial bias

We observed no funnel plot asymmetry for all-cause mortality, all-cause hospital admissions, and HRQoL by MLWHF only (Egger test P > 0.05) at any time point. We found evidence of asymmetry for heart failure-related hospital admission (Egger test P = 0.015) and HRQoL by all scales (Egger test P = 0.002).

DISCUSSION

Summary of main results

This review update shows that compared with no-exercise control there was no evidence that participation in ExCR resulted in a difference in the risk of all-cause mortality in the short term (up to 12 months' follow up; Summary of findings 1). Benefits of ExCR included evidence of a likely reduction in both all-cause and heart failure-related hospitalisation risk in both the short and long term, and a likely clinically meaningful improvement in HRQoL. A small number of trial-based economic evaluations support the acceptable cost-effectiveness of ExCR compared to control. Trials of home- and hybrid- (i.e. both home- and centre-) based ExCR delivery were associated with similar improvements in outcome compared to traditional, centre-based programmes.

Overall completeness and applicability of evidence

Consistent with the previous version of this Cochrane review, we found included trials with a greater proportion of women, older patients, and patients with HFpEF, and therefore more reflective of the wider heart failure population in clinical practice. The increasing evidence for home and hybrid mode of ExCR delivery is particularly important given the need to improve rehabilitation access and uptake for heart failure patients (Laoutaris 2022). However, only two trials identified patients with acute decompensated heart failure (Kitzman 2021; Reeves 2017).

Quality of the evidence

Whilst the majority of included trials poorly reported their methodology in full, especially random sequence generation and allocation concealment, more recently published trials are better reported (Figure 2).

Overall, the evidence ranged in certainty from high to very low (Summary of findings 1). All-cause mortality outcomes were the strongest certainty; we deemed long-term findings to be high certainty and downgraded short-term findings to low certainty due to risk of bias concerns and imprecision. We downgraded short-term and long-term all-cause hospitalisation outcomes for risk of bias concerns and inconsistency, respectively. We downgraded heart failure-related hospitalisation to moderate certainty due to suspected publication bias. We downgraded short-term overall MLWHF due to risk of bias and inconsistency but uprated it as the effect size included the minimal clinically important difference; a change of approximately 5 points in overall MLWHF score has been associated with a clinically meaningful patient-perceived change in their health status (Gonzalez-Saenz 2019). The other HRQoL outcomes (long-term overall MLWHF and all HRQoL measures), we downgraded to very low certainty due to concerns about risk of bias, inconsistency, and high imprecision due to small numbers of participants (long-term overall MLWHF).

Potential biases in the review process

We believe this is the most comprehensive systematic review to date of RCT evidence on the impact of ExCR on people with heart failure. However, our review has some limitations. The overall risk of bias in included trials was generally low or unclear, although evidence shows improvement in the level of reporting in trials published in more recent years. However, details of random sequence generation, allocation concealment, and blinding were particularly poorly reported and therefore were subject to bias. Also, funnel plot asymmetry for heart failure-related hospitalisation and HRQoL (all scales) is indicative of small-trial bias and possible publication bias. Clinical heterogeneity was high, as there was wide variation among both intervention and control regimes. As this review employed a broad definition of ExCR, included trials covered a range of rehabilitation programmes that varied in terms of their inclusion of educational and psychological interventions, and exercise training dose. To reflect this clinical heterogeneity, we employed a random-effects meta-analysis model. The control regime also varied greatly between trials. For example, some control regimes included medication review, heart failure-related educational programmes, or attention control, such as a flexibility programme, while others included only basic care. This variation in clinical heterogeneity of interventions and controls likely contributed to the considerable level of statistical heterogeneity observed for some outcomes.

This updated review (or its previous versions) does not separately report adverse events. However, it is important to note that all-cause mortality and HRQoL are both included outcomes that 'net' the potential benefits and harms of ExCR. Furthermore, all-cause hospitalisations, a key contributor to serious adverse events, are also reported. However, we do acknowledge that this review does not report more minor adverse events such as falls or chest pain.

The prescribed dose of exercise training ranged widely across trials (e.g. session duration: 8 to 120 minutes, 1 to 7 sessions per week). While trials reported a prescribed dose of exercise (and in some cases, delivery of other interventions), few, if any, reported the actual level of participation by participants. So, we were not able to assess the impact of ExCR intervention adherence, either in terms of actual engagement in exercise or other intervention components.

Whilst there was considerable statistical heterogeneity in HRQoL outcome across trials, in meta-regression analyses, the only consistent trial-level predictive factor was risk of bias - there being larger ExCR effects in trials of overall high compared to low risk of bias (Table 3).

Readers should note that the evidence base presented is from December 2021 and with the COVID-19 social restrictions being lifted in 2022 across many countries, evidence not yet captured by

the current search may impact the review conclusions. We intend to update the evidence base as soon as possible.

Agreements and disagreements with other studies or reviews

The individual patient data (IPD) meta-analysis, Exercise Training Meta-Analysis of Trials for Chronic Heart Failure (ExTraMATCH) was originally published in 2004 (ExTraMatch 2004); recently the ExTraMATCH II Collaboration updated this IPD meta-analysis based on RCTs included in the 2014 Cochrane Review (ExTraMATCH II; Taylor 2014). The ExTraMATCH II events analysis included data obtained from 18 trials including 3912 participants with HFrEF. The ExTraMATCH Collaboration authors reported that, compared to control data, they found no statistically significant differences in pooled time-to-event estimates in favour of ExCR, although confidence intervals were wide (all-cause mortality: hazard ratio (HR) 0.83, 95% CI 0.67 to 1.04; heart failure-specific mortality: HR 0.84, 95% CI 0.49 to 1.46; all-cause hospitalisation: HR 0.90, 95% CI 0.76 to 1.06; and heart failure-specific hospitalisation: HR 0.98, 95% CI 0.72 to 1.35). Lack of statistically significant impact of ExCR on all-cause mortality is consistent with the findings of this updated Cochrane review. However, the finding of no reduction in all-cause or heart-failure hospitalisations with ExCR contrasts with the information provided in this update, and in the 2014 version of this Cochrane review. A possible explanation for this difference is that the ExTraMATCH II authors were not able to obtain participant data from all trial authors, and that not all included trials collected hospitalisation data as a time-to-event outcome. The ExTraMATCH II authors also noted a limitation of their analysis, which showed lack of consistency in how our included trials with IPD defined and collected clinical event outcome data. As noted in recent commentaries on clinical events, in heart failure trials, with the exception of all-cause mortality, the collection and reporting of other outcomes including cause-specific mortality and hospitalisation can be prone to confounding and bias (Zannad 2013). In accord with this Cochrane review update, ExTraMATCH II found no strong evidence of differential effects of ExCR across patient characteristics (i.e. age, sex, ethnicity, NYHA functional class, ischaemic aetiology, ejection fraction, exercise capacity) on mortality or hospitalisation outcomes.

Our findings are consistent with those of other systematic reviews and meta-analyses of RCTs for cardiac rehabilitation for heart failure published since the 2014 version of this review. Zhang 2018 collated trial-level data from 2533 patients with heart failure enroled in 28 published RCTs. Based on the MLWHF questionnaire, trial authors reported a similar magnitude of pooled improvement in HRQoL (mean −6.8, 95% CI −3.9 to −9.7; P < 0.0001). Similarly, based on eight RCTs including 317 participants with HFpEF, Chan 2016 reported a pooled improvement in MLWHF score of −6.8 (95% CI −9.7 to −3.8; P < 0.0001). In accord with our updated Cochrane review, Vromen 2018 found in a meta-regression analysis that ExCR programme characteristics of frequency, intensity, and session duration were not predictive of ExCR outcomes, although programmes with higher overall energy expenditure were associated with greater improvement in exercise capacity. Like the present review, the Cardiac Rehabilitation Outcome Study in Heart Failure (CROS-HF), included RCTs of ExCR but focused on the subgroup of trials with a more precise definition of HFrEF (left ventricular ejection fraction < 40%) and published after 1999 (therefore receiving contemporary drug and secondary prevention of heart failure) with a follow-up of six-months or more (Bjarnason-Wehrens 2020). Whilst CROS-HF reported no clear improvement in either mortality or hospitalisation, it confirms the improvement in exercise capacity and HRQoL with participation in ExCR.

AUTHORS' CONCLUSIONS

Implications for practice

Results of this update review show that although there was no evidence of a difference in the risk of all-cause mortality between exercise for cardiac rehabilitation (ExCR) and control, participation in ExCR likely reduces the risk of all-cause and heart failure-specific hospitalisation and health-related quality of life in the short-term (up to 12-months' follow up) as measured by the Minnesota Living With Heart Failure questionnaire amongst people with heart failure. These effects of ExCR appear to be consistent across ExCR programme characteristics (including centre-based, home-based and digitally supported ExCR settings) and support the recommendations provided in current international clinical guidelines that the offer of ExCR should be made taking account of patient's preference for ExCR setting (ACCF/AHA 2013; ESC 2021; NICE 2018).

Implications for research

Despite clinical guidelines recommending ExCR for the management of heart failure, internationally the provision and uptake of rehabilitation in heart failure remains poor (Bjarnason-Wehrens 2010; Golwala 2015). Further randomised controlled trials are needed to assess the clinical effectiveness and economic value (costs and cost-effectiveness) of alternative models of ExCR relative to traditional centre-based programmes, especially home-based and digitally supported programmes. Future trials need to consider the generalisability of trial populations (women, older people, and people with heart failure with preserved ejection fraction remain under-represented in trial populations); the application of interventions to enhance long-term maintenance of exercise training and outcomes (Karmali 2014); and costs and cost-effectiveness of ExCR programmes.

ACKNOWLEDGEMENTS

We thank the Cochrane Heart Group for running our updated search strategy, and Claudia Armengol and Soumeen Jin (both University of Glasgow, College of Medical, Veterinary, and Life Sciences) for their assistance with translation of two of the new trials included in this latest update.

Editorial and peer-reviewer contributions

Cochrane Heart supported the authors in the development of this review update. The following people conducted the editorial process for this review update:

- Sign-off Editor (final editorial decision): Michael Brown, Michigan State University, College of Human Medicine;
- Managing Editor (selected peer reviewers, collated peer-reviewer comments, provided editorial guidance to authors, edited the article): Joey Kwong, Cochrane Central Editorial Service;
- Editorial Assistant (conducted editorial policy checks, selected peer reviewers, collated peer-reviewer comments, supported

editorial team): Sara Hales-Brittain, Cochrane Central Editorial Service;

- Copy Editor (copy editing and production): Denise Mitchell, Cochrane Central Production Service
- Peer-reviewers (provided comments and recommended an editorial decision): Christian Lewinter, Karolinska Institute (clinical/content review); Malcolm Brewster, Ferry Road Health Centre, East Sussex, UK (consumer review); Aditi Bauskar, Independent Consultant, USA (consumer review); Nuala Livingstone, Cochrane Evidence Production and Methods Directorate (methods review); Ina Monsef, Cochrane Haematology, Department of Internal Medicine, Center for Integrated Oncology, Aachen Bonn Cologne Duesseldorf, Faculty of Medicine; University Hospital Cologne, University of Cologne, Cologne, Germany (search review). One additional peer reviewer provided content/clinical review but chose not to be publicly acknowledged.

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* Indicates the major publication for the study

CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Andryukhin 2010

Study characteristics	
Methods	Parallel-group RCT
Participants	**N Randomised:** 100 (exercise 50, control 50)

Andryukhin 2010 *(Continued)*

	Diagnosis (% of participants) • Aetiology: not reported • NYHA: I 17% II 35%; III 48% • LVEF: HFpEF only **Case mix:** as above **Age:** 67 (range 59-71): excercise 66.5, control 68 **Male:** 31% **White:** not reported **Inclusion/exclusion criteria** **Inclusion:** ≥ 50 years with an established diagnosis of HFPEF in a stable condition….based on symptoms (dyspnoea at rest or during exercise, fatigue, tiredness, ankle swelling) or signs (tachycardia, tachypnea, raised jugular venous pressure, oedema) of congestive HF plus the results of an echocardiographic examination by a cardiologist: presence of a normal LV systolic function (LVEF 50%), and evidence of abnormal LV relaxation, diastolic distensibility or diastolic stiffness. **Exclusion:** a history of an acute coronary syndrome within the last 6 months, a haemodynamically significant valvular stenosis, the presence of physical conditions that limited participation in a rehabilitation programme, insulin-dependent DM or confirmed COPD i.e. an FEV1/FVC < 70, a negative reversibility test, and a history of chronic cough, sputum production and dyspnoea
Interventions	**Exercise** • Total duration: 24 weeks • Aerobic/resistance/mix: mix • Frequency: 4 times/week • Duration: 30 min/session • Intensity: not defined • Modality: walking, weight training. • Setting: home • Other: “In the first month, the patients attended four weekly introductory sessions of 30 min each, under the supervision of a physiotherapist who had been trained in the study protocol. The personal intensity level, frequency and duration of training were determined and an individualized programme was recommended for further practice at home during the next five months (months two-to-six).” **Control:** prescription of medication as well as non-pharmacological measures. The basic medications are ACEIs, ARBs, β-blockers, aldosterone antagonists, diuretics and digoxin if needed. Non-pharmacological measures included recommendations concerning diet, alcohol intake, weight reduction, smoking cessation, activity and exercise training, given by the GP during consultation.
Outcomes	• NYHA class of CHF • BMI • WC • 6MWT • Biochemical parameters of blood plasma levels of fasting blood glucose, total cholesterol, LDL, CRP (high sensitivity method) and (NT-proBNP) (Biomedica Gruppe Austria) • HADS • HRQoL by MLWHF* • LASI • LVEDVI • LVMI • (E/A ratio)

Andryukhin 2010 *(Continued)*

Country and setting	Russia, single centre
Follow-up	BL (prerandomisation), and 6-months and 18-months post-randomisation
Notes	*Outcomes relevant to review AND converted from median and IQR to mean and SD Authors reported no external funding

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	“Selected patients were stratified by sex and randomized with the ‘randomization by envelopes’ method into two equal groups: a control group (usual care group) and an intervention group (usual care + nursing intervention group). An external collaborator that did not know the patients performed this procedure”
Allocation concealment (selection bias)	Unclear risk	"randomization by envelopes" method
Blinding (performance bias and detection bias) All outcomes	Low risk	“The subjects were tested… by nurses and physicians, who did not know whether the patient belonged to the intervention or the control group (single blinded).”
Incomplete outcome data (attrition bias)	High risk	Intervention 40/50 (80%), control 35/50 (70%) provided outcomes for analysis at 6 months
Selective reporting (reporting bias)	Low risk	All outcomes discussed in the methods are reported.
Groups balanced at baseline?	Low risk	"No significant differences were observed between the control and intervention groups in age, sex, NYHA class or number of prescribed medications. In addition, there were no significant differences regarding the outcome parameters between both groups, only the LVMI was significantly higher in the intervention group”
Groups received comparable care?	Low risk	It appears that the intervention group also recieved standard care in addition to intervention.
Intention-to-treat analysis?	High risk	It appears a per-protocol analysis was performed (i.e. analysed patients who received intervention)

Antonicelli 2016

Study characteristics

Methods	Parallel-group RCT
Participants	**N randomised:** 343 (exercise 170, control 173) **Diagnosis (% of participants)** • Aetiology: ischaemic 49%, hypertension 36%, valvular 15% • LVEF: total 48.4 ± 13.4%, exercise 47.9 ± 13.3%, control 49 ± 13.4% • NYHA: not reported

Antonicelli 2016 *(Continued)*

	Case mix: not reported **Age (mean ± SD), years:** total 76.9 ± 5.67, exercise 76.21 ± 5.21, control 77.6 ± 6.02 **Male:** total 56.9%, exercise 60.6%, control 53.2% **White:** not reported **Inclusion/exclusion criteria** **Inclusion:** inpatients or outpatients > 70 years of age, CHF from any cause with HFrEF or HFPEF, NYHA functional class ≥ II, MMSE score > 24 **Exclusion:** survival prognosis < 6 months, severe uncontrolled diabetes, acute heart decompensation in previous 2 months, severe COPD, severe liver failure with survival prognosis < 12 months; severe CKD with glomerular filtration rate < 15 mL/min/1.73 m^2, severe disabling systemic disease, severe cognitive impairment, inability to perform exercise training
Interventions	**Exercise** • Total duration: 24 weeks • Aerobic/resistance/mix: aerobic (cycling) • Frequency: 3 sessions/week (for 24 weeks) • Duration: 50 min (30 min on cycle ergometer) • Intensity: 20 min intense exercise on cycle ergometer/exercise session (60 rpm, achieving 60% to 70% maximum predicted HR) • Modality: cycle ergometer • Settings: hospital and home • Other: supervised (face-to-face by physiotherapist in hospital and remotely by nurse via telemonitoring at home) **Control group/comparison** • Usual care (medication, education/advice on discharge from hospital) • GP appointment within 2 weeks of discharge • hospital cardiologist appointment at 12 months
Outcomes	• All-cause hospital admissions • HRQoL (MLWHF)
Country and setting	Italy, single centre
Follow-up	3 months and 6 months
Notes	Exercise group received HF education **Source of funding:** strategic project grant of the Italian Ministry of Health, 2007: "Modelli riabilitativi multi-disciplinari: i nuovi farmaci per il paziente anziano con scompenso cardiaco cronico?". Part of the 2007 I.N.R.C.A. Strategic Program, RFPS-2007-6-654027: "Assessment of biological parameter changes induced by the rehabilitation program in elderly patients with congestive heart failure". "This work was also supported by grants from TERPAGE project POR Marche FESR 2007-2013 Italy to RA and FO; and Universita Politecnica delle Marche, Italy, to FO"

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No description of the randomisation process provided

Antonicelli 2016 *(Continued)*

Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding (performance bias and detection bias) All outcomes	Unclear risk	Not reported
Incomplete outcome data (attrition bias)	Low risk	All withdrawals and dropouts were described Exercise: 20/170 (11.8%) lost to follow-up Control: 10/173 (5.8%) lost to follow-up
Selective reporting (reporting bias)	Unclear risk	No protocol identified
Groups balanced at baseline?	Low risk	"There were no differences between the two groups at baseline"
Groups received comparable care?	Low risk	All participants continued with usual medication and received education/advice before discharge from the hospital
Intention-to-treat analysis?	Low risk	Although the term ITT was not stated, it appears from the CONSORT diagram that ITT analysis was undertaken

Austin 2005

Study characteristics	
Methods	Parallel-group RCT
Participants	**N randomised:** 200 (exercise 100, control 100) **Diagnosis (% of participants)** • Aetiology: ischaemia 77%, hypertension 15.5%, DCM 5.5%, other 2% • NYHA: Class II 51.5%, Class III 48.5% • LVEF: 40% to 35%: 16.5%; < 35% to 30%: 45%; < 30%: 38.5% **Case mix:** 100%, as above **Age, years:** exercise 71.9 (SD 6.3), control 71.8 (SD 6.8) **Male:** 43% **White:** not reported **Inclusion/exclusion criteria** **Inclusion:** age > 60 years, NYHA Class II or III, LVSD < 40% as confirmed by echocardiography **Exclusion:** diastolic dysfunction, significant co-morbidity preventing entry into the study because of terminal disease or inability to exercise (e.g. severe musculoskeletal disorder, unstable IHD, advanced valvular disease), resident outside the catchment area or in a long-term care establishment
Interventions	**Exercise** • Total duration: 24 weeks

Austin 2005 *(Continued)*

	• Aerobic/resistance/mix: aerobic endurance training and low resistance training/high repetitive muscular strength work • Frequency: 2 sessions/week (for 8 weeks), 1 session/week (for 16 weeks) plus 3 sessions/week at home • Duration: 2.5-h class (for 8 weeks) and 1-h class (for next 16 weeks) • Intensity: not reported • Modality: not reported • Settings: hospital and home • Other: none **Control group/comparison** Standard care group (including monitoring of clinical status, explanation of HF and its treatment, self-monitoring, dietary advice, and contact details of clinical nurse specialist)
Outcomes	• HRQoL (MLWHF questionnaire and EuroQol/EQ-5D) • healthcare utilisation (length of stay in hospital, admissions arising from heart disease, prescribed HF medication) • mortality
Country and setting	UK, single centre
Follow-up	6 months and 5 years (after randomisation)
Notes	**Source of funding:** Nevill Hall Coronary and Research Thrombosis Fund, North Gwent Cardiac After Care Charity, Gwent Healthcare Trust, University of Glamorgan

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	"A computer was used to generate a list of random numbers"
Allocation concealment (selection bias)	Low risk	"The numbers, placed in plain sealed envelopes by a university colleague prior to patient recruitment, were allocated to the participants by a hospital colleague unconnected with the study. The allocation schedule was not broken until the trial was completed"
Blinding (performance bias and detection bias) All outcomes	High risk	Not for HRQoL; data on deaths, admissions from hospital records department
Incomplete outcome data (attrition bias)	Low risk	CONSORT diagram was presented, showing participant flow. No imputation or sensitivity analysis was done to assess the impact of loss to follow-up.
Selective reporting (reporting bias)	Low risk	All outcomes described in the methods were reported in the results.
Groups balanced at baseline?	Low risk	"There are no significant differences in the baseline parameters of the standard care and experimental groups"
Groups received comparable care?	Low risk	Both groups received usual medical care; the only difference between groups was the exercise intervention provided
Intention-to-treat analysis?	Low risk	Although the term ITT was not stated, it appears from the CONSORT diagram that ITT analysis was undertaken

Belardinelli 1999

Study characteristics	
Methods	Parallel-group RCT
Participants	**N randomised:** 99 (exercise 50, control 49) **Diagnosis (% of participants)** • Aetiology: ischaemic cardiomyopathy 85%, idiopathic DCM 15% • NYHA: Class II 49%, Class III 34%, Class IV 17% • LVEF: exercise 28.4 (SD 6), control 27.9 (SD 5) **Case mix:** see above **Age, years:** exercise 56 (SD 7), control 53 (SD 9) **Male:** 89% **White:** not reported **Inclusion/exclusion criteria** **Inclusion:** HF, LVEF < 40%, sinus rhythm, diagnosis of CHF based on clinical symptoms and signs with or without radiological evidence of pulmonary congestion **Exclusion:** unstable angina, recent acute MI, decompensated congestive HF, haemodynamically significant valvular heart disease, significant chronic pulmonary illness, uncontrolled hypertension, renal insufficiency (serum creatinine > 2.5 mg/dL), orthopaedic or neurological limitations
Interventions	**Exercise** • Total duration: 14 months; 8 weeks supervised, then 12 months maintenance • Aerobic/resistance/mix: aerobic • Frequency: 2 to 3 sessions/week • Duration: 40 min/session • Intensity: 60% max VO_2 • Modality: cycling • Setting: hospital-based programme **Other:** all sessions were supervised by a cardiologist **Control group/comparison:** standard medical care
Outcomes	• HRQoL (MLWHF questionnaire) • mortality • morbidity • cost-effectiveness
Country and setting	Italy, single centre
Follow-up	14 months and 26 months (after randomisation)
Notes	**Source of funding:** none reported
Risk of bias	

Bias	Authors' judgement	Support for judgement

Belardinelli 1999 *(Continued)*

Random sequence generation (selection bias)	Unclear risk	Not reported
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding (performance bias and detection bias) All outcomes	Unclear risk	Not reported
Incomplete outcome data (attrition bias)	Low risk	Losses to follow-up were reported.
Selective reporting (reporting bias)	Low risk	All outcomes described in the methods were reported in the results.
Groups balanced at baseline?	Low risk	"The baseline characteristics of the study population are shown in Table 1. The 2 groups were well balanced with respect to most characteristics, including peak VO2, NYHA functional class, and LVEF. There were no differences in type and doses of medications, blood chemistry, and previous cardiac events"
Groups received comparable care?	Unclear risk	Not reported
Intention-to-treat analysis?	Unclear risk	Not reported

Belardinelli 2012

Study characteristics	
Methods	Parallel-group RCT
Participants	**N randomised:** 123 (exercise 63, control 60) **Diagnosis (% of participants)** • Aetiology: ischaemic 80%, non-ischaemic 20% • NYHA: Class II 59%, Class III 41% • LVEF: 37 (SD 8) **Case mix:** see above **Age, years:** 59 (SD 14) **Male:** 78% **White:** not reported **Inclusion/exclusion criteria** **Inclusion:** clinical stability for 3 months before enrolment, LVEF < 40%, ability to exercise **Exclusion:** haemodynamically significant valvular heart disease, uncontrolled DM and hypertension, orthopaedic or neurological problems, renal insufficiency (creatinine > 2.5 mg/dL)
Interventions	**Exercise**

Belardinelli 2012 *(Continued)*

- Total duration: 10 years; 8 weeks' supervised, then 12 months' maintenance
- Aerobic/resistance/mix: aerobic
- Frequency: 2-3 sessions/week
- Duration: 40 min/session
- Intensity: 60% max VO_2 for first 2 months, thereafter at 70% max VO_2
- Modality: cycling
- Settings: hospital and home

Other: trained participants were encouraged to exercise without supervision at home at least a third time, performing aerobic activities at the same HR as the other 2 supervised sessions

Exercise sessions held at the hospital were supervised by cardiologists. Study authors emphasise that the supervised element was maintained over 10 years of follow-up

Control group/comparison: standard medical care. Participants were instructed to continue with their usual home daily physical activities, avoiding exercise training in a supervised environment. They were free to perform aerobic activities such as walking, cycling (home or outside), and swimming, avoiding a duration longer than 30 min. Study authors advised control group participants to walk and perform usual physical activities

Outcomes	• HRQoL (MLWHF questionnaire) • Mortality • Morbidity (including hospitalisation) • Cost-effectiveness
Country and setting	Italy, single centre
Follow-up	10 years (every 12 months) (after randomisation)
Notes	Every 6 months participants exercised at the hospital, then returned to a coronary club, where they exercised the rest of the year **Source of funding:** no external funding

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not reported
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding (performance bias and detection bias) All outcomes	Unclear risk	Not reported
Incomplete outcome data (attrition bias)	Low risk	Losses to follow-up were reported. Dropout rate was 3% on average in the exercise group. 2/63 did not complete the protocol - 1 because of a car accident and the other for personal reasons. 3/60 in the control group decided to withdraw from the study for reasons unrelated to their clinical status.
Selective reporting (reporting bias)	Low risk	All outcomes described in the methods were reported in the results.

Belardinelli 2012 *(Continued)*

Groups balanced at baseline?	Low risk	"The baseline characteristics of the study population are shown in Table 1. The 2 groups were well balanced with respect to most characteristics, including peak VO2, New York Heart Association functional class, left ventricular ejection fraction. There were no difference in type and doses of medication, blood chemistry, and previous cardiac events"
Groups received comparable care?	Low risk	Both groups appeared to receive the same interventions apart from the CR intervention.
Intention-to-treat analysis?	Low risk	"All analyses were performed with an intention-to-treat principle"

Bocalini 2008

Study characteristics	
Methods	Parallel-group RCT
Participants	**N randomised:** 53 (exercise 28, control 25) **Diagnosis (% of participants)** • Aetiology: MI 45.2%, systemic hypertension 19%, dilated Chagas' cardiomyopathy 11.9%, DM 4.8%, other 19.1% • NYHA: Class II or III • LVEF: ≤ 45% **Case mix:** 100%, as above **Age, years:** exercise 61 (SD 12), control 60 (SD 11) **Male:** 88% **White:** not reported **Inclusion/exclusion criteria** **Inclusion:** EF < 45%, symptoms of NYHA functional Class II or III, optimised pharmacological therapy established at least 4 weeks before inclusion in the study, compensated HF state at least 2 months before **Exclusion:** age < 50 years, NYHA functional Class IV, clinical instability in the preceding 2 months, non-optimised therapy, uncontrolled arrhythmias, MI within the last 2 months, surgery-associated cardiomyopathy, pulmonary disease or other co-morbid conditions that limit physical exercise, accentuated severe cardiac symptoms (hypotension, complex ventricular arrhythmia, progressive worsening of dyspnoea, and significant ischaemia at low rates) during ergometric tests, regular participation in some exercise programme within the last 6 months, frequency in the training protocol < 80%
Interventions	**Exercise:** Total duration: 6 months • Aerobic/resistance/mix: mix • Frequency: 3 sessions/week • Duration: 90 min • Intensity: target HR (50% of work at maximum HR) • Modality: walking on a treadmill, dumbell resistance exercises • Setting: not reported • Other: relaxation and stretching exercises before and after every session

Bocalini 2008 *(Continued)*

	Control group/comparison: usual medical therapy - individual dietary guidance and pharmacological therapy
Outcomes	• HRQoL (shortened version of World Health Organization Quality of Life questionnaire) • Hospitalisation
Country and setting	Brazil, single centre
Follow-up	6 months (after randomisation)
Notes	Initially randomised 53 participants; excluded data from participants who withdrew, were lost to follow-up, etc.; hence analysed 42 participants Although setting was not reported, the exercise programme was described as "supervised" **Source of funding:** none reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not reported
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding (performance bias and detection bias) All outcomes	Unclear risk	Not reported
Incomplete outcome data (attrition bias)	High risk	Only 42/53 (79%) provided data at follow-up
Selective reporting (reporting bias)	Low risk	All outcomes described in the methods were reported in the results
Groups balanced at baseline?	Low risk	Table 1 of the publication shows that groups were well balanced
Groups received comparable care?	Low risk	"All patients continued with pharmacological therapy and individual dietary guidance"
Intention-to-treat analysis?	High risk	"During the follow-up, medicine doses were not modified except for those that presented impairment of symptoms and, consequently, these patients were excluded from the analysis"

Chen 2018

Study characteristics	
Methods	Parallel-group RCT
Participants	**N randomised:** 62 (exercise 31, control 31) **Diagnosis (% of participants)**

Chen 2018 *(Continued)*

- Aetiology: coronary artery disease 41.9%, cardiomyopathy 35.5%, rheumatic heart disease 9.7%, hypertension 6.5%, valvular 6.5%
- NYHA: Class II to IV
- LVEF: mean 43.5%, SD 13.8

Case mix: 100%, as above

Age, years: exercise 61 (SD 14), control 62 (SD 15)

Male: 59.7%

White: not reported

Inclusion/exclusion criteria

Inclusion: heart failure diagnosis, NYHA class II to IV, > 18 years old

Exclusion: cognitive impairment, unable to be contacted by telephone or home visit, included in other study, COPD, life expectancy < 1 year, other diagnosis-limiting activity

Interventions	**Exercise** • Total duration: 26 weeks • Aerobic/resistance/mix: mix • Frequency: up to 3 sessions/week • Duration: 20 to 40 min/session • Intensity: as tolerated by participant • Modality: walking • Setting: hospital • Other: education, depression therapy, home visits **Control group/Comparison:** standard care (telephone call at 2 weeks, 2 clinic reviews at 90 and 180 days), mortality, hospitalisation
Outcomes	• HRQoL (MLWHF questionnaire and Short Physical Performance Battery - SPPB)
Country and setting	China, single centre
Follow-up	6 months
Notes	**Source of funding:** none reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	"A computer generated randomization list was created by a statistician for patient randomization"
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding (performance bias and detection bias) All outcomes	Unclear risk	Data collectors (nurses) were blinded to randomisation; whether they were blinded to outcomes is not clear.
Incomplete outcome data (attrition bias)	Low risk	Only 2 deaths were reported; no other losses to follow-up were described.

Chen 2018 *(Continued)*

Selective reporting (reporting bias)	Low risk	All outcomes were reported (no protocol publication is available).
Groups balanced at baseline?	Low risk	"Baseline demographic and clinical characteristics were not significantly different between the SC group and MDMP group (Table 1)"
Groups received comparable care?	Low risk	"Medications recommended by the 2013 American College of Cardiology Foundation/American Heart Association Guideline for the Management of Heart Failure.50 were prescribed for all the patients in this study at optimal dosage if there was no contradiction"
Intention-to-treat analysis?	Low risk	Although the term ITT was not stated, it appears that groups were analysed according to initial random allocation.

Cowie 2014

Study characteristics	
Methods	Parallel-group RCT, 2 arms
Participants	**N randomised:** 46; 15 hospital, 15 home, 16 control **Diagnosis (% of participants)** • Aetiology: not reported • NYHA: Class II: exercise (home 60%, hospital 53.3%), control 56.3% • NYHA: Class III: exercise (home 40%, hospital 46.7%), control 43.7% • LVEF: not reported (severe LVSD: exercise (home 60%, hospital 53.3%), control 56.3%) **Case mix:** 100%, as above **Age, years:** exercise (home 63.3, hospital 69.2), control 60.4 **Male:** 91.3%(total), exercise (home 86.7%, hospital 86.7%), control 100% **White:** not reported **Inclusion/exclusion criteria** **Inclusion:** LVSD on echocardiography, clinically stable for at least 1 month, receiving optimised medication **Exclusion:** significant ischaemic symptoms at low workloads, uncontrolled diabetes, acute systemic illness/fever, recent embolism, active pericarditis or myocarditis, moderate to severe aortic stenosis, regurgitant valvular heart disease requiring surgery, MI within past 3 weeks, new-onset AF, signs and symptoms of decompensation, other co-morbidities (life-threatening, uncontrolled, infectious, or exacerbated by exercise)
Interventions	**Exercise** • Total duration: 8 weeks • Aerobic/resistance/mix: aerobic • Frequency: 2 sessions/week • Duration: 60 min • Intensity: not specified • Modality: circuit training • Setting: hospital-based (intervention 1) and home-based (intervention 2)

Cowie 2014 *(Continued)*

	• Other: hospital group with a senior CR physiotherapist, a physiotherapy technical instructor, and a senior cardiac nurse present at each class; home group monitored by a senior CR physiotherapist by telephone, twice during their 8-week intervention (estimated as two 20-min calls, plus 10-min documentation, i.e. 1 h per participant) **Control group/comparison** usual care, which included specialist HF nursing input
Outcomes	• Hospitalisations • Costs
Country and setting	UK
Follow-up	5.2 years
Notes	**Source of funding:** NHS Ayrshire and Aaran's Coronary Heart Disease Managed Clinical Network

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No details of randomisation sequence generation process were provided.
Allocation concealment (selection bias)	Low risk	Concealed envelopes were used.
Blinding (performance bias and detection bias) All outcomes	Unclear risk	The researcher collating and analysing data was blind to participants' randomisation groups when measuring long-term activity levels, but blinding was unclear for outcomes.
Incomplete outcome data (attrition bias)	High risk	46/60 (77%) provided follow-up data.
Selective reporting (reporting bias)	High risk	Number of hospitalisations was not reported (obtained from study lead investigator).
Groups balanced at baseline?	Unclear risk	Hospital group participants were almost 10 years older than control participants and so were at high risk of bias, whereas the home group and the control group were similar and so were at low risk of bias.
Groups received comparable care?	Low risk	Usual care was standard in all 3 groups.
Intention-to-treat analysis?	Low risk	Although the term ITT was not stated, it appears that groups were analysed according to initial random allocation.

Dalal 2018

Study characteristics

Methods	Parallel-group RCT
Participants	**N randomised:** 216; 107 exercise, 109 control **Diagnosis (% of participants)** • Aetiology: exercise 45%, control 46%

Dalal 2018 *(Continued)*

- Female: exercise 24%, control 19%
- NYHA: Class II: exercise 59%, control 58%; Class III: exercise 19%, control 24%
- LVEF: mean 34%

Case mix: 100%, as above

Age: exercise mean 69.7 (SD 10.9), control mean 69.9 (SD 11.0)

Male: 78% (total); exercise 76, control 81%

White: 100%

Inclusion/exclusion criteria

Inclusion: men and women aged ≥ 18 years with a confirmed diagnosis of HFrEF on echocardiography or angiography (LVEF < 45% within the preceding 5 years), no deterioration of HF symptoms in prior 2 weeks resulting in hospitalisation or alteration of HF medication

Exclusion:cardiac rehabilitation (CR) within the past 12 months; received an intracardiac defibrillator (ICD); cardiac re-synchronisation therapy (CRT) or combined CRT/ICD device in prior 6 months; contraindications to exercise testing or exercise training; in a long-term care establishment or unwilling or unable to travel to research assessments, or to accommodate home visits; unable to understand study information or unable to complete outcome questionnaires

Interventions	**Exercise** • Total duration: 12 weeks • Aerobic/resistance/mix: aerobic • Frequency: 2-3 times/week • Duration: 12 weeks • Intensity: not reported • Modality: not reported • Setting: home-based Participants received the REACH-HF Manual (including a choice of 2 exercise programmes); a participant 'Progress Tracker' booklet to record symptoms, physical activity, and other actions related to self-care; support for caregivers and facilitation by cardiac nurses or physiotherapists, including assessing individual participant and caregiver needs and concerns and tailoring the intervention content to address these; this element was supported by a 3-day training course for facilitators on how to deliver the intervention using a patient-centred style of communication **Control group/comparison:** usual care ("...intervention and control group patients received usual medical management for HF according to current guidelines")
Outcomes	**Primary outcome:** MLWHF questionnaire **Secondary outcomes:** death; hospitalisation; HeartQoL; EQ-5D-3L; costs
Country and setting	UK, multicentre (4 sites)
Follow-up	4, 6, and 12 months
Notes	**Funding source:** NIHR under its Programme Grants for Applied Research Programme (Grant Reference Number RP-PG-1210-12004)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	"Participants were randomly allocated in a 1:1 ratio, stratified by investigator site and baseline plasma N-terminal proB-type natriuretic peptide (NT-pro-

Dalal 2018 *(Continued)*

		BNP) levels (≤2000 vs >2000 pg/mL), using minimisation to facilitate balance between the groups. Randomisation numbers were computer generated and assigned in strict sequence at the point of randomisation"
Allocation concealment (selection bias)	Low risk	"To maintain concealment, the Peninsula Clinical Trials Unit used a password protected, web based randomisation system to allocate participants after completion of consent and entry of baseline assessment data"
Blinding (performance bias and detection bias) All outcomes	Low risk	Outcome assessors and statistician were blinded
Incomplete outcome data (attrition bias)	Low risk	All participants were accounted for in a CONSORT flow diagram.
Selective reporting (reporting bias)	Low risk	All prespecified outcomes were reported as in the published protocol.
Groups balanced at baseline?	High risk	"Patient level characteristics at baseline were well balanced between the groups, apart from more frequent cardiac comorbidity (history of myocardial infarction and atrial fibrillation) and, consequently, a higher Charlson comorbidity score in the control group (table 1). Mean baseline MLHFQ scores for the REACH-HF group were higher (poorer) than for the control group, but secondary baseline outcomes were similar for the two groups"
Groups received comparable care?	Low risk	Both groups received usual care.
Intention-to-treat analysis?	Low risk	"Primary analyses were based on ITT complete case analyses"

DANREHAB 2008

Study characteristics	
Methods	Parallel-group RCT
Participants	**N randomised:** 91 (exercise 45, control 46) **Age, years:** exercise median 66 (range 33-91), control median 65 (range 29-94) **Male:** 90% **White:** not reported **Inclusion/exclusion criteria** **Inclusion:** symptoms of CHF and objective findings or effect of medication **Exclusion:** mental disorders and social problems (such as dementia, alcoholism, or drug addiction); transferred to other department or hospital at discharge; severe illness, including NYHA Class IV; living at nursing home; did not speak Danish; refused consent
Interventions	**Exercise** • Total duration: 12 weeks • Aerobic/resistance/mix: mix • Frequency: 3 sessions/week

DANREHAB 2008 *(Continued)*

- Duration: 90 min/session
- Intensity: 50% max HR
- Modality: not reported
- Setting: supervised centre-based plus home-based also encouraged to continue

Other: physical exercise was conducted as a mixture of endurance and strengthening training using various upper and lower body modalities easily implemented as activities that participants could perform at home. CR included participant education, exercise training, dietary counselling, smoking cessation, psychosocial support, risk factor management, and clinical assessment. All components reflected theoretical and practical approaches followed by individual follow-up and feedback. The lifestyle intervention strategy was based on the stages of change model and the self-efficacy theory. The lifestyle intervention was designed as a group intervention, but individual counselling was also provided

Control group/comparison

Usual care participants were offered follow-up treatment prescribed by the discharging physician as outpatient control or by the GP. Pharmaceutical treatment followed routine clinical practice based on current national guidelines. The discharging nurse or physician determined whether participants were referred to smoking cessation and dietary counselling parallel to outpatient treatment.

Outcomes	**Primary outcomes:** composite outcome measure included overall mortality, MI, or acute first-time readmission due to heart disease other than MI **Secondary outcomes:** collected data based on an adapted standardised interview questionnaire and a postal questionnaire (e.g. SF-36, HADS); clinical examination; blood tests
Country and setting	Demark, single centre
Follow-up	12 months
Notes	HF subset of 770 participants were randomised; this study included other participants without HF (coronary heart disease and individuals ar high risk but no diagnosed disease). Only data on HF patients used in this review. Randomisation was stratified by indication. **Funding source:** Copenhagen Hospital Corporation Research Council, Danish Heart Foundation, Danish Pharmacy Foundation of 1991, Danish Research Council, Danish Centre for Evaluation and Health Technology Assessment, Danish Ministry of the Interior and Health, Development Fund of Copenhagen County, Villadsen Family Foundation, Eva and Henry Fraenkel's Memorial Foundation, Builder LP Christensen's Foundation, Danish Animal Protection Foundation, Bristol-Myers Squibb, Merck Sharp and Dohme, and AstraZeneca

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	"Patients who gave informed consent were randomized using a centralized randomization procedure administered by the Copenhagen Trial Unit. The randomization was stratified according to risk group (CHF, IHD, or HR) based on a random-permuted multiblock within-stratum method"
Allocation concealment (selection bias)	Low risk	As above
Blinding (performance bias and detection bias) All outcomes	Low risk	"Because of the nature of CR, the interventions were open to the investigators and the patients. Investigator independent outcome data from registries were chosen to ensure blinded assessment and outcome analysis"
Incomplete outcome data (attrition bias)	Low risk	81% overall follow-up at 12 months

DANREHAB 2008 *(Continued)*

Selective reporting (reporting bias)	Low risk	All outcomes listed in the methods were reported in the results.
Groups balanced at baseline?	Low risk	"Patients were well matched at entry"
Groups received comparable care?	Low risk	Both groups received control care.
Intention-to-treat analysis?	Low risk	ITT analysis was stated.

Davidson 2010

Study characteristics	
Methods	Parallel-group RCT
Participants	**N randomised:** 105 (exercise 53, control 52) **Diagnosis (% of participants)** • Aetiology: not reported • NYHA: Class I: exercise 2%, control 0%; Class II: exercise 38%, control 33%; Class III: exercise 60%, control 67%; Class IV: exercise 0%, control 0% • LVEF: not reported **Case mix:** as above **Age, years:** exercise 71.6 (SD not reported), control 73.9 (SD not reported) **Male:** 67% **White:** not reported **Inclusion/exclusion criteria** **Inclusion:** patients of any age with diagnosis of HF of any aetiology and NYHA Class I-IV. All participants were cleared by their physician to participate in the exercise group. **Exclusion:** participants with unstable angina pectoris were ineligible to participate.
Interventions	**Exercise** • Total duration: 12 weeks • Aerobic/resistance/mix: mix • Frequency: 1 session/week • Duration: 30-50 min • Intensity: not reported • Modality: gymnasium: treadmills, stationary cycles, recumbent cycles • Home-based: hall walks, stairs, and sporting activities such as lawn bowls • Setting: supervised gymnasium, home-based programme tailored to participant's needs **Other:** also attended a nurse-co-ordinated CR clinic with emphasis on self-management. A group-based educational session was conducted for study participants and their families. The exercise group attended the nurse-co-ordinated CR clinic, where comprehensive assessment was performed by the physiotherapist, the CR co-ordinator, and the occupational therapist.

Davidson 2010 *(Continued)*

	Control group/comparison: information session, then usual medical care
Outcomes	• HRQoL (MLWHF questionnaire) • All-cause and cardiovascular-related hospital admission • Mortality
Country and setting	Australia, single centre
Follow-up	12 months (after randomisation)
Notes	The trial had to be stopped prematurely at 12 months following introduction of chronic and complex care for people with CHF by the New South Wales Health Department. "In view of trends in favour of the intervention group and emerging evidence from other studies, it was considered unethical and untenable to continue randomization in view of the policy mandate. When the trial was stopped there were 53 participants in the intervention group and 52 participants in the usual care group" **Source of funding:** none reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	"Participants were randomized to either the intervention or control group by means of a computer-generated program"
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding (performance bias and detection bias) All outcomes	Low risk	"The randomization technique was blinded to the investigators until the close of the study"
Incomplete outcome data (attrition bias)	Low risk	"No participants were lost to follow-up"
Selective reporting (reporting bias)	Low risk	All outcomes were described and all methods were reported.
Groups balanced at baseline?	Low risk	"…there were few differences between intervention and usual care groups, indicating success of randomization. The most important difference on clinical variable was that a significantly greater proportion of people in the intervention group were taking spironolactone at baseline"
Groups received comparable care?	Low risk	Both groups appeared to receive the same interventions apart from the CR intervention.
Intention-to-treat analysis?	Low risk	Although this was not reported as an ITT analysis, groups did appear to be analysed according to original randomised allocation.

Dehkordi 2015

Study characteristics

Methods	Parallel-group RCT
Participants	**N randomised:** 61 (exercise 30, control 31)

Dehkordi 2015 *(Continued)*

	Diagnosis (% of participants) • Aetiology: ischaemic cardiomyopathy 67.2%, hypertension 26.2%, DCM 4.9% • NYHA: Class I: exercise 0, control 0; Class II: exercise 20%, control 19.33%; Class III: exercise 83%, control 81% • LEVF: exercise 32 ± 4%; control 33 ± 5% **Case mix:** as above **Age (mean ± SD), years:** exercise 60 ± 4.25, control 58 ± 4.22 **Male:** 67.2% (exercise 60%, control 74%) **White:** not reported **Inclusion/exclusion criteria** **Inclusion:** patients admitted to hospital with diagnosis of HF, with LVEF ≤ 40%, and in sinus rhythm **Exclusion:** difficulty with movement; no heart transplant 3 months after exercise programme; no advanced HF; not available throughout the study; coronary bypass surgery during the study; other neurological, orthopaedic, peripheral vascular, or pulmonary disease, making it impossible to complete exercise; unwilling to co-operate
Interventions	**Exercise** • Total duration: 24 weeks • Aerobic/resistance/mix: aerobic only (walking) • Frequency: 3 sessions/week • Duration: 40 min • Intensity: in short term (up to 6 weeks), < 3 MET (simple walking until HR reaches 60% of HR reserve); in longer term (≥ 6 weeks), HR 70% of HR reserve • Modality: walking • Setting: hospital sport facility or gymnasium (supervised) **Control group/comparison:** usual care (medication and lifestyle advice)
Outcomes	HRQoL (MacNew Questionnaire)
Country and setting	Iran, hospital
Follow-up	6 months
Notes	Exercise group supervised by nurse or cardiologist; control group supervised by physician **Source of funding:** Research and Technology Deputy of Shahrekord University of Medical Sciences

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	The randomisation code was developed with a computer random-number generator
Allocation concealment (selection bias)	Unclear risk	Method of allocation was not described
Blinding (performance bias and detection bias) All outcomes	Low risk	HRQoL assessment was self-administered.

Dehkordi 2015 *(Continued)*

Incomplete outcome data (attrition bias)	Low risk	No loss to follow-up was reported in either arm.
Selective reporting (reporting bias)	Unclear risk	No protocol was identified.
Groups balanced at baseline?	Low risk	No differences were noted between groups.
Groups received comparable care?	Low risk	Medications were unchanged in both groups.
Intention-to-treat analysis?	Low risk	Although the term ITT was not stated, it appears from the CONSORT diagram that ITT analysis was undertaken.

Dracup 2007

Study characteristics	
Methods	Parallel-group RCT
Participants	**N randomised:** 173 (exercise 86, control 87) **Diagnosis (% of participants)** • Aetiology: ischaemic; idiopathic; valvular; DCM; other • NYHA: Class II-IV • LVEF: 26.4 (SD 6.8) **Case mix:** 100%, as above **Age, years:** 54 (SD 12.5) **Male:** 71.7% **White:** 60.1 **Inclusion/exclusion criteria** **Inclusion:** English-speaking, age 18-80 years, NYHA II-IV, and LVSD with LVEF < 40% as documented by echocardiogram or radionuclide ventriculography within 6 months, and sinus rhythm **Exclusion:** MI or recurrent angina within 3 months, orthopaedic impediments to exercise, severe obstructive pulmonary disease with FEV < 1 L in 1 second as measured by spirometry, stenotic valvular disease as measured by echocardiogram, history of uncontrolled ventricular tachyarrhythmias (documented by electrophysiology study or 24-h Holter monitor), or absence of an implantable cardioverter-defibrillator despite a history of sudden cardiac death
Interventions	**Exercise** • Total duration: unclear (6 months or 1 year) • Aerobic/resistance/mix: mix • Frequency: 4 sessions/week • Duration: 10-45 min • Intensity: 40%-60% max HR • Modality: walking • Setting: home-based

Dracup 2007 *(Continued)*

	Other: "After six weeks resistive training component involved both upper and lower extremity strengthening. Resistance training was prescribed at 80% of one repetition maximum, which is the maximal weight lifted one time, for 2 sets of 10 repetitions using seated biceps curls to strengthen the arms & seated lateral raises to strengthen shoulders. A second set of 10 repetitions at 80% of one repetition maximum was also prescribed…" **Control group/comparison:** maintained usual level of daily activities; no exercise component
Outcomes	• HRQoL (MLWHF questionnaire) • Mortality • Hospitalisation
Country and setting	USA, single centre
Follow-up	6 months and 12 months (after randomisation)
Notes	Home-based exercise programme **Subgroup analysis reported:**Evangelista 2010 **Source of funding:** American Heart Association Western Division (NCR 133-09)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not reported
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding (performance bias and detection bias) All outcomes	Unclear risk	Blinding reported for physical activity (accelerometer) outcome but not reported for other outcomes
Incomplete outcome data (attrition bias)	Low risk	"Two patients (one from the experimental and one from the control group) were lost to follow-up within the first three months of enrollment. One was incarcerated and the second left the geographic area with no forwarding information. The remaining 173 patients compose the final study"
Selective reporting (reporting bias)	Low risk	All outcomes described in the methods were reported in the results.
Groups balanced at baseline?	Low risk	There were no significant differences in any of baseline characteristics between the 2 groups, except for angiotensin-converting enzyme (ACE) inhibitor; adherers were more likely to use ACE inhibitors than nonadherers (84% vs 60%; P = 0.039)
Groups received comparable care?	Low risk	"Research nurses made home visits weekly for the first two weeks and then monthly to assess protocol adherence, correct use of the pedometer, and tolerance to the exercise program. The home visits also served as a form of attention control in the care- as-usual group. All clinical questions were referred to the patient's cardiologist"
Intention-to-treat analysis?	Low risk	Although not reported as ITT analysis, groups did appear to be analysed according to original randomised allocation.

Du 2018

Study characteristics	
Methods	Parallel-group RCT
Participants	**N randomised:** 132 (exercise 67, control 65) **Diagnosis (% of participants)** • Aetiology: ischaemic: total 60 (45%), exercise 33 (49%), control 27 (42%) • NYHA: Class II: total 92 (70%), exercise 49 (73%), control 43 (66%); Class III: total 40 (30%), exercise 18 (27%), control 22 (34%) • LVEF: total 32.6 (SD 12.5), exercise 32 (SD 11.6), control 33 (SD 13.5) **Case mix:** 100%, as above **Age, years:** total 60 (SD 15); exercise 62 (SD 15), comparator 58 (SD 15) **Male:** total 104 (78.8%); exercise 56 (83.6%), control 48 (73.8%) **White:** not reported I**nclusion/exclusion criteria** **Inclusion:** symptomatic heart failure, NYHA II-III **Exclusion:** unstable angina pectoris, unexplained syncope in previous 3 months, resting heart rate > 120 bpm, participating in any structured exercise programme, inability to give informed consent, significant cognitive impairment
Interventions	**Exercise** • Total duration: 24 weeks • Aerobic/resistance/mix: aerobic • Frequency: 1 session/week • Duration: 6 min/session • Intensity: tailored to individual • Modality: walking (home heart walk) • Setting: home-based **Other:** usual care **Control group/comparison:** usual care consisting of bedside education, cardiology appointments
Outcomes	HRQoL (SF-36 and MLWHF questionnaire)
Country and setting	Australia, multicentre
Follow-up	3 months and 6 months
Notes	Australian New Zealand Clinical Trial Registry 12609000437268. Participants in this study were younger than the average age of the HF population **Source of funding:** Australian Department of Health and Ageing, as part of the Sharing Health Care Initiative

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**

Du 2018 *(Continued)*

Random sequence generation (selection bias)	Low risk	"Participants were randomized at a 1:1 ratio through a central phone randomization centre using computer generated random numbers"
Allocation concealment (selection bias)	Low risk	"Participants were randomized at a 1:1 ratio through a central phone randomization centre using computer generated random numbers"
Blinding (performance bias and detection bias) All outcomes	Low risk	A blinded assessor conducted outcome assessments at follow-up (3 months and 6 months).
Incomplete outcome data (attrition bias)	High risk	16/67 were lost to follow-up in the exercise group. 9/65 were lost to follow-up in the control group. All reasons for losses to follow-up were reported but no explanation was given for differences between groups.
Selective reporting (reporting bias)	Low risk	No differences were noted between the protocol and the study.
Groups balanced at baseline?	Low risk	Tables 1 and 2
Groups received comparable care?	Low risk	Both groups received usual care.
Intention-to-treat analysis?	Low risk	"Data were analysed according to the intention-to-treat principle"

Gary 2010

Study characteristics	
Methods	Parallel-group RCT, 2 arms
Participants	**N randomised:** total 65; intervention 1 (comprehensive): 28 (CBT 10; CBT and exercise 18); intervention 2 (ex alone): 37 (exercise alone 20; control 17) **Diagnosis (% of participants)** • Aetiology: not reported • NYHA: Class II 43.3%; Class III 56.7% (as a whole) • LVEF: ≥ 15% **Case mix:** 100%, as above **Age, years:** 65.8 (SD 13.5) **Male:** 41.9% **White:** not reported **Inclusion/exclusion criteria** **Inclusion:** documented medical diagnosis of HF; LVEF ≥ 15% documented within the last year by echocardiogram, cardiac catheterisation, ventriculography, or radionuclide ventriculography; receiving therapy for HF according to guidelines published by the American College of Cardiology/American Heart Association recommendations (ACEIs, diuretics, beta blockers, ARBs, hydralazine and nitrate

Gary 2010 *(Continued)*

	combination, etc.); HAM-D score ≥ 11; positive results on the Mini for minor or major depression; DSM-IV diagnosis for depression for 14 days, or for 7 days if history of major depressive disorder in the last 6 months. Participants also had to be English speaking; living independently (non-institutionalised) within 100 miles of Atlanta, Georgia; able to respond to questions appropriately; able to hear adequately to respond to verbal questions; not involved in any structured exercise programme or walking 3 times/week for a minimum of 20 min; not participating in any psychotherapy; and not hospitalised within the last 60 days **Exclusion:** suicide ideation according to psychiatric assessment or Mini evaluation; major psychiatric co-morbidity such as schizophrenia, personality disorder, or dementia; planned surgery; not given a diagnosis of HF in the past 3 months; renal insufficiency (serum creatinine > 2.5 mg/dL); uncontrolled hypertension; acute bereavement or loss of significant other within the last month or currently involved in family crisis such as divorce; any disorder interfering with independent ambulation; and terminal illness such as cancer
Interventions	**Exercise** • Total duration: 12 weeks • Aerobic/resistance/mix: aerobic • Frequency: 3 sessions/week • Duration: 30-45 min/session, maximum 1 h • Intensity: Borg < 15 ('moderate') • Modality: walking • Setting: home-based **Other:** exercise + CBT group also received 12 weeks of weekly 1-h sessions of CBT. No other co-interventions were mentioned. **Control group/comparison:** usual care "Participants assigned to the UC [usual care] group received no information or counselling from their health care provider other than that normally provided"
Outcomes	• HRQoL (MLWHF questionnaire) • Mortality
Country and setting	USA, single centre
Follow-up	24 weeks (after randomisation)
Notes	Exercise group participants had 12 weekly face-to-face home visits by a research nurse to monitor walking progress and to tailor the exercise prescription. "At the first home visit for EX, the research nurse (1) educated the patient on the rationale for EX in HF; (2) instructed on self-monitoring of symptoms [dyspnoea, heart rate (HR), fatigue] during walking; (3) provided the patient with a Polar monitor and instruction on how to use it; (4) provided patient with EX logs and instructions; (5) instructed on use of the 6- to 20-point Borg's rate of perceived exertion (RPE) scale; (6) provided patient with blood pressure cuff and weight scale, if not available; and (7) observed participant response to walking out side home" **Source of funding:** Southeast Affiliate of the American Heart Association Beginning Grant-in-Aid, Atlanta Clinical and Translational Science Institute at Emory University School of Medicine

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not reported

Gary 2010 *(Continued)*

Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding (performance bias and detection bias) All outcomes	Low risk	"Data collectors were blinded to group assignment"
Incomplete outcome data (attrition bias)	Low risk	QUORUM diagram and details of losses to follow-up were reported. In exercise group, 1 patient died and 3 withdrew at 24 weeks. In usual care group, 2 participants and 1 participant withdrew at 12 and 24 weeks, respectively. In combined CBT/exercise group, 2 withdrew at 12 weeks. 1 was lost to follow-up and 1 withdrew at 24 weeks. In CBT group, 1 withdrew at 12 weeks and 24 weeks. 1 died and 1 was lost to follow-up at 24 weeks
Selective reporting (reporting bias)	Low risk	Outcomes were described in the Methods and were reported in the Results.
Groups balanced at baseline?	Low risk	"There were no BL differences between groups on any demographic or outcome variables"
Groups received comparable care?	Low risk	Groups appeared to receive the same care other than exercise and CBT interventions.
Intention-to-treat analysis?	Low risk	Although not stated, CONSORT diagram suggests that groups were analysed according to initial randomised allocation.

Gary 2019

Study characteristics	
Methods	Parallel-group RCT
Participants	**N randomised:** 69 (2 intervention arms: exercise only [EX only] 24, and combined exercise and cognitive training program [EX/CT] 18, and control: usual care attention control [UCAC] 17) **Diagnosis (% of participants)** • Aetiology: not reported • NYHA: class II 55%, class III 45% • LVEF: 35 (15) **Case mix:** as above **Age:** 61 (SD 10) years **Male:** 46% **White:** 39% **Inclusion/exclusion criteria** I**nclusion:** ambulatory, between 40–75 years of age, have a LVEF ≥ 10% documented within the last year by echocardiogram, cardiac catheterisation ventriculography, or radionuclide ventriculography, stable NYHA class II-III HF, receiving medication therapy for HF according to the American College of Cardiology/ American Heart Association recommendation guidelines 14 for at least 3 months prior to study enrolment, English speaking and live independently, score ≤ 26 on the Montreal Cognitive Assessment (MOCA)15 and have access to a computerised device

Gary 2019 *(Continued)*

	Exclusion: unstable angina or hypertension, end-stage organ failure, and any identified or diagnosed neurological or psychological disorder that would interfere with physical or cognitive functioning
Interventions	**Exercise only** • Total duration: 24 weeks • Aerobic/resistance/mix: aerobic • Frequency: 3 days/week • Duration: 30 min up to 45 min • Intensity: 60% up to 70% of maximum HR • Modality: walking • Setting: home-based + weekly telephone supervision by member of research team for first 12 weeks and then every 2-6-months **Exercise and cognitive training:** as above, plus "The Brain Fitness" cognitive training program. Brain Fitness computerised program designed to be completed over 8 weeks in 40 x 1-h sessions **Control:** attentional control usual care – received education, flexibility and stretching over same time-time equivalence.
Outcomes	Depressive symptoms, programme adherence, exercise capacity, neurocognition*
Country and setting	USA, single centre
Follow-up	6-months
Notes	N/A "Pilot trial" *None of the outcomes reported were relevant to this review **Source of funding:** US National Institutes of Health National Institute of Nursing Research

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	"Once baseline measurements were completed, participants were randomized using a table of random numbers prepared by a statistician"
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding (performance bias and detection bias) All outcomes	Low risk	"Data collection was conducted by trained research assistants (RAs) blinded to group assignment"
Incomplete outcome data (attrition bias)	High risk	From the 69 patients randomised, only 39 completed the study (57%).
Selective reporting (reporting bias)	Low risk	All discussed outcomes in methods were reported.
Groups balanced at baseline?	High risk	"There were a greater number of comorbidities in the EX [exercise] group and was controlled as a covariate"
Groups received comparable care?	High risk	Intervention groups were not reported to have received the "education, flexibility and stretching protocols" which the control group received.

Gary 2019 *(Continued)*

Intention-to-treat analysis?	Low risk	"An intent to treat approach was used for data analysis"

Giallauria 2008

Study characteristics	
Methods	Parallel-group RCT
Participants	**N randomised:** 61 (exercise 30, control 31) **Diagnosis (% of participants)** • Aetiology: anteroseptal acute MI: total 55.7%, exercise 60%, control 55% • NYHA: exercise 2.7 ± 0.7, control 2.6 ± 0.5 • LVEF: exercise 41.6 ± 11.3%, control 42.0 ± 7.6% **Case mix:** 100%, as above **Age (mean ± SD), years:** exercise 55.9 ± 3.1, control 55.1 ± 3.7 **Male:** total 72.1%, exercise 73.3%, control 71% **White:** not reported **Inclusion/exclusion criteria** **Inclusion:** consecutive patients immediately post STEMI **Exclusion:** residual myocardial ischaemia, severe ventricular arrhythmias, atrioventricular block, valvular disease requiring surgery, pericarditis, severe renal dysfunction (i.e. creatinine > 2.5 mg/dL)
Interventions	**Exercise** • Total duration: 12 weeks • Aerobic/resistance/mix: aerobic • Frequency: 3 sessions/week • Duration: 40 min (30 min plus 5 min of warm-up and 5 min of cool-down) • Intensity: tailored to individual (target 60%-70% of VO_2 peak achieved at initial symptom-limited cardiopulmonary exercise test) • Modality: cycling • Setting: hospital (supervised) **Other:** usual care co-interventions **Control group/comparison:** usual care (generic instructions re exercise and diet plus a visit at 6 months)
Outcomes	Hospital admissions
Country and setting	UK, single centre
Follow-up	6 months
Notes	**Source of funding:** study authors state there was no conflict of interest related to sponsorship.
Risk of bias	

Giallauria 2008 *(Continued)*

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not reported
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding (performance bias and detection bias) All outcomes	Unclear risk	Unclear whether clinician prescribing hospitalisation following dyspnoea was blinded
Incomplete outcome data (attrition bias)	Low risk	All participants were accounted for.
Selective reporting (reporting bias)	Unclear risk	No protocol available
Groups balanced at baseline?	Low risk	No differences between groups were noted (Table 1).
Groups received comparable care?	Low risk	Medications were uptitrated to maximal in both groups.
Intention-to-treat analysis?	Unclear risk	Not stated whether intention-to-treat analysis was performed, but looks as if groups were analysed to original random allocation

Giannuzzi 2003

Study characteristics	
Methods	Parallel-group RCT
Participants	**N randomised:** 90; 45 each group **Diagnosis (% of participants)** • Aetiology: HF secondary to idiopathic DCM; ischaemic heart disease; valvular disease • NYHA: Class II-III • LVEF: exercise 25% (SD 4), control 25% (SD 4) **Case mix:** 100% **Age, years:** exercise 60 (SD 7), control 61 (SD 7) **Male:** not reported **White:** not reported **Inclusion/exclusion criteria** **Inclusion**: HF secondary to idiopathic DCM, ischaemic heart disease, or valvular disease; echocardiographic EF < 35%; clinical stability for at least 3 months under optimised therapy; NYHA functional Class II-III; peak oxygen uptake (VO_2) < 20 mL/kg/min; echocardiographic images of adequate quality for quantitative analysis **Exclusion:** any systemic disease limiting exercise; hypertrophic cardiomyopathy; valvular disease requiring surgery; angina pectoris; sustained ventricular arrhythmias; severe hypertension; excess vari-

Giannuzzi 2003 *(Continued)*

	ability (> 10%) at baseline cardiopulmonary exercise test; inability to participate in a prospective study for any logistical reason
Interventions	**Exercise** • Total duration: 24 weeks • Aerobic/resistance/mix: aerobic • Frequency: 3-5 sessions/week • Duration: 30 min • Intensity: 60% peak VO_2 • Modality: exercise cycle, daily brisk walk, calisthenics. In addition, requested to take brisk daily walk for > 30 min • Setting: supervised cycling sessions at rehabilitation centre; unsupervised sessions at home **Other:** not reported **Control group/comparison:** educational support but no formal exercise protocol was provided
Outcomes	• Mortality • Morbidity
Country and setting	Italy, multicentre (15 CR units)
Follow-up	6 months (after randomisation)
Notes	**Source of funding:** not reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not reported
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding (performance bias and detection bias) All outcomes	Unclear risk	Not reported
Incomplete outcome data (attrition bias)	Low risk	45/45 (100%) in exercise training group, 44/45 (98%) available at 6 months' follow-up.
Selective reporting (reporting bias)	Low risk	All outcomes described in the methods were reported in the results.
Groups balanced at baseline?	Low risk	"No significant differences were observed between the 2 groups with respect to demographic and clinical data, including age, weight, cause of heart failure, or New York Heart Association functional class. Furthermore, there was no difference between the 2 groups in the medications received during the 6-month period of the study"
Groups received comparable care?	Unclear risk	Not clearly stated whether co-treatments (i.e. cardiovascular medication) in the 2 groups were the same
Intention-to-treat analysis?	Low risk	Although not stated, it is clear from the CONSORT diagram that 2 groups were analysed according to ITT.

Gielen 2003

Study characteristics	
Methods	Parallel-group RCT
Participants	**N randomised:** 20 (exercise 10, control 10) **Diagnosis (% of participants)** • Aetiology: IHD, DCM • NYHA: Class II 90%, Class III 10% • LVEF: exercise mean 26.1% (SD 6), control mean 24.7% (SD 8) **Case mix:** 100%, as above **Age, years:** exercise 55 (SD 6), control 53 (SD 9) **Male:** 100% **White:** not reported **Inclusion/exclusion criteria** **Inclusion:** age < 70 years with CHF (NYHA II-III) as a result of DCM or IHD as assessed by cardiac catheterisation. All had clinical, radiological, and echocardiographic signs of CHF and an LVEF of 40% as assessed by ventriculography and clinically stable condition for > 3 months before enrolment **Exclusion:** significant valvular heart disease, uncontrolled hypertension, peripheral vascular disease, pulmonary disease, musculoskeletal abnormalities precluding exercise training
Interventions	**Exercise** • Total duration: 2 weeks inpatient followed by 6 months outpatient • Aerobic/resistance/mix: aerobic • Frequency: 7 sessions/week • Duration: 20 min/session • Intensity: 70% symptom-limited VO_2 max • Modality: cycle ergometers • Setting: supervised sessions at hospital and home-based unsupervised sessions **Other:** expected to participate in 1 group training session (walking, calisthenics, and non-competitive ball games) of 60 minutes each week. Participants were asked to exercise for 20 min/d at home **Control group/comparison:** continued sedentary lifestyle and remained on individually tailored cardiac medication supervised by private physicians
Outcomes	Mortality
Country and setting	Switzerland, single centre
Follow-up	26 weeks (after randomisation)
Notes	**Source of funding:** none reported
Risk of bias	
Bias	**Authors' judgement** **Support for judgement**

Gielen 2003 *(Continued)*

Random sequence generation (selection bias)	Unclear risk	Not reported
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding (performance bias and detection bias) All outcomes	Unclear risk	Not reported
Incomplete outcome data (attrition bias)	Low risk	No loss to follow-up
Selective reporting (reporting bias)	Low risk	All outcomes described in the methods were reported in the results
Groups balanced at baseline?	Low risk	"Patients in the training group and in the control group showed a significantly reduced left ventricular ejection fraction (training group: 26.1 ±3.1%, control group: 24.7± 2.4%; NS [not significant]) and exercise capacity as determined by peak oxygen uptake (training group: 20.3 ± 1.0 ml/kg min, control group: 17.9 ± 1.6 ml/kg min; P NS)"
Groups received comparable care?	Unclear risk	Details of co-interventions not reported
Intention-to-treat analysis?	Low risk	Although ITT analysis not reported, groups do appear to be analysed according to original randomised allocation

Gottlieb 1999

Study characteristics	
Methods	Parallel-group RCT
Participants	**N randomised:** 33 **Diagnosis (% of participants)** • Aetiology: ischaemic or primary • NYHA: Class II or III • LVEF: exercise 22% (SD 8), control 25% (SD 10) **Case mix:** 100%, as above **Age, years:** exercise 67 (SD 7), control 64 (SD 10) **Male:** exercise 15/16 (94%), control 11/14 (79%), total 87% **White:** not reported **Inclusion/exclusion criteria** **Inclusion:** NYHA Class II-III for at least 3 months and on stable medications for the past 1 month. All participants were on maximal medical therapy with ACEIs, diuretic, and digoxin. All participants had EF < 40% by nuclear ventriculography. No participants had obstructive valvular disease, MI within 3 months, or limitation of exercise secondary to angina or new arrhythmias

Gottlieb 1999 *(Continued)*

	Exclusion: not reported
Interventions	**Exercise** • Total duration: 3 months • Aerobic/resistance/mix: aerobic • Frequency: 3 sessions/week • Duration: 30 min • Intensity: Borg 12-13 • Modality: bike and treadmill • Setting: supervised sessions at medical centre by a nurse or an exercise physiologist **Other:** care provided by a specialist HF physician **Control group/comparison:** usual medical care **Other:** care provided by specialist HF physicians
Outcomes	• HRQoL (MLWHF questionnaire and MOS SF-36 questionnaire) • Mortality • Morbidity
Country and setting	USA, single centre
Follow-up	6 months (after randomisation)
Notes	MLWHF, MOS, SF-36 results not reported for the control group **Source of funding:** not reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not reported
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding (performance bias and detection bias) All outcomes	Unclear risk	Not reported
Incomplete outcome data (attrition bias)	Low risk	Yes, QUORUM flow diagram reported Unclear how loss to follow-up, dropout, and cross-over were dealt with
Selective reporting (reporting bias)	Low risk	All outcomes described in the methods were reported in the results.
Groups balanced at baseline?	Low risk	"There were no differences at baseline between patients randomised to the control group and those randomised to the exercise program"
Groups received comparable care?	Low risk	"Medical follow-up of both the control and intervention patient groups was provided by specialized heart failure physicians"

Gottlieb 1999 *(Continued)*

Intention-to-treat analysis?	Unclear risk	Not reported

Hagglund 2018

Study characteristics	
Methods	Parallel-group RCT
Participants	**N randomised:** 45 (exercise 25, control 20) **Diagnosis (% of participants)** • Aetiology: not reported • NYHA: not reported (75% reported > 12 on MFI-20 = NYHA II-III) • LVEF: not reported (LVEF < 50%) **Case mix:** as above **Age:** 75 years:exercise 75.6 (range: 71-85), control 75.5 (range: 71-83) **Male:** 78% **White:** not reported **Inclusion/exclusion criteria** **Inclusion:** verified CHF; stable medication, perceived fatigue, age ≥ 70 **Exclusion:** unstable angina pectoris, MI within last 3 months, cognitive impairment, no perceived fatigue
Interventions	**Exercise** • Total duration: 16 weeks • Aerobic/resistance/mix: mix • Frequency: 2 times/week • Duration: 60 min • Intensity: not defined • Modality: Tai Chi • Setting: training centre • Other: performed sitting in a chair
Outcomes	• MFI-20 • MLWHF* • SPPB - Swedish version
Country and setting	Sweden, multicentre (3 sites)
Follow-up	Baseline, and end of training (16 weeks from baseline), and 6 months post-training (10 months from baseline)
Notes	*Outcome relevant to this review **Source of funding:** not reported

Hagglund 2018 *(Continued)*

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	"the participants were randomly assigned to either a control or training group"
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding (performance bias and detection bias) All outcomes	Unclear risk	Not reported
Incomplete outcome data (attrition bias)	High risk	Exercise 21/25 (84%), control 12/20 (60%) provided outcomes for primary analysis at 12-months
Selective reporting (reporting bias)	High risk	Not all outcomes discussed in methods were reported i.e. MLWHF
Groups balanced at baseline?	High risk	"At baseline, participants in the control group rated a higher degree of mental fatigue compared with the training group (mean 11.3 vs. 10.3, p = .034) and had higher BMI than participants in the training group (mean 28 vs. 26, p = .055)"
Groups received comparable care?	Low risk	"the control group continued their normal living habits"
Intention-to-treat analysis?	Unclear risk	Not reported

Hambrecht 1995

Study characteristics

Methods	Parallel-group RCT
Participants	**N randomised:** 22 (exercise 12, control 10) **Diagnosis (% of participants)** • Aetiology: DCM 86%, ischaemic heart disease 14% • NYHA: Class II (55%), Class III (45%) • LVEF: exercise 26% (SD 9), control 27% (SD 10) **Case mix:** 100%, as above **Age, years:** exercise 50 (SD 12), control 52 (SD 8) **Male:** 100% **White:** not reported **Inclusion/exclusion criteria** **Inclusion:** EF < 40% as assessed by radionucleotide scintigraphy and reduced fractional shortening < 30% as assessed by echocardiography; willingness to participate in the study for the next 6 months; permanent residence within 25 km of the training facility; physical work capacity at baseline > 25 watts

Hambrecht 1995 *(Continued)*

	without signs of myocardial ischaemia (i.e. angina or ST segment depression); clinically stable > 3 months **Exclusion:** exercise-induced myocardial ischaemia or ventricular tachyarrhythmias (> Lown Class IVa), valvular heart disease, uncontrolled hypertension, PVD, COPD, orthopaedic or other conditions precluding regular participation in exercise sessions
Interventions	**Exercise** • Total duration: 6 months • Aerobic/resistance/mix: aerobic • Frequency: 4-6 sessions/week • Duration: 10-60 min/session, 1 h at home • Intensity: 70% VO_2 max • Modality: cycling, walking, ball games, and calisthenics • Setting: first 3 weeks supervised hospital-based training; thereafter, home-based **Other:** none **Control group/comparison:** after discharge, medical therapy was continued and participants were supervised by private physician
Outcomes	Morbidity and mortality
Country and setting	Germany, single centre
Follow-up	6 months (after randomisation)
Notes	**Source of funding:** not reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not reported
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding (performance bias and detection bias) All outcomes	Unclear risk	Not reported
Incomplete outcome data (attrition bias)	Low risk	Dropouts and clinical events were fully reported for both groups. No imputation was undertaken.
Selective reporting (reporting bias)	Low risk	All outcomes described in the methods were reported in the results.
Groups balanced at baseline?	Low risk	"There were no significant differences in baseline variables between the training and control groups"
Groups received comparable care?	Unclear risk	The exercise group had a 3-week hospital stay; the control group stayed only 3 days. Control group followed up with private physician. No comment was included on follow-up of the intervention group.

Hambrecht 1995 *(Continued)*

Intention-to-treat analysis?	Unclear risk	Not reported

Hambrecht 1998

Study characteristics	
Methods	Parallel-group RCT
Participants	**N randomised:** 20 (exercise 10, control 10) **Diagnosis (% of participants)** • Aetiology: IHD 35%, DCM 65% • NYHA: Class II 65%, Class III 35% • LVEF: exercise mean 24% (SD 13), control mean 23% (SD 10%) **Case mix:** as above **Age, years:** exercise 54 (SD 9), control 56 (8) **Male:** 100% **White:** not reported **Inclusion/exclusion criteria** **Inclusion:**age < 70 years, with CHF as a result of DCM or IHD; LVEF < 40% **Exclusion:** DM, hypertension, overt atherosclerotic PVD, hypercholesterolaemia, ventricular tachycardia, COPD, primary valvular disease
Interventions	**Exercise** • Total duration: 6 months • Aerobic/resistance/mix: aerobic • Frequency: 2-6 sessions/d • Duration: 10-20 min/session • Intensity: 70% VO_2 max • Modality: bike ergometer • Setting: supervised hospital-based sessions and unsupervised home-based sessions **Other:** not reported **Control group/comparison:** stayed on previous medication, continued sedentary lifestyle, and supervised by private physicians
Outcomes	Mortality
Country and setting	Germany, single centre
Follow-up	6 months (after randomisation)
Notes	**Source of funding:** Grant Ha 2155/3-2 from the Deutsche Forschungsgemeinschaft (DFG), Bonn, Germany
Risk of bias	

Hambrecht 1998 *(Continued)*

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not reported
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding (performance bias and detection bias) All outcomes	Unclear risk	Not reported
Incomplete outcome data (attrition bias)	Low risk	Detailed description of losses to follow-up and dropouts was provided.
Selective reporting (reporting bias)	Low risk	All outcomes described in the methods were reported in the results.
Groups balanced at baseline?	Low risk	"At baseline, patients in the control group did not differ significantly from those in the training group with respect to age, aetiology of heart failure, NYHA functional class, duration of heart failure, LVEF (left ventricular ejection fraction) or LVEDD (left ventricular end diastolic diameter)"
Groups received comparable care?	Low risk	"Patients were on angiotensin-converting enzyme inhibitors (100% in both groups), diuretics (training group 82%, control 70%), and digoxin (training 73%, control 70%, P5NS). Drug treatment did not change between 4 weeks before enrolment and study termination"
Intention-to-treat analysis?	Low risk	It appears that groups were analysed according to original randomised allocation.

Hambrecht 2000

Study characteristics	
Methods	Parallel-group RCT
Participants	**N randomised:** 73 (exercise 36, control 37) **Diagnosis (% of participants)** • Aetiology: IHD 16%, DCM 84% • NYHA: Class I and II 74%, Class III 26% • LVEF: 29% (SD 9) **Case mix:** 100%, as above **Age, years:** exercise 54 (SD 9), control 54 (SD 8) **Male:** 100% **White:** not reported **Inclusion/exclusion criteria** **Inclusion:** documented HF by signs, symptoms, and angiographic evidence of reduced LVEF (< 40%) as a result of DCM or IHD; physical work capacity at baseline > 25 watts; clinical stability ≥ 3 months before study start

Hambrecht 2000 *(Continued)*

	Exclusion: significant valvular heart disease, uncontrolled hypertension, DM, hypercholesterolaemia, PVD, pulmonary disease, musculoskeletal abnormalities precluding exercise training
Interventions	**Exercise** • Total duration: 6 months • Aerobic/resistance/mix: aerobic • Frequency: 6 or 7 sessions/week • Duration: 10-20 min/session • Intensity: 70% of peak VO_2 • Modality: cycle ergometer • Setting: first 2 weeks in hospital, remainder home based **Other:** plus group sessions 1 h twice weekly, walking, ball games, and calisthenics **Control group/comparison:** continued individually tailored cardiac medications, supervised by physicians
Outcomes	Mortality
Country and setting	Germany, single centre
Follow-up	6 months (after randomisation)
Notes	**Source of funding:** Grant Ha 2155/3-2, from the Deutsche Forschungsgemeinschaft (DFG), Bonn, Germany

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	"Patients were randomly assigned to either a training group or an inactive group using a list of random numbers"
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding (performance bias and detection bias) All outcomes	Unclear risk	Not reported
Incomplete outcome data (attrition bias)	Low risk	QUORUM diagram and details of losses to follow-up were reported.
Selective reporting (reporting bias)	Low risk	All outcomes described in the methods were reported in the results
Groups balanced at baseline?	Low risk	"No significant differences were observed between the two groups with regard to demographic or clinical data, including age, weight, LVEF, LVEDD (left ventricular end diastolic diameter), NYHA or maximum oxygen uptake"
Groups received comparable care?	Unclear risk	Co-interventions in the control group were not reported.
Intention-to-treat analysis?	Low risk	Not reported

Hasanpour-Dehkordi 2020

Study characteristics	
Methods	Parallel-group RCT
Participants	**N randomised:** 52 (exercise 26, control 26) **Diagnosis (% of participants)** • Aetiology: not reported • NYHA: II 23%; III 77% • LVEF: not reported (≤ 40%) **Case mix:** as above **Age:** 60 ± 5 years **Male:** 60% **White:** not reported **Inclusion/exclusion criteria** **Inclusion:**patients suffering from chronic heart disease, age 60 ± 5 years, volunteering to participate in the study, as well as the diagnosis of congestive HF by a cardiologist, clinical symptoms, echocardiography, LVEF ≤ 40%, the ability to do the exercise in question after pharmacotherapy, the physician's approval, lack of other chronic diseases (rheumatoid arthritis, fractures, etc.), as well as lack of traveling and heart transplantation until 3 months after the exercise programme **Exclusion:** coronary artery bypass surgery during the study, withdrawing from the study at any stage of this study, and percutaneous transluminal coronary angioplasty/coronary artery bypass grafting surgery in the previous year.
Interventions	**Exercise** • Total duration: 24 weeks • Aerobic/resistance/mix: aerobic • Frequency: 3 times/week • Duration: 40 min • Intensity: 60%-70% HR • Modality: walking • Setting: gym in hospital • Other: supervised by nursing or medical team **Control:** educational support Both intervention and control groups received usual medication
Outcomes	QoL SF-36: Physical functioning, Role-physical, Bodily, General, Energy, Social functioning, Role-emotional, Mental, Fatigue, Total QoL
Country and setting	Iran, single site
Follow-up	Baseline (prerandomisation) and 6 months post-randomisation
Notes	**Source of funding:** Deputy of Research and Technology of Shahrekord University of Medical Sciences
Risk of bias	

Hasanpour-Dehkordi 2020 *(Continued)*

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	"based on random allocation rule, the participants were randomly divided into case (Class II and III) and control (Class II and III) groups."
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding (performance bias and detection bias) All outcomes	Unclear risk	Not reported
Incomplete outcome data (attrition bias)	Low risk	Exercise 26/26 (100%), control 26/26 (100%) provided outcomes at 24 weeks
Selective reporting (reporting bias)	Low risk	Whilst some outcomes appear to be named differently in results table 2 to the outcomes described in the methods, all outcomes are reported fully.
Groups balanced at baseline?	Low risk	"At baseline, no significant difference was observed in blood pressure, pulse, physical functioning, `role-physical, role-emotional,` social functional, mental status, general health, fatigue level, and body pain between the two groups"
Groups received comparable care?	Low risk	"patients in both the groups received their medications as prescribed by the cardiologist."
Intention-to-treat analysis?	Low risk	Although not formally stated, the groups appear to be analysed by initial random allocation.

HF ACTION 2009

Study characteristics	
Methods	Parallel-group RCT
Participants	**N randomised:** 2331 (exercise 1159, control 1172) **Diagnosis (% of participants)** • Aetiology: IHD 51% • NYHA: Class II 63%, Class III 35%, Class IV 1% • LVEF: 25% (SD not reported) **Case mix:** 100%, as above **Age, years:** exercise 59 (SD not reported), control 59 (SD not reported) **Male:** 72% **White:** 62% **Inclusion/exclusion criteria** **Inclusion:**LVEF < 35%; NYHA Class II to IV HF for previous 3 months despite a 6-week period of treatment; optimal HF therapy at stable doses for 6 weeks before enrolment or documented rationale for variation, including intolerance, contraindication, participant preference, and personal physician's judgement; sufficient stability, by investigator judgement, to begin an exercise programme

HF ACTION 2009 *(Continued)*

	Exclusion*:* (selected) age < 18 years; co-morbid disease or behavioural or other limitations that interfere with performing exercise training or preventing the completion of 1 year of exercise training; major cardiovascular event or cardiovascular procedure, including implantable cardioverter-defibrillator use and cardiac re-synchronisation, within previous 6 weeks
Interventions	**Exercise** • Total duration: 30 months • Aerobic/resistance/mix: aerobic • Frequency: 3-5 sessions/week • Duration: 15-35 min/session • Intensity: 60%-70% HR reserve • Modality: cycling or walking • Setting: first 36 sessions were supervised, then participant was advised to follow a 5 days/week home-based exercise programme **Other:** none reported **Control group/comparison:** usual care: all participants, regardless of group allocation, received self-management educational materials consistent with guidelines of American College of Cardiology and American Heart Association
Outcomes	• Mortality • Hospitalisation • HRQoL (KCCQ) • Cost-effectiveness
Country and setting	USA, multicentre
Follow-up	Median 30.1 months (after randomisation)
Notes	Study authors were contacted for further details of outcome findings, but no information was provided **Source of funding:** study authors were funded by various bodies, including NIH and various pharmaceutical companies, particularly GE Medical and Roche

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	"The trial uses a permuted block randomization scheme stratified by center and by the etiology of the patient's heart failure (ischemic vs nonischemic)"
Allocation concealment (selection bias)	Low risk	"Patients are randomized at the enrolling centers using an interactive voice response"
Blinding (performance bias and detection bias) All outcomes	Low risk	Event outcomes were blinded.
Incomplete outcome data (attrition bias)	Low risk	QUORUM diagram and details of losses to follow-up were reported.
Selective reporting (reporting bias)	Low risk	All outcomes described in the methods were reported in the results.
Groups balanced at baseline?	Low risk	Table 1 of the publication shows that the 2 groups were well balanced.

HF ACTION 2009 *(Continued)*

Groups received comparable care?	Low risk	"All patients, regardless of group allocation, received self-management educational materials...consistent with guidelines of American College of Cardiology and American Heart Association"
Intention-to-treat analysis?	Low risk	"Statistical comparisons of the treatment arms with respect to clinical outcomes were performed according to the intention-to-treat principle"

Hieda 2021

Study characteristics	
Methods	Parallel-group RCT
Participants	**N randomised:** 56 (exercise 38, control 18) **Diagnosis (% of participants)** • Aetiology: unreported • NYHA: unreported • LVEF: unreported **Case mix:** as above **Age:** exercise 53 (5), control 53 (7) **Male:** 57% **White:** 52% **Inclusion/exclusion criteria** **Inclusion:** EF > 50% and documented LVH by MRI (125 g/m2) or echocardiography (left ventricular septum > 11 mm) **Exclusion: (as extracted from the Dallas Heart Study*):** dilated LV at baseline, defined by LV end-diastolic volume indexed to body surface area (LVEDV/BSA) > 97.5th percentile of a normal subpopulation 30 (82.8 mL/m2 for men and 80.3 mL/m2 for women, those who developed cardiovascular disease (CVD) (defined as MI, coronary bypass surgery, percutaneous intervention, stroke, or HF)
Interventions	**Exercise** • Total duration: 52 weeks (details) • Aerobic/resistance/mix: mix • Frequency: 4-6 times/week (3-4 aerobic + 1-2 resistance) • Duration: 30-60 min • Intensity: varies: > 95% HR to “HR = Maximal Steady State – 20” • Modality: walk, cycle, swim • Setting: not specified • Other: individually designed with a personal trainer, every session HR data recorded **Control** • Yoga, balance, and strength training (light weights) • 3 times per week for 1 year • Home-based
Outcomes	Outcomes not explicitly stated. Measurements include:

Hieda 2021 *(Continued)*

- VO2 max
- Mean pulmonary capillary wedge pressure
- Right atrial pressure
- LV end diastolic volume
- HR
- Blood pressure
- Lean body mass

Country and setting	USA, centre(s) not reported
Follow-up	Baseline (prerandomisation) and 12 months post-randomisation
Notes	*Cohort recruited from Dallas Heart Study 2017 **Source of funding:** American Heart Association Strategically Focused Research Network; NIH

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	"Subjects were stratified by sex and allocated to either exercise or yoga interventions using a stratified block randomization at a 2:1 exercise-to-control ratio (allowing for greater attrition for the exercise group). The randomization schema was programmed using SAS Proc Plan and performed by the study biostatistician"
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding (performance bias and detection bias) All outcomes	Unclear risk	Not reported
Incomplete outcome data (attrition bias)	High risk	Exercise 20/38 (53%), control 11/18 (61%) of those randomised completed the trial and provided outcome data for analysis at 12 months
Selective reporting (reporting bias)	High risk	Outcomes not explicitly stated
Groups balanced at baseline?	Low risk	"The 2 groups were comparable in age, sex, race, blood pressure, and maximal oxygen uptake."
Groups received comparable care?	High risk	The control group were prescribed a 12-month yoga programme. The intervention group were not prescribed yoga as part of their intervention.
Intention-to-treat analysis?	High risk	"The primary analysis included all participants who completed the 1-year follow-up."

Jaarsma 2020

Study characteristics

Methods	Parallel group RCT
Participants	**N randomised:** 605 (exercise 305, control 300)

Jaarsma 2020 *(Continued)*

	Diagnosis (% of participants) • Aetiology: ischaemic 42% • NYHA: I 9% II 60%; III 30% IV 1% • LVEF: HFrEF 47%, HFmrEF 30%, HFpEF 22% **Case mix:** as above **Age:** 67 (12):Intervention 66 (12) Control 67 (11) **Male:** 71% **White:** not reported **Inclusion/exclusion criteria** **Inclusion:**> 18 years diagnosed with HF (NYHA class I–IV])by a cardiologist according to European Society of Cardiology Guidelines (HFrEF or HFpEF), spoke the language of the including country **Exclusion:** unable to use the computer game due to visual impairment (not able to see a TV at 3 m), hearing impairment (not able to telephone), cognitive impairment (assessed by an HF team), motor impairment (not able to swing arm > 10 times), or unable to complete questionnaires, having a life expectancy < 6 months
Interventions	**Exercise:** • Total duration: 12 weeks • Aerobic/resistance/mix: aerobic • Frequency: 5 times/week • Duration: 30 min • Intensity: not defined • Modality: exergaming (Nintendo Wii – Wii Sports Game) (baseball, bowling, boxing, golf, tennis) • Setting: home • Other: if patients were not able to be active for 30 min a day, they were advised to play for as many min as possible with an increasing length of time until they reached 30 min a day **Control:** protocol-based physical activity advice and motivational telephone follow-up from a HF team member
Outcomes	Primary: submaximal aerobic capacity (6MWT) Secondary: muscle function, exercise motivation, exercise self-efficacy, self-reported physical activity, heart failure symptoms (visual analogue scale), HRQoL (MLwHFQ), well-being (cantril Ladder), mortality and readmission (registration), anxiety/depression (HADS), insomnia (MISS), self-care (EHFScBS), costs
Country and setting	Sweden, Italy, Israel, the Netherlands, Germany, and the USA; multi-centre (10 sites)
Follow-up	Baseline (prerandomisation) and 3 months and 6 months and 12 months post-randomisation
Notes	Funding from the Swedish National Science Council. Study authors undertook a number of subgroup analyses. They provided us with HRQoL outcome data not yet published as of 15 March 2022.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	"Randomization was in a 1:1 ratio, stratified by study centre…..randomization was done in blocks comprising an equal number of patients (8 or 12) per

Jaarsma 2020 *(Continued)*

		group." "A clinical trial centre (Forum Östergötland) provided a list of computer-generated randomized block allocations for each study centre."
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding (performance bias and detection bias) All outcomes	Low risk	"Blinding to treatment allocation for patients was impossible, but outcome assessors of the 6MWT and personnel who entered and checked data were blinded to group assignment."
Incomplete outcome data (attrition bias)	High risk	Exercise 234/305 (77%), control 230/300 (76%) provided outcomes for primary analysis at 12 months
Selective reporting (reporting bias)	High risk	Not all outcomes published in protocol are reported in the main paper.
Groups balanced at baseline?	Low risk	"Groups were well balanced regarding baseline characteristics"
Groups received comparable care?	Low risk	"All patients received regular treatment as well as information about cardiac rehabilitation and physical activity according to standard practice at their referring centre (usual care)." "To balance for extra attention in the intervention group, controls received motivational telephone follow-up at 2, 4, 8, and 12 weeks following a standard script discussing their physical activity"
Intention-to-treat analysis?	Low risk	"an intention-to-treat analysis was performed"

Jolly 2009

Study characteristics	
Methods	Parallel-group RCT
Participants	**N randomised:** 169 (exercise 84, control 85) **Diagnosis (% of participants)** • Aetiology: data not available • NYHA: Class I 6%, Class II 74%, Class III 20% • LVEF: ≤ 40% **Age, years:** exercise 65.9 (SD 12.5), control 70 (SD 12.5) **Male:** 75% **White:** 85.1% **Inclusion/exclusion criteria** **Inclusion:**LVEF ≤ 40% on echocardiogram and severity of at least NYHA group II in the previous 24 months; had to have been clinically stable for 4 weeks and in receipt of optimal medical treatment and in care of a specialist HF nurse team from 2 acute hospital trusts and 1 primary care trust, not considered high-risk for a home-based exercise programme **Exclusion:**NYHA Class IV; MI or re-vascularisation within past 4 months; hypotension; unstable angina; ventricular or symptomatic arrhythmias; obstructive abortive valvular disease; COPD; hypertrophic ob-

Jolly 2009 *(Continued)*

	structive cardiomyopathy; severe musculoskeletal problems preventing exercise; case note-reported dementia or current severe psychiatric disorder
Interventions	**Exercise** Total duration: 6-month programme progressive with aim that participants would achieve the following. • Aerobic/resistance/mix: mix • Frequency: 5 times/week • Duration: 20-30 min • Intensity: 70% peak VO_2 or Borg 12-13 • Modality: aerobic and resistance elements (upper and lower limb exercises) • Setting: first 3 sessions supervised centre-based followed by home-based programme with home visits by nurse at 4, 10, and 20 weeks and telephone support at 6, 15, and 24 weeks; intervention manual provided **Other:** specialist HF nurse care **Control group/comparison:** specialist HF nurse care
Outcomes	HRQoL (MLWHF questionnaire); composite of death, hospital admissions, generic quality of life (EQ-5D)
Country and setting	West Midlands, UK, community
Follow-up	6-month and 12-month follow-up (after randomisation)
Notes	**Source of funding:** Department of Health's Policy Research Programme, as part of a joint DH/British Heart Foundation Heart Failure research initiative

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	"An independent clinical trials unit using a computerized programme undertook randomization after each patient had consented and undergone the baseline tests and questionnaire"
Allocation concealment (selection bias)	Low risk	"An independent clinical trials unit using a computerized programme undertook randomization after each patient had consented and undergone the baseline tests and questionnaire"
Blinding (performance bias and detection bias) All outcomes	High risk	"…, the nurse undertaking the assessment was blinded to the treatment allocation of the patient, but owing to staffing issues, this occurred in only 62% of participants followed up at 6 months"
Incomplete outcome data (attrition bias)	Low risk	Dropouts and clinical events were fully reported. Outcomes available for 161 (95%) participants at 6 months and for 157 (92%) participants at 12 months. Non-imputed data were reported, and sensitivity analysis was undertaken to examine the impact of missing data.
Selective reporting (reporting bias)	Low risk	All primary outcomes and most secondary outcomes described in the methods were reported. Stated in the methods that blood pressure and incremental shuttle walking test were not collected at 12 months

Jolly 2009 *(Continued)*

Groups balanced at baseline?	Unclear risk	"Baseline characteristics were broadly comparable, the exception being that the exercise group was somewhat younger and had higher HADS depression scores and a lower systolic blood pressure"
Groups received comparable care?	Low risk	"Both groups received specialist heart failure nurse input in primary and secondary care through clinic and home visits that included the provision of information about heart failure, advice about self-management and monitoring of their condition, and titration of beta-blocker therapy"
Intention-to-treat analysis?	Low risk	"...between- and within-group analyses for primary and secondary outcomes at 6 and 12 months were performed according to intention to treat"

Jónsdóttir 2006

Study characteristics	
Methods	Parallel-group RCT
Participants	**N randomised:** 43 (exercise 21, control 22) **Diagnosis (% of participants)** • Aetiology: ischaemic 79%, AF 12%, valvular 7%, hypertension 2% • NYHA: Class II and III • LVEF: exercise 41.5 (SD 13.6), control 40.6% (SD 13.7) **Case mix:** as above **Age, years:** exercise 68 (SD 7), control 69 (SD 5) **Male:** 79% **White:** not reported **Inclusion/exclusion criteria** **Inclusion:** CHF diagnosis; on CHF medication; clinical symptoms of CHF; clinically stable > 3 months before study entrance; fulfilling 1 of the following criteria: previous MI, hospitalised because of CHF, lung oedema, and cardiac enlargement on X-ray **Exclusion:** COPD, orthopaedic disabilities, psychiatric disabilities, cancer, senility, age > 80 years
Interventions	**Exercise** • Total duration: 5 months • Aerobic/resistance/mix: mix • Frequency: 2 sessions/week • Duration: 45 min • Intensity: not reported • Modality: cycling, free weights, and elastic rubber bands (Thera-bands) • Setting: hospital outpatients, supervised by physiotherapists **Other:** training group given 3 educational lectures about nutrition, physical activity, and relaxation, in addition to the exercise programme **Control group/comparison:** usual medical care (continued previous level of physical activity, which varied from performing little physical activity to taking a daily walk outdoors)

Jónsdóttir 2006 *(Continued)*

Outcomes	• Rehospitalisation • Mortality
Country and setting	Iceland, single centre
Follow-up	12 months and 28 months (after randomisation)
Notes	**Source of funding:** none reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not reported
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding (performance bias and detection bias) All outcomes	Unclear risk	Not reported
Incomplete outcome data (attrition bias)	Low risk	No losses to follow-up
Selective reporting (reporting bias)	Low risk	All outcomes described in the methods were reported in the results
Groups balanced at baseline?	Low risk	Table 2 of the publication suggests that the 2 groups were well balanced
Groups received comparable care?	Low risk	Yes, both groups appeared to receive the same interventions apart from the CR intervention
Intention-to-treat analysis?	Low risk	Although not reported as an ITT analysis, groups did appear to be analysed according to the original randomised allocation

Kaltsatou 2014

Study characteristics

Methods	Parallel-group RCT, 2 arms
Participants	**N randomised:** 57 (dance 19, formal exercise 19, control 19) **Diagnosis (% of participants)** • Aetiology: coronary artery disease 29.8%, hypertension 24.6%, valvular heart disease 24.6%, arrhythmia 21.1% • NYHA: not reported • LVEF: dance 49.3 ± 3.4%, formal exercise 49.1 ± 2.4%, control 49.6 ± 3.5% **Case mix:** as above **Age, years:** dance 67.2 (SD 4.2), formal exercise 67.1 (SD 7.2), control 67.2 (SD 5)

Kaltsatou 2014 *(Continued)*

	Male: 100% **White:** not reported **Inclusion/exclusion criteria** **Inclusion:**NYHA II/III, HF with at least 3 months' clinical stability, no participation in any form of regular exercise **Exclusion:** unstable angina, MI within last 5 months, uncontrolled hypertension, COPD, insulin-dependent DM, severe neurological or orthopaedic problems that would hinder the patient's participation in the exercise programme
Interventions	**Exercise** • Total duration: 32 weeks • Aerobic/resistance/mix: mix (resistance training included in the formal exercise group) • Frequency: 3 sessions/week • Duration: 60 min • Intensity: moderate: exercise perceived exertion 13-14 (somewhat hard) on the Borg 6-20 category scale • Modality: dancing, cycling, or treadmill • Setting: home setting (supervised training at a public gym) **Other:** not reported **Control group/comparison:** usual care (no formal intervention was provided, and participants were asked to continue with usual sedentary lifestyle).
Outcomes	HRQoL (Greek version of SF-36)
Country and setting	Greece, single centre
Follow-up	8 months
Notes	Formal exercise was structured by a group of experienced exercise trainers specialising in cardiac rehabilitation. Dance intervention was designed by a dance teacher with experience in rehabilitation **Source of funding:** no specific grant from any funding agency in public, commercial, or not-for-profit sectors

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	"simple random allocation (drawing lots)"
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding (performance bias and detection bias) All outcomes	Low risk	"All tests were conducted and interpreted by the same researcher blinded to the identity of the subjects"
Incomplete outcome data (attrition bias)	Low risk	Loss to follow-up comparable and low in all groups, with reasons reported. • In the dance group, 1/19 were lost to follow-up • In the formal exercise group, 3/19 were lost to follow-up

Kaltsatou 2014 *(Continued)*

		• In the control group, 2/19 were lost to follow-up
Selective reporting (reporting bias)	Unclear risk	No protocol available
Groups balanced at baseline?	Low risk	No differences between groups
Groups received comparable care?	Low risk	"The participants had to be in a clinically stable condition for at least three months before entering the study and remained in a stable medication regimen and diet during the study"
Intention-to-treat analysis?	Low risk	Although the term ITT was not stated, it appears from the CONSORT diagram that ITT analysis was undertaken.

Keteyian 1996

Study characteristics	
Methods	Parallel-group RCT
Participants	**N randomised:** 40 (exercise 21, control 19) **Diagnosis (% of participants)** • Aetiology: DCM 40%, IHD 60% • NYHA: Class II 67.5%, Class III 32.5% • LVEF: 21% (SD 7) **Case mix:** 100%, as above **Age, years:** 56 (SD 11) **Male:** 100% **White:** 62.5% (remainder black) **Inclusion/exclusion criteria** **Inclusion:**NYHA Class II or III, resting EF < 35% measured by echocardiography or gated equilibrium radionuclide angiography, no change in medical therapy ≥ 30 days before randomisation **Exclusion:** AF, acute MI 3 months, angina pectoris at rest or induced by exercise, current enrolment in another clinical trial, current participation in a regular exercise programme (at least twice weekly)
Interventions	**Exercise** • Total duration: 24 weeks • Aerobic/resistance/mix: aerobic • Frequency: 3 sessions/week (rate of perceived exertion 12-14) • Duration: 33 minutes • Intensity: 60%-80% peak HR • Modality: treadmills, stationary cycles, rowing machines, arm ergometers **Setting:** outpatient clinic **Other:** none reported

Keteyian 1996 *(Continued)*

	Control group/comparison: usual medical care. Participants were instructed to maintain their normal daily activity habits and not to begin an exercise regimen
Outcomes	• Mortality • Hospital admissions
Country and setting	USA, single centre
Follow-up	6 months (after randomisation)
Notes	Study authors were contacted for further details of outcome findings but provided no information. Each participant's physician was asked to not change the drug regimen during the study, if possible **Source of funding:** Astra Merck

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	"Patients were randomly assigned to the exercise group or the control group"
Allocation concealment (selection bias)	Unclear risk	"Each patient's assignment was sealed in an envelope until completion of the second exercise test"
Blinding (performance bias and detection bias) All outcomes	Unclear risk	Not reported
Incomplete outcome data (attrition bias)	Low risk	"Fifteen patients in the exercise group completed the study. Two patients dropped out because of noncardiac medical conditions (progressive, limiting arthritis in one patient and newly diagnosed cancer in the other) that developed within 1 month of the start of the exercise program. One patient developed atrial fibrillation between week 12 and week 24; 3 other patients stopped exercising for personal reasons before week 12 and refused follow-up testing. Fourteen of the 19 patients in the control group completed the study. Two dropped out for personal reasons and refused follow-up testing, one developed atrial fibrillation between week 12 and week 24, one was hospitalized at week 22 for an acute myocardial infarction, and one died suddenly"
Selective reporting (reporting bias)	Low risk	All outcomes described in the methods were reported in the results.
Groups balanced at baseline?	Low risk	"Among patients who completed the study, no differences in demographic characteristics were seen between the two study groups after randomization"
Groups received comparable care?	Unclear risk	Co-interventions in the control group were not reported.
Intention-to-treat analysis?	Low risk	"Of the 40 patients entered into the study, only those who also completed the exercise tests at weeks 12 and 24 were considered in the data analysis"

Kitzman 2021

Study characteristics

Kitzman 2021 *(Continued)*

Methods	Parallel-group RCT

Participants	**N eandomised:** 348 (exercise 175, control 174)
	
	Diagnosis (% of participants)
	
	• Aetiology: not reported
	• NYHA: exercise II 19%; III 57%; IV 23%, control II 20%; III 52%; IV 29%
	• LVEF: not reported
	
	Case mix: as above
	
	Age: 72.7 +- 8.1
	
	Male: 48%
	
	White: 51%
	
	Inclusion/exclusion criteria
	
	Inclusion
	
	• Age ≥ 60 years old
	• In the hospital setting > 24 h for the management of ADHF, or diagnosed with ADHF after being hospitalised for another reason. ADHF will be confirmed by the study physician, and will be defined according to the Food and Drug Administration definition of hospitalised HF as a combination of symptoms, signs, and HF-specific medical treatments, and requires that all 4 of the following are met:
	  ◦ 1) At least one symptom of HF which has worsened from baseline:
	  ▪ dyspnea at rest or with exertion
	  ▪ exertional fatigue
	  ▪ orthopnea
	  ▪ paroxysmal nocturnal dyspnoea (PND)
	  ◦ 2) At least two of the following signs of HF:
	  ▪ pulmonary congestion or oedema on exam (rales or crackles) or by chest X-ray;
	  ▪ elevated jugular venous pressure or central venous pressure ≥ 10 mm Hg
	  ▪ peripheral oedema
	  ▪ wedge or left ventricular end diastolic pressure ≥ 15 mmHg
	  ▪ rapid weight gain (≥ 2.7kg)
	  ▪ increased BNP (≥ 100 pg/mL) or N-terminal prohormone BNP (≥ 220pg/mL)
	  ◦ 3) Change in medical treatment specifically targeting HF defined as change in dose or initiation of or augmentation of at least one of the following therapies:
	  ▪ diuretics
	  ▪ vasodilators
	  ▪ inotropes (including digoxin if for HF)
	  ▪ other neurohormonal modulating agents, including ACEIs, ARBs, beta-blockers, aldosterone or direct renin inhibitors
	  ◦ 4) The primary cause of symptoms and signs is judged by the investigator to be due to HF
	• Adequate clinical stability has been achieved in the judgment of the investigator to allow participation in study assessments and the intervention
	• Prior to admission and HF decompensation, patient was independent with basic activities of daily living (ADLs) including the ability to ambulate independently (with or without the use of an assistive device)
	• Able to walk 4 meters (with or without the use of an assistive device) at the time of enrolment
	• Signed informed consent document indicating that the patient understands the purpose of and procedures required for the study and is willing to participate in the study
	
	Exclusion

Kitzman 2021 *(Continued)*

- Acute MI (Note: given that cardiac biomarkers such as troponin are frequently elevated in HF patients, the diagnosis of acute MI should be based on clinical diagnosis, not biomarkers alone)
- Planned discharge other than to home or a facility where the participant will live independently
- Already actively participating in formal, facility-based cardiac rehabilitation
- Prior cardiac transplantation or planned within the next 6 months
- Severe aortic valve stenosis
- Ventricular assist device or anticipated within the next 6 months
- Already engaging in regular moderate to vigorous exercise conditioning defined as > 30 min/day, ≥ twice/week consistently during the previous 6 weeks
- Terminal illness other than HF with life expectancy < 1 year
- Impairment from stroke, injury or other medical disorder that precludes participation in the intervention
- Dementia that precludes ability to participate in rehabilitation and follow study protocols
- Enrollment in a clinical trial not approved for co-enrollment
- Expected use of continuous intravenous inotropic therapy after discharge 5
- Implantable cardioverter defibrillator with heart rate limits < expected heart rates for exercise and unable to be reprogrammed
- Advanced CKD defined as estimated glomerular filtration rate < 20 mL/min/1.73 m2 based upon the Modification of Diet in Renal Disease study equation, current ultrafiltration, or on chronic or intermittent dialysis or dialysis anticipated within the next 6 months
- High risk for non-adherence as determined by screening evaluation
- Inability or unwillingness to comply with the study requirements
- Anticipated hospital discharge before baseline study measures could be complete

Interventions	**Exercise** • Total duration: 24 weeks • Aerobic/resistance/mix: mix • Frequency: 3 days/week • Duration: 60 min • Intensity: not specified • Modality: walking, bodyweight exercises • Setting: inpatient for 3 months, then outpatient facility for 3 months • Other: progressive training plan, across 4 ‘levels’ **Control:** usual care
Outcomes	**Primary** • SPPB at 3 months **Secondary** • All-cause hospitalisation at 6 months • Cardiovascular hospitalisation at 6 months • HF hospitalisation at 6 months • 6MWT at 3 months • Frailty status at 3 months • QoL (KCCQ, EQ-5D-5L) at 3 months • Geriatric Depression Scale -15 at 3 months • Montreal Cognitive Assessment score at 3 months
Country and setting	USA, multicentre (5 sites)
Follow-up	Baseline (prerandomisation) and 9 weeks and 14-26 months postrandomisation

Kitzman 2021 *(Continued)*

Notes	**Source of funding:** NIH, the Kermit Glenn Phillips II Chair in Cardiovascular Medicine, the Oristano Family Fund at Wake Forest School of Medicine

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	"After eligible patients provided written informed consent and completed baseline testing, they were randomly assigned with equal probability to the rehabilitation intervention (intervention group) or to usual care (control group) by a centralized, Web-based system, with the use of block randomization. Randomization was stratified according to ejection fraction (<45% and >45%) and clinical site"
Allocation concealment (selection bias)	Low risk	"Outcome measures of physical and cognitive function were assessed by personnel who were unaware of the trial-group assignments."
Blinding (performance bias and detection bias) All outcomes	Unclear risk	Not reported
Incomplete outcome data (attrition bias)	Low risk	Exercise 174/175 (99%), control 173/174 (99%) provided outcomes for secondary outcomes at 6-month follow-up. Exercise 149/175 (85%), control 155/174 (89%) provided outcomes for primary outcomes at 3-month follow-up.
Selective reporting (reporting bias)	High risk	Outcome data for 'another cardiovascular rehospitalisation' (ie cardiovascular non-HF related) were not reported.
Groups balanced at baseline?	Low risk	Groups appear balanced at baseline, except for diabetes incidence: "The incidence of diabetes mellitus was higher in the intervention group than in the control group (58% vs. 47%)"
Groups received comparable care?	Low risk	"Patients who had been randomly assigned to the control group received a telephone call every 2 weeks and had in-person clinic visits at 1 month and 3 months after discharge from the index hospitalization.17 Information regarding the occurrence of symptoms or clinical events and the receipt of rehabilitation therapy unrelated to the trial was collected. Patients received no specific recommendations with respect to exercise, but they were encouraged to adhere to prescribed usual-care therapy and follow-up appointments."
Intention-to-treat analysis?	Low risk	Although not explicitly stated, it appears an intention-to-treat analysis was applied according to the CONSORT diagram.

Klecha 2007

Study characteristics

Methods	Parallel-group RCT
Participants	**N randomised:** 50 (exercise 25, control 25) **Diagnosis (% of participants)** • Aetiology: IHD 100% • NYHA: Class II: exercise 56%, control 60%; Class III: exercise 44%, control 40%

Klecha 2007 *(Continued)*

- LVEF: exercise mean 27.4% (SD 5.7), control mean 28.5% (SD 5.2)

Case mix: 100%, as above

Age, years: exercise 59.6 (SD 10.2), control 61.2 (SD 9.5)

Male: exercise 80%, control 72%

White: not reported

Inclusion/exclusion criteria

Inclusion: ischaemic HF in NYHA Classes II and III > 6 months, clinically stable > 6 weeks, LVEF < 35%

Exclusion: uncontrolled arterial hypertension; history of major ventricular arrhythmias, acute coronary syndrome, percutaneous coronary intervention, or brain event 3 months before the study; AF or other arrhythmia making it impossible to perform MRI; previous coronary artery bypass grafting; implantable cardioverter-defibrillator; permanent pacemaker or presence of metal parts in the body; signs of osteoarticular dysfunction excluding participation in physical training; DM; COPD; anaemia

Interventions	**Exercise** • Total duration: 6 months • Aerobic/resistance/mix: aerobic • Frequency: 3 sessions/week • Duration: 25 min/session • Intensity: 80% predicted HR at VO_2 max • Modality: cycling **Setting:** centre-based **Other:** none reported **Control group/comparison:** standard medical care only
Outcomes	Mortality
Country and setting	Poland, single centre
Follow-up	26 weeks (after randomisation)
Notes	**Source of funding:** KBN (The Polish State Committee for Scientific Research), grant no. 3 PO5D 047 23

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not reported
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding (performance bias and detection bias) All outcomes	Unclear risk	Not reported
Incomplete outcome data (attrition bias)	Low risk	No participants were lost to follow-up.

Klecha 2007 *(Continued)*

Selective reporting (reporting bias)	Low risk	All outcomes described in the methods were reported in the results.
Groups balanced at baseline?	Low risk	"At baseline the groups did not differ significantly in clinical characteristics. The only exception was smoking, the training group consisted of significantly more ex-smokers"
Groups received comparable care?	Unclear risk	Not reported
Intention-to-treat analysis?	Low risk	Not implicit, but numbers used suggest that groups were analysed according to randomised allocation

Klocek 2005

Study characteristics	
Methods	Parallel-group RCT
Participants	**N randomised:** 42 (exercise group A 14, exercise group B 14, control group 14) **Diagnosis (% of participants)** **Exercise group A** • Aetiology: ischaemic 100% • NYHA: Class II/III exercise group A 55%, control group 100% • LVEF: exercise group A mean 33.6% (SD 3.6), control group 33.2% (SD 3.8) **Exercise group B** • Aetiology: ischaemic 100% • NYHA: Class II/III exercise group B 75%, control group 100% • LVEF: exercise group B mean 34.2% (SD 4.2), control group 33.2% (SD 3.8) **Case mix:** 100%, as above **Age, years:** exercise group A 54 (SD 7), control 55 (SD 9), exercise group B 57 (SD 8), control 55 (SD 9) **Male:** 100% **White:** not reported **Inclusion/exclusion criteria** **Inclusion:**stable CHF, LVEF < 40% on echocardiography ≤ 1 month before inclusion, age < 65 years **Exclusion:** moderate or severe pulmonary disease; orthostatic blood pressure fall (> 20 mmHg); MI, unstable angina, heart surgery, or coronary angioplasty within 3 months before inclusion as well as inability to perform bicycle training
Interventions	**Exercise** • Total duration: 6 months • Aerobic/resistance/mix: aerobic • Frequency: 3 sessions/week • Duration: group A: 20 min/session (4 min constant workload with 1 min rest repeated 5 times) • Intensity: group A: 60% max HR

Klocek 2005 *(Continued)*

	• Duration: group B: 25 min/session (exercise workload gradually increased after each 5-min training period to a total of 25 min) • Intensity: group B: up to 75% max HR • Modality: cycle ergometer • Setting: CR, outpatient unit under supervision of the physician and the rehabilitation specialist **Other:** none reported **Control group/comparison:** controls were asked to not change their degree of physical activity during the study
Outcomes	HRQoL (Psychological General Wellbeing Index)
Country and setting	Poland, single centre
Follow-up	26 weeks (after randomisation)
Notes	**Source of funding:** not reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not reported
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding (performance bias and detection bias) All outcomes	Unclear risk	"Results of baseline QoL examinations were not known to the patients and their physicians or to the persons performing the randomisation"
Incomplete outcome data (attrition bias)	Unclear risk	No information was presented on loss to follow-up nor dropouts.
Selective reporting (reporting bias)	Low risk	All outcomes described in the methods were reported in the results.
Groups balanced at baseline?	Low risk	"At baseline there were no significant differences in between groups in left ventricular ejection fraction and other basic parameters of left ventricular function" "At the start of the study, mean PGWB [Psychological General Wellbeing Index] total index was similar in groups A and B. Controls had lower total index than patients in group B"
Groups received comparable care?	Unclear risk	Details of co-interventions were not reported, although the degree of follow-up was stated to be equivalent.
Intention-to-treat analysis?	Low risk	It appears that groups were analysed according to initial random allocation.

Koukouvou 2004

Study characteristics

Koukouvou 2004 *(Continued)*

Methods	Parallel-group RCT
Participants	**N randomised:** 26 (exercise 16, control 10) **Diagnosis (% of participants)** • Aetiology: DCM 7%, ischaemic 100% • NYHA: Class II 58%, Class III 42% • LVEF: < 40% **Case mix:** 100%, as above **Age, years:** exercise 52 (SD 9), control 53 (SD 11) **Male:** 100% **White:** not reported **Inclusion/exclusion criteria** **Inclusion:** aetiology of CHF either ischaemic heart disease or DCM; diagnosis of CHF mainly based on clinical signs (NYHA Class II and III), radiological findings, and echocardiographically determined EF < 40% and shortening fraction < 30% **Exclusion:** recent MI or unstable angina; aortic stenosis; DM; uncontrolled hypertension; musculoskeletal limitations or other contraindications for participating in an exercise training programme; documented exercise-induced severe ischaemia or serious arrhythmias, or both
Interventions	**Exercise** • Total duration: 6 months • Aerobic/resistance/mix: mix • Frequency: 3 or 4 sessions/week • Duration: 60 min/session • Intensity: 50%-75% peak VO_2 • Modality: cycle ergometer, walking or jogging, stair climber, and step-aerobics ○ Plus 'light' resistance exercise (not defined) • Setting: supervised exercise training programme at institution **Other:** none reported **Control group/comparison:** not reported
Outcomes	HRQoL (MLWHF questionnaire and Spritzer Quality of Life Index)
Country and setting	Greece, single centre
Follow-up	6 months (after randomisation)
Notes	**Source of funding:** not reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not reported

Koukouvou 2004 *(Continued)*

Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding (performance bias and detection bias) All outcomes	Low risk	"The psychological tests were assessed from all patients in the first week of admission, before randomization to study groups and the end of the study by the same physician, who was not familiar with the patients"
Incomplete outcome data (attrition bias)	Unclear risk	Losses to follow-up, dropouts not reported
Selective reporting (reporting bias)	Low risk	All outcomes outlined in the methods were reported.
Groups balanced at baseline?	Low risk	"The two groups of patients participating in the study were similar as regards their clinical data"
Groups received comparable care?	Unclear risk	Not reported
Intention-to-treat analysis?	Low risk	Not stated explicitly, but analysis appears to be done according to initial group allocation.

Lang 2018

Study characteristics	
Methods	Parallel-group RCT
Participants	**N randomised:** 50 (exercise 25, control 25) **Diagnosis (% of participants)** • Aetiology: ischaemic exercise 32%, control 64% • NYHA: Class II: exercise 60%, control 64%; Class III: exercisse 36%, control 32% • LVEF: ≥ 45% **Case mix:** 100%, as above **Age, years:** exercise 71.8 (SD 9.9), control 76.0 (SD 6.6) **Male:** exercise 36%, control 56% **White:** not reported **Inclusion/exclusion criteria** **Inclusion:** LVEF ≥ 45% within 6 months of randomisation **Exclusion:**cardiac rehab within 6 months, contraindication to exercise
Interventions	**Exercise** • Total duration: 12 weeks • Aerobic/resistance/mix: aerobic • Frequency: 2-3 times/week • Duration: not reported • Intensity: not reported

Lang 2018 *(Continued)*

	• Modality: walking or chair-based • Setting: home-based The REACH-HF Manual; a participant 'Progress Tracker' booklet to record symptoms, physical activity, and other actions related to self-care; support for caregivers; and facilitation by cardiac nurses or physiotherapists, including assessment of individual patient and caregiver needs and concerns and tailoring of the intervention content to address these were provided; this element was supported by a 3-day training course for facilitators on how to deliver the intervention using a patient-centred style of communication. **Control group/comparison:** usual care ("...intervention and control group patients received usual medical management for HF according to current guidelines")
Outcomes	**Primary outcome:** MLWHF questionnaire **Secondary outcomes:** mortality, hospitalisation, Heart-QoL, EQ-5D-3L, costs
Country and setting	UK, single centre
Follow-up	4 months and 6 months
Notes	**Funding source:** NIHR under its Grants for Applied Research Programme (Grant Reference No. RP-PG-1210-12004)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	"Participants will be randomly allocated in a 1:1 ratio to either intervention or control group arms without stratification or minimisation. Randomisation numbers will be computer generated and assigned in strict sequence. At the point of randomisation, participants will be assigned the next randomisation number in the sequence. To maintain concealment and minimise selection bias, randomisation will be performed after the baseline visit by a member of Peninsula Clinical Trials Unit (CTU), independent from investigator teams, using a secure, web-based randomisation system"
Allocation concealment (selection bias)	Low risk	As above
Blinding (performance bias and detection bias) All outcomes	Low risk	"We assessed the fidelity of blinding by asking outcome assessors at each follow-up visit to guess patient group allocation. Unblinding of groups did not take place until after data analysis and the blinded results had been presented to the Trial Management Group and interpretation of results was agreed"
Incomplete outcome data (attrition bias)	Low risk	All participants were accounted for in a CONSORT flow diagram.
Selective reporting (reporting bias)	Low risk	All prespecified outcomes were reported as in the published protocol.
Groups balanced at baseline?	High risk	"There was evidence of imbalance between intervention and control group patients in terms of their baseline demographic characteristics (see Table 1). Compared with the control group, the intervention group included a higher proportion of females, and lower proportions of patients with an ischaemic diagnosis, with atrial flutter/atrial fibrillation, and with chronic renal failure; also, the intervention group had a younger mean age"

Lang 2018 *(Continued)*

Groups received comparable care?	Low risk	Both groups received usual care.
Intention-to-treat analysis?	Low risk	"All analyses are based on the intention to treat principle (patients are analysed according to their original random allocation) using observed data only"

Liu 2018

Study characteristics	
Methods	Parallel-group RCT
Participants	**N randomised:** 212 (Multidisciplinary disease management programme with exercise 71, Multidisciplinary disease management programme without exercise 70, control 71) **Diagnosis (% of participants)** • Aetiology: not reported • NYHA: II 37%; III&IV 63% • LVEF: control38.6 ± 14.6; MDP-EX 35.8 ± 15.2; MDP+EX 37.6 ± 15.2 **Case mix:** as above **Age:** control 61.7 ± 13.8; Multidisciplinary disease management programme without exercise 65.1 ± 12.6; Multidisciplinary disease management programme with exercise 62.7 ± 11.1 **Male:** Control 67.6%; MDP-EX 66.2; MDP+EX 62.2 **White:** not reported **Inclusion/exclusion criteria** **Inclusion** • "aged 20-80 years • presented with the typical signs and symptoms of HF and NYHA functional classifications II to IV and were hospitalised for acute cardiogenic pulmonary congestion based on chest X-rays (grade ≥ I according to the classification by Mao and colleagues (see secondary ref for Liu 2018) after non-cardiogenic causes were excluded • displayed a LVEF ≤ 40% by echocardiogram • could complete a 6MWT and questionnaires regarding their disease knowledge before discharge • were alert and orientated and able to speak and write Chinese; • were willing to sign the informed consent after an explanation of the study was provided" **Exclusion:** • "had been bedridden for > 3 months • had a disorder other than heart failure that might compromise survival within 6 months • were pregnant"
Interventions	**Exercise** • Total duration: 2-12 weeks • Aerobic/resistance/mix: aerobic • Frequency: 2-3 times/week • Duration: 30 min

Liu 2018 *(Continued)*

	• Intensity: not reported • Modality: walking • Setting: outpatient clinic and home • Other: participants were encouraged to home exercise after outpatient sessions ended **Control:** MDP-EX: multidisciplinary disease management programme including an educational booklet and disease coaching without an exercise intervention
Outcomes	**Primary:** HF-related rehospitalisation* **Secondary:** disease knowledge, 6MWD
Country and setting	Taiwan, single centre
Follow-up	Baseline (prerandomisation) and 12 months postrandomisation
Notes	*Although outcome was reported, it was not in a suitable format for meta-analysis Secondary study based off original trial population in Mao 2015 (see secondary ref under Liu 2018) **Source of funding:** not reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	"Of the patients who participated in the MDP (n = 141), data for 71 patients without contraindications who were willing to receive outpatient exercise training were included in the MDP with exercise training group; data for the other 70 patients who did not undergo exercise training due to unwillingness (n = 39) or contraindications to exercise training (n = 31), including cardiac arrhythmia (n = 8), incomplete revascularization (n = 10), unstable angina (n = 5), valvular heart diseases (n = 6), or intraventricular thrombus (n = 2) were included in the MDP without exercise training group"
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding (performance bias and detection bias) All outcomes	Unclear risk	Not reported
Incomplete outcome data (attrition bias)	High risk	MDP-EX 53/70 (76%) MDP+EX 63/71 (89%) provided outcomes for primary analysis at 12-months
Selective reporting (reporting bias)	Low risk	All outcomes described in protocol publication are reported in main trial publications.
Groups balanced at baseline?	High risk	"No significant differences were observed among the three groups in the demographic variables, laboratory variables, and comorbidities, but a difference was observed in the use of guideline-based medications, including angiotensin-converting enzyme inhibitors/angiotensin II receptor blockers"
Groups received comparable care?	Low risk	"The patients in the MDP with outpatient exercise training group received the same programme as the MDP without exercise training group but with the addition of outpatient-based exercise training."
Intention-to-treat analysis?	Low risk	Figure 1 (flow diagram of the study) shows an apparent ITT analysis used at follow-up.

Lugo 2018

Study characteristics	
Methods	Parallel-group RCT
Participants	**N randomised:** 49 (exercise 23, control 26) **Diagnosis (% of participants)** • Aetiology: not reported • NYHA: II 15.2%; III 63.0%; IV 21.7% • LVEF: exercise 30.0 (20.0-60.0); control 35.0 (25.0-75.0) **Case mix:** as above **Age:** exercise 54.4 (13.6); control 56.5 (11.0) **Male:** 53.1% **White:** not reported **Inclusion/exclusion criteria** **Inclusion***:* aged > 18 years with diagnosed HF diagnosed for over 6 months **Exclusion:**NHYA I; previous CR; uncontrolled DM; poorly controlled arterial hypertension; ischaemic heart disease in the past month; previous pulmonary embolism; COPD; pulmonary restrictive disease; aortic valve stenosis; new episode of AF; musculoskeletal disease that limits exercise capacity
Interventions	**Exercise** • Total duration: 8 weeks • Aerobic/resistance/mix: aerobic • Frequency: 2 times/week • Duration: 1 h • Intensity: 60%-80% of HR reserve • Modality: running • Setting: in clinic • Other: monitored via telemetric device; supervised by doctor and nurse; also had a 1-h physical therapy session once a week; also 2 occupational therapy sessions across the 8 weeks **Control:** usual care with education programme
Outcomes	**Primary** • Exercise capacity (VO_2 max) • Functionality (NYHA) **Secondary** • 6MWT • Quality of life (SF-36)* • Depression • Echocardiographic data • All-cause mortality*^
Country and setting	Colombia, single-centre

Lugo 2018 *(Continued)*

Follow-up	Baseline and post-test (8 weeks) and 4 months post-test (6 months)
Notes	Data extraction completed with support of Spanish translator (Claudia Armengol, BSc Neuroscience student) *outcomes relevant to this review ^identified from CONSORT flow diagram HRQOL (SF-36) was reported in a form not suitable for meta-analysis. **Source of funding:** Investigation Development Committee of The University of Antioquia (CODI)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	"Patients allocated randomly."
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding (performance bias and detection bias) All outcomes	Low risk	Evaluators blinded to participant's trial group
Incomplete outcome data (attrition bias)	High risk	Exercise 15/23 (65%); control 16/26 (62%) reported complete outcome data at 6 months
Selective reporting (reporting bias)	High risk	NYHA class not reported after intervention, as described in methods
Groups balanced at baseline?	Low risk	There were no significant differences between the 2 groups, in demographics, clinical measures, or echocardiographic measures.
Groups received comparable care?	Low risk	Both control and exercise groups received an education programme discussing risk factors, lipid control, hypertension control, smoking cessation advice, weight control, and diabetes control.
Intention-to-treat analysis?	High risk	An analysis by treatment was performed.

McKelvie 2002

Study characteristics

Methods	Parallel-group RCT
Participants	**N randomised:** 181 (exercise 90, control 91) **Diagnosis (% of participants)** • Aetiology: ischaemic 76%, hypertensive 7%, valvular 5%, other 12% • NYHA: Class I-III • LVEF: < 40% **Case mix:** 100%, as above

McKelvie 2002 *(Continued)*

Age, years: exercise 64.8 ± 1.1 (SD 10.5), control 66.1 (SD 9.4)

Male: control 80, exercise 82

White: not reported

Inclusion/exclusion criteria

Inclusion: documented clinical signs and symptoms of HF; LVEF < 40%; NYHA functional class I-III; 6MWT < 500 m

Exclusion:inability to attend regular exercise training sessions; exercise testing limited by angina or leg claudication; abnormal blood pressure response to exercise testing (systolic blood pressure during exercise > 250 mmHg or diastolic blood pressure response > 15 mmHg, systolic blood pressure response decrease > 20 mmHg after normal increase or decrease below the resting level); cerebrovascular or musculoskeletal disease preventing exercise testing or training; respiratory limitation (FEV in 1 second, or vital capacity < 60% of predicted, or both); poorly controlled cardiac arrhythmias; any noncardiac condition affecting regular exercise training or decreasing survival

Interventions	**Exercise** • Total duration: 9 months (3 supervised, 6 home-based) • Aerobic/resistance/mix: mix • Frequency: 2 sessions/week • Duration: aerobic; 30 min/session • Intensity: aerobic: 60%-70% max HR. Resistance: 40% of 1-repetition maximum, with 10 repetitions for arm exercises and 15 repetitions for leg exercises, with an increase over 5 weeks to an intensity of 60% for 1-repetition maximum and a total of 3 sets of each exercise per session • Modality: aerobic: cycle, treadmill, and arm ergometry exercise. Resistance: arm curl, knee extension, and leg press performed individually with each limb. After 3 months of supervised training, participants in the exercise group were provided an exercise cycle and a set of free weights with instructions to continue training at home 3 times/week for the remainder of the study **Setting:** supervised for 3 months at rehabilitation centre and unsupervised for 9 months at home **Other:** none reported **Control group/comparison:** usual medical care. Control participants were not provided a formal exercise prescription but were encouraged to continue their usual level of physical activity and were not discouraged from regular physical activity.
Outcomes	• HRQoL (MLWHF questionnaire) • Mortality • Composite of mortality and hospital admission for HF
Country and setting	Canada, multicentre
Follow-up	12 months (after randomisation)
Notes	**Source of funding:** not reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	"The predetermined allocation sequence was based on a stream of computer-generated pseudorandom numbers from a uniform distribution stratified by center and with a blocking factor of 4"

McKelvie 2002 *(Continued)*

Allocation concealment (selection bias)	Low risk	"Eligible patients were registered in a log and treatment group determined by opening the next sequential study allocation envelope"
Blinding (performance bias and detection bias) All outcomes	Low risk	"Outcome measures were performed in a blinded fashion. Individuals responsible for supervising and recording the results of the outcome measurements were unaware of the patients group assignment"
Incomplete outcome data (attrition bias)	Low risk	"In the control group, 83 patients completed 3 months of follow-up (reasons for incompletion: death 3; other problems 4; worsening heart failure 1) and 75 patients completed 12months of follow-up (reasons for incompletion: death 8; withdrawal 2; other problems 3; worsening heart failure 2; refused testing 1). For the exercise group, 80 patients completed 3 months of follow-up (reasons for incompletion: death 1; withdrawal 5; other problems 1; worsening failure 2; refused testing 1) and 64 patients completed 12 months of follow-up (reasons for incompletion: death 9; withdrawal 6; other problems 7; worsening heart failure 3; refused testing 1)" No imputation nor sensitivity analysis was undertaken to assess the impact of loss to follow-up
Selective reporting (reporting bias)	Unclear risk	All outcomes described in the methods were reported in the results.
Groups balanced at baseline?	Low risk	"There were no differences between the control and exercise training groups with respect to age, resting ejection fraction, New York Heart Association class, cause of heart failure, or duration of heart failure"
Groups received comparable care?	Unclear risk	"All patients were reviewed monthly throughout the study"
Intention-to-treat analysis?	Low risk	Although ITT analysis was not reported, groups appear to have been analysed according to the original randomised allocation.

Mehani 2013

Study characteristics	
Methods	Parallel-group RCT
Participants	**N randomised:** 40 (exercise 20, control 20) **Diagnosis (% of participants)** • Aetiology: ischaemic 76%, hypertensive 7%, valvular 5%, other 12% • NYHA: Class I-III • LVEF: exercise 33.09 ± 4.77%, comparator 35.8 ± 6.87% **Case mix:** 100%, as above **Age, years:** exercise 56.4 (SD 5.829), control 54.6 (SD 9.264) **Male:** 100% **White:** not reported **Inclusion/exclusion criteria** **Inclusion:** > 8 months' history of DCM with 3 months' clinical stability on optimal medical therapy

Mehani 2013 *(Continued)*

	Exclusion: significant coronary disease by history or angiography to exclude ischaemic causes; evidence for secondary causes of cardiomyopathy as long-standing or uncontrolled hypertension; primary valvular disease; AF; severe functional MR; clinical evidence of pulmonary disease (COPD, moderate to severe pulmonary hypertension)
Interventions	**Exercise** • Total duration: 28 weeks • Aerobic/resistance/mix: aerobic • Frequency: 3 sessions/week • Duration: aerobic; 45 min/session • Intensity: aerobic: maximal 80% of HR reserve • Modality: aerobic: circuit training (Stairmaster, bicycle, treadmill) **Setting:** hospital (supervised) **Other:** none reported **Control group/comparison:** usual care (2 weekly physician visits with medication adjustments)
Outcomes	Hospital admissions, mortality
Country and setting	Iran, single centre
Follow-up	7 months
Notes	**Source of funding:** not reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	"the patients were randomly assigned into two groups (training and control groups) by arrangement into numerical numbers from 1 to 40, then odd numbers were allocated as a training group and the even numbers were allocated as a control group"
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding (performance bias and detection bias) All outcomes	Unclear risk	HRQoL assessment was self-administered. Blinding was not reported for other outcomes.
Incomplete outcome data (attrition bias)	Low risk	Loss to follow-up similar across groups, with reasons given Exercise: 5/20 were lost to follow-up Control: 5/20 were lost to follow-up
Selective reporting (reporting bias)	Unclear risk	No protocol was available.
Groups balanced at baseline?	Low risk	"At baseline, there were no statistical significant differences between both groups as regards to age, body mass index, NYHA classification, left ventricular internal dimensions at diastole and systole"

Mehani 2013 *(Continued)*

Groups received comparable care?	Low risk	With the exception of the exercise-based intervention, all participants underwent the same visits, except for exercise, and received the same disease information.
Intention-to-treat analysis?	Low risk	Although the term ITT was not stated, it appears from the CONSORT diagram that an ITT analysis was undertaken.

Mueller 2007

Study characteristics	
Methods	Parallel-group RCT
Participants	**N randomised:** 50 (exercise 25, control 25) **Diagnosis (% of participants)** • Aetiology: ischaemic, DCM (% not reported) • NYHA: not reported • LVEF: < 40% (% not reported) **Case mix:** 100%, as above **Age, years:** 55 (SD 10) **Male:** 100% **White:** not reported **Inclusion/exclusion criteria** **Inclusion:** CHF documented by clinical, angiographic, or echocardiographic criteria; resting EF < 40% **Exclusion:** not reported
Interventions	**Exercise** • Total duration: 1 month • Aerobic/resistance/mix: aerobic • Frequency: 5 sessions/week • Duration: 30 min/session cycling, 90 min walking each day • Intensity: Borg 12-14 (60%-80% max HR) • Modality: cycling and walking • Setting: indoor cycling sessions were supervised directly by a medical resident; outdoor walking sessions were supervised by exercise physiologists **Other:** resided at the rehabilitation centre for 1 month; programme also included education and low-fat meals prepared daily by the centre's cook **Control group/comparison:** usual medical care
Outcomes	Morbidity, mortality
Country and setting	Switzerland, single centre
Follow-up	6.2 years (after randomisation)

Mueller 2007 *(Continued)*

Notes	**Source of funding:** RAHN-Medizinfonds, Zurich; Schweizerische Herzstiftung, Switzerland

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not reported
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding (performance bias and detection bias) All outcomes	Unclear risk	Not reported
Incomplete outcome data (attrition bias)	Low risk	"Data from one patient in the control group was not available at the two-month evaluation due to refusal to complete testing." "Among subjects in the exercise group, 9 died, and one refused repeat testing. Among patients in the control group, 12 died and two refused repeat testing. Therefore, 14 and 13 patients performed six-year evaluations in the exercise and control groups, respectively" QUORUM diagram reported and detailed text provided; no imputation undertaken
Selective reporting (reporting bias)	Low risk	Outcomes described in the methods were reported in the results.
Groups balanced at baseline?	Low risk	"No differences were observed between the exercise and control groups initially in clinical or demographic data, including age, height, weight, pulmonary function or medication status"
Groups received comparable care?	Unclear risk	"Patients in the exercise group resided at the rehabilitation centre for one month. Control subjects received usual clinical care, including verbal encouragement to remain physically active"
Intention-to-treat analysis?	Low risk	ITT was not stated explicitly; however, groups appear to have been analysed according to the original allocation.

Mueller 2021

Study characteristics

Methods	Parallel-group RCT
Participants	**N randomised:** 180 (HIIT 60, moderate-intensity continuous training 60, control 60) **Diagnosis (% of participants)** • Aetiology: not reported • NYHA: HIIT II 76%, III 24%; moderate intensity II 76%, III 24%; control II 70%; III 30% • LVEF: < 50% **Case mix:** as above **Age:** mean (SD): exercise 69.7 (10.9), control 69.6 (11.0)

Mueller 2021 *(Continued)*

	Male: 33% **White:** not reported **Inclusion/exclusion criteria** **Inclusion:** sedentary patient, on-site measures of E/e' medial ≥ 15 or E/e' medial ≥ 8 and NT-proBNP ≥ 220 pg/mL or E/e' medial ≥ 8 and BNP ≥ 80 pg/mL; **Exclusion:** not reported
Interventions	**HIIT** • Total duration: 12 months • Aerobic/resistance/mix: aerobic endurance training • Frequency: 3 times/week • Duration: 38 min • Intensity: 80%-90% HR reserve • Modality: cycling • Setting: all sessions supervised in clinic for first 3 months, then all home-based • Other: 10-min warm-up at 35%-50% of HR reserve, 4 × 4-min intervals at 80%-90% of HR reserve, interspaced by 3 min of active recovery In case of a decline in attendance to < 70% of scheduled exercise sessions or a decline in exercise intensity during sessions, patients were encouraged by telephone contact to increase adherence to meet study targets. **Moderate-intensity continuous training** • Total duration: 12 months • Aerobic/resistance/mix: aerobic • Frequency: 5 times/week • Duration: 40 min • Intensity: 35%-50% HR reserve • Modality: cycling • Setting: supervised 3 times/week and at home twice/week for first 3 months, then twice/week home-based **Control:** 1-time advice on physical activity according to guidelines.
Outcomes	**Primary** • VO_2 max at 3 months **Secondary** • Echocardiographic measures of diastolic function at 3 and 12 months • HRQoL (KCCQ score)
Country and setting	Berlin, Leipzig, Munich (Germany), Antwerp (Belgium), Trondheim (Norway); multi-centre (5 sites)
Follow-up	Baseline (prerandomisation) and 4 and 12 months post-randomisation
Notes	**Source of funding:** European Commission; Deutsche Forschungsgemeinschaft; Flemish Research Funds

Risk of bias

Bias	Authors' judgement	Support for judgement

Mueller 2021 *(Continued)*

Random sequence generation (selection bias)	Low risk	“A web-based system was used to assign patients in a 1:1:1 ratio to high-intensity interval training, moderate continuous training, or guideline control. Randomization was stratified by study site using block sizes of 12 (first block) and 6 (following blocks)”
Allocation concealment (selection bias)	Low risk	“The staff members conducting the evaluations were not blinded to treatment groups” "...the staff conducting the evaluations was not blinded to the treatment group assignment, which could have had an effect on the maximal exhaustion during cardiopulmonary exercise testing. However, the respiratory exchange ratio at peak exercise did not significantly differ between groups and time points" "Cardiopulmonary exercise testing was performed according to current recommendations and analyzed in a blinded manner at the study core laboratory in Munich" "All echocardiograhic analyses were performed centrally by the Academic Echocardiography Core Lab at Charité Berlin, blinded to treatment group assignment."
Blinding (performance bias and detection bias) All outcomes	Low risk	“All echocardiographic analyses were performed centrally by the Academic Echocardiography Core Lab at Charité Berlin, blinded to treatment group assignment.”
Incomplete outcome data (attrition bias)	Low risk	HIIT 48/60 (80%), moderate continuous training 53/60 (88%), control 55/60 (88%) provided outcomes for analysis at 12-months
Selective reporting (reporting bias)	Low risk	All outcomes described in protocol publication are reported in main trial publications.
Groups balanced at baseline?	Low risk	Baseline characteristics appeared balanced in table 1, however there was no formal analysis to show this, and the trial authors did not explicitly state this either.
Groups received comparable care?	Low risk	“Patients assigned to guideline control received 1-time advice on physical activity according to guidelines”
Intention-to-treat analysis?	Low risk	“All patients were analysed according to their randomization group”

Myers 2000

Study characteristics	
Methods	Parallel-group RCT
Participants	**N randomised:** 25 (exercise 12, control 13) **Diagnosis (% of participants)** • Aetiology: ischaemic 100% • NYHA: not reported • LVEF: exercise 31.5% (SD 7), control 33.3% (SD 6) **Case mix:** 100%, as above **Age, years:** exercise 56 (SD 5), control 55 (SD 7)

Myers 2000 *(Continued)*

	Male: 100% **White:** not reported **Inclusion/exclusion criteria** **Inclusion:**MI, diagnosis of HF and stable symptoms, LVEF < 40% **Exclusion:** pulmonary disease
Interventions	**Exercise** • Total duration: 2 months • Aerobic/resistance/mix: aerobic • Frequency: walking: 2 sessions daily; cycling: 4 sessions/week • Duration: walking: 1 h; cycling: 45 min • Intensity: walking: not reported; cycling: 60%-70% peak VO_2 • Modality: walking and cycling • Setting: centre-based; supervised by physicians **Other:** exercise groups received educational sessions and low-fat meals prepared 3 times daily **Control group/comparison:** usual clinical follow-up
Outcomes	• Hospitalisation • Mortality
Country and setting	Switzerland, single centre
Follow-up	2 months and 12 months (after randomisation)
Notes	"After the initial 2-months exercise training or control period, both groups were encouraged to remain physically active over the subsequent 10 months, although no formal program was implemented" **Source of funding:** supported in part by a grant from Schweizerische Herzstiftung, Switzerland

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not reported
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding (performance bias and detection bias) All outcomes	Unclear risk	Not reported
Incomplete outcome data (attrition bias)	Low risk	Losses to follow-up were reported.
Selective reporting (reporting bias)	Low risk	All outcomes described in the methods were reported in the results.
Groups balanced at baseline?	Low risk	"No differences were observed between the 2 groups initially in clinical or demographic data, including age, height, weight, resting blood pressure, pulmonary function, ejection fraction, or maximal oxygen uptake"

Myers 2000 *(Continued)*

Groups received comparable care?	Low risk	Yes, both groups appeared to receive the same interventions, apart from the CR intervention.
Intention-to-treat analysis?	Low risk	Although not explicit, participants appeared to be analysed according to the initial random allocation.

Nilsson 2008

Study characteristics	
Methods	Parallel-group RCT
Participants	**N randomised:** 80 (exercise 40, control 40) **Diagnosis (% of participants)** • Aetiology: ischaemic cardiomyopathy 69%, idiopathic DCM 18%, hypertensive HF 13% • NYHA: Class II 47%, Class III 35% • LVEF: exercise 31% (SD 8), control 31% (SD 9) **Case mix:** 100%, as above **Age, years:** 70.1 (SD 7.9) **Male:** 79% **White:** not reported **Inclusion/exclusion criteria** **Inclusion:** stable CHF and LVEF < 40% or ≥ 40% with clinical symptoms of diastolic HF **Exclusion:** acute MI within 4 weeks; unstable angina pectoris; serious rhythm disturbance; symptomatic PVD; severe COPD, with FVC < 50% of expected measured by spirometry; 6MWD > 550 m; workload on the cycle ergometer test > 110 watts; significant co-morbidities that would prevent entry into the study due to terminal disease or inability to exercise (e.g. severe musculoskeletal disorder, advanced valvular disease); in long-term care establishment
Interventions	**Exercise** • Total duration: 4 months • Aerobic/resistance/mix: aerobic • Frequency: 2 sessions/week • Duration: 50 min • Intensity: 15-18 on Borg scale • Modality: fast walking, side-stepping, and leg lifts in combination with overhead arm reaches • Setting: hospital outpatient department **Other:** 15-30 min of counselling with CHF nurse for participants in the exercise group (4 hours in total) **Control group/comparison:** control group was not provided with exercise prescriptions and was encouraged to continue usual levels of physical activity
Outcomes	• HRQoL (MLWHF questionnaire) • Mortality
Country and setting	Norway, single centre

Nilsson 2008 *(Continued)*

Follow-up	12 months (after randomisation)
Notes	All training sessions were supervised by a physiotherapist - a specialist in CR **Source of funding:** not reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	"computer-generated table of random numbers"
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding (performance bias and detection bias) All outcomes	Low risk	"Three physicians and 3 nurses who were blinded to the clinical data and group assignments of the patients carried out all the follow-up tests. Patients were told not to reveal to which groups they belonged"
Incomplete outcome data (attrition bias)	Low risk	35/40 (88%) in the exercise training group and 37/40 (93%) in the control group were available at 12 months.
Selective reporting (reporting bias)	Low risk	All outcomes described in the methods were reported in the results.
Groups balanced at baseline?	Low risk	Table 1 of the publication suggests no differences between the 2 groups.
Groups received comparable care?	Low risk	Yes
Intention-to-treat analysis?	Low risk	"Intention-to-treat analyses were performed"

Norman 2012

Study characteristics

Methods	Parallel-group RCT
Participants	**N randomised:** 42 (exercise 22, control 20) **Diagnosis (% of participants)** • Aetiology: ischaemic 50%, non-ischaemic 50% • NYHA: Class II: exercise 64%, control 45%; Class III: exercise 36%, control 55% • LVEF: exercise: mean 33% (SD 7), control: mean 32% (SD) **Age, years:** exercise 57 (SD 12), control 63 (SD 15) **Male:** 57.5% **White:** not reported **Inclusion/exclusion criteria**

Norman 2012 *(Continued)*

	Inclusion: age ≥ 21 years with HF; oriented to person, place, and time; able to speak and read English; resting LVEF ≤ 40% and stable on optimal medical therapy for at least 30 days **Exclusion:** clinical evidence of decompensated HF; unstable angina pectoris; MI; coronary artery bypass surgery; biventricular pacemaker < 3 months ago; orthopaedic or neuromuscular limitations preventing participation in aerobic or resistance exercise training; participation in an aerobic exercise programme during the past 12 months
Interventions	**Exercise** • Total duration: 24 weeks • Aerobic/resistance/mix: mix • Frequency: aerobic 3 days/week, resistance 2 days/week • Duration: aerobic: 30 min/session (30-min warm-up); resistance: 8-10 exercises (upper and lower extremities) performed for 1 set of 10-15 repetitions • Intensity: aerobic: 40%-70% HR reserve, or Borg 11-14; resistance: not reported • Modality: aerobic: not reported; resistance: weight machines, free weights, or elastic bands based on exercise performance • Setting: 3 weeks: supervised, 21 weeks: hospital's wellness centre or home **Other:** group meetings that addressed the same educational topics as were addressed in the control group but also information on problem-solving barriers to exercise, relapse management, and symptoms experienced during exercise **Control group/comparison:** "Attention control". Instructions to continue with normal level of activity; no instructions given to withhold or stop activity
Outcomes	• HRQoL (KCCQ) • SF-36; mortality
Country and setting	USA, single centre
Follow-up	24 weeks (after randomisation)
Notes	Study conducted in 2 sequential 12-week phases • Phase 1: separate weekly group meetings of both groups during weeks 1-3, then separate biweekly meetings during weeks 4-12 • Phase 2: following the groups for an additional 12 weeks without group sessions See secondary ref under Norman 2012 for other trial report: Pozehl 2010 **Source of funding:** R-15 AREA Grant from the National Institute of Health (# NR0092 15-01)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not reported
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding (performance bias and detection bias) All outcomes	High risk	"Research assistants who were blinded to group assignment assisted in some of the data collection. However, because of budget constraints, the investigators who were not blinded to group assignment were also involved in data collection"

Norman 2012 *(Continued)*

Incomplete outcome data (attrition bias)	Low risk	Due to mortality and dropout, KCCQ scores were available for 37 participants (88%) at 24 weeks.
Selective reporting (reporting bias)	Low risk	All outcomes described in the methods were reported in the results.
Groups balanced at baseline?	Low risk	"…no significant difference noted between groups"
Groups received comparable care?	Low risk	Both groups received group sessions (attention control), so the only difference between groups was the exercise-based intervention.
Intention-to-treat analysis?	Low risk	Not stated, but groups were analysed according to randomised allocation.

Passino 2006

Study characteristics	
Methods	Parallel-group RCT
Participants	**N randomised:** 85 (training 44, control 41) **Diagnosis (% of participants)*** • Aetiology: ischaemic 59%, DCM 41% • NYHA: Class I 16%, Class II 69%, Class III 34% • LVEF: training 35% (SD 9.3), control 32.3 (SD 14.1) **Case mix:** 100%, as above **Age, years:** exercise 60 (SD 13), control 61 (SD 13) **Male:** 87% **White:** not reported **Inclusion/exclusion criteria** **Inclusion:**impaired left ventricular systolic function (EF < 45%) and exercise capacity (peak VO_2 < 25 mL/min/kg) **Exclusion:** NYHA Class IV; MI or unstable angina < 6 months before the examination; exercise-limiting disease; severe pulmonary or renal disease *Baseline data available for only 85 participants
Interventions	**Exercise** • Total duration: 9 months • Aerobic/resistance/mix: aerobic • Frequency: > 3 sessions/week • Duration: 30 min/session • Intensity: 65% max VO_2 • Modality: cycle • Setting: home-based **Other:** not reported

Passino 2006 *(Continued)*

	Control group/comparison: not reported
Outcomes	• HRQoL (MLWHF questionnaire) • Morbidity
Country and setting	Italy, not reported
Follow-up	9 months (after randomisation)
Notes	**Source of funding:** not reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not reported
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding (performance bias and detection bias) All outcomes	Unclear risk	Exercise test assessor was blinded.
Incomplete outcome data (attrition bias)	Low risk	Outcomes described in the methods were reported in the results.
Selective reporting (reporting bias)	Unclear risk	Not reported
Groups balanced at baseline?	Low risk	"The two groups did not differ as to age, gender, NYHA functional class, EF, pharmacologic treatment, or HF etiology (Table 1)"
Groups received comparable care?	Low risk	"Patients in [control] group underwent follow-up visits at the third and ninth month to exclude changes in their usual lifestyle and physical activity"
Intention-to-treat analysis?	Low risk	Although ITT was not stated, groups appear to have been analysed according to the original randomisation.

Peng 2018

Study characteristics

Methods	Parallel-group RCT
Participants	**N randomised:** 98 (exercise 49, control 49) **Diagnosis (% of participants)** • Aetiology: ischaemic 60.2% • NYHA: I 24.5% II 36.7%; III 38.8% IV 0% • LVEF: not reported **Case mix:** as above

Peng 2018 *(Continued)*

Age: < 60 years 30.6%; > 60 years 69.4%

Male: 59.2%

White: not reported

Inclusion/exclusion criteria

Inclusion: a primary diagnosis of CHF for at least 3 months; NYHA classification I-III; > 18 years of age; a clinically stable condition with a regular medication regimen for at least 4 weeks before enrolment in the study; the ability to use Wechat or QQ software via a smart phone; discharged to home; and the ability to understand and speak Chinese

Exclusion: MI within the last month, unstable angina, uncontrolled hypertension, severe respiratory diseases, decompensated non-cardiac disease, malignancy, physical disability, mental disease, or other contraindications that affected participation in this study, surgical treatment within the last month; and previous participation in exercise CR programmes

Interventions	**Exercise** • Total duration: 8 weeks • Aerobic/resistance/mix: aerobic (stage 1), mix (stage 2) • Frequency: 3 times/week • Duration: 10-14 min (stage 1), 20-24 min (stage 2) • Intensity: 40%-70% of HR reserve • Modality: walking, jogging (stage 1), walking, jogging, weight-bearing exercise, calisthenics (stage 2) • Setting: participant's home, supervised via webcam • Other: assessing, supervising and adjusting the training intensity by the physiotherapists **Control:** usual care that included simple discharge education and regular follow-up visits at the clinic. Participants in the control group in the usual care setting were not given any type of instruction regarding exercise.
Outcomes	**Primary:** QoL (MLWHF) **Secondary:** • QoL (HADS: anxiety, depression) • 6MWT • NYHA class • LVEF • Resting HR
Country and setting	Chengdu, China, single-centre
Follow-up	Baseline and post-test (8 weeks) and 4 months post-test (6 months)
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	"Simple randomization was used in this study. The 98 eligible patients were randomly assigned to either the experimental group (n=49) or the control group (n=49) prior to discharge by the researchers using a computer-generated random sequence."

Peng 2018 *(Continued)*

Allocation concealment (selection bias)	Low risk	"Allocation concealment was assured by enclosing the assignments in sequentially numbered, opaque envelopes."
Blinding (performance bias and detection bias) All outcomes	Unclear risk	Not reported
Incomplete outcome data (attrition bias)	Low risk	"A total of 15 participants (7 in the experimental group and 8 in the control group) did not complete the 4-month follow-up. The attrition rates of the experimental and control groups at 4 months post-test were 14.3% and 16.3%, respectively"
Selective reporting (reporting bias)	Unclear risk	Not reported
Groups balanced at baseline?	Low risk	"There were no significant differences between the experimental and control groups with respect to patients' demographic and clinical variables"
Groups received comparable care?	Low risk	"The patients in the control group received usual care that included simple discharge education and regular follow-up visits at the clinic. The patients in the control group in the usual care setting were not given any type of instruction regarding exercise, while the patients in the experimental group received usual care plus telehealth exercise training"
Intention-to-treat analysis?	Unclear risk	Not reported

Pozehl 2008

Study characteristics	
Methods	Parallel-group RCT
Participants	**N randomised:** 21 (exercise 15, control 6) **Diagnosis (% of participants)** • Aetiology: ischaemic 71%, non-ischaemic 29% • NYHA: Class II 39%, Class III 52%, Class IV 9% • LVEF: exercise 27.9% (SD 7.0), control 29.7% (SD 8.7) **Case mix:** 100%, as above **Age, years:** exercise 66.3 (SD 9.6), control 66 (SD 12.6) **Male:** 90% **White:** 100% **Inclusion/exclusion criteria** **Inclusion:** ability to speak and read English; stable NYHA Class II to IV; no change in medical therapy for 30 days; resting LVEF < 40% as measured by echocardiography or gated equilibrium radionuclide angiography; medical diagnosis of HF ischaemic or non-ischaemic; standard pharmacological therapy for HF (diuretics, angiotensin-converting enzyme inhibitors, and beta blockers)

Pozehl 2008 *(Continued)*

	Exclusion:participation in a formal exercise programme < 30 days before this study; clinical evidence of decompensated HF; any of the following medical conditions: AF, acute MI < 3 months, unstable angina pectoris, end-stage renal disease, or orthopaedic impediments to exercise
Interventions	**Exercise** • Total duration: 24 weeks • Aerobic/resistance/mix: mix • Frequency: 3 sessions/week • Duration: 30 min aerobic, 20 min resistance • Intensity: 60%-85% max VO_2, 12-14 Borg scale • Modality: aerobic: treadmill, stationary bike, rower, arm ergometer; resistance: light upper body exercises (military press, biceps curl, lateral deltoid raises), and lower body exercises (knee extension, side hip raise, hip extension) with 0.45kg to 4.5kg hand and ankle weights. Wall push-ups, abdominal curl-ups, pelvic tilts, or a combination • Setting: first 12 weeks at the hospital and remaining sessions were unsupervised at the rehabilitation centre **Other:** strategies from social learning theory (goal-setting, feedback, problem-solving guidance) utilised to facilitate, improve adherence to the training programme **Control group/comparison:** usual medical care
Outcomes	Mortality
Country and setting	USA, single centre
Follow-up	6 months (after randomisation)
Notes	**Source of funding:** American Heart Association #9806406S and University of Nebraska Medical Center #OC-10-98

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not reported
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding (performance bias and detection bias) All outcomes	Unclear risk	Not reported
Incomplete outcome data (attrition bias)	Low risk	"One subject in the control group died of myocardial infarction and one subject in the exercise training group was diagnosed with cancer and unable to continue the exercise training" No imputation undertaken
Selective reporting (reporting bias)	Low risk	Outcomes described in the methods were reported in the results.
Groups balanced at baseline?	Low risk	"Subjects did not differ in fatigue or dyspnea by type of HF (ischemic vs. nonischemic) or years since diagnosis of HF (length of time since diagnosis)"

Pozehl 2008 *(Continued)*

Groups received comparable care?	Unclear risk	Not reported
Intention-to-treat analysis?	Low risk	Although not stated, groups appear to have been analysed according to the initial randomised allocation.

Reeves 2017

Study characteristics	
Methods	Parallel-group RCT
Participants	**N randomised:** 27 (exercise 15, control 12) **Diagnosis (% of participants)** • Aetiology: preserved EF: exercise 42%, control 40% • NYHA: not reported • LVEF: exercise 40 ± 13%, control 34 ± 18% **Case mix:** 100%, as above **Age, years:** exercise 72.7 (SD 10.8), control 71.8 (SD 9.1) **Male:** exercise 47%, control 33% **White:** 47% in exercise group, 42% in control group **Inclusion/exclusion criteria** **Inclusion:**ADHF diagnosed by acute worsening of HF symptoms; at least 1 sign of HF and change in medical treatment consistent with HF; aged ≥ 60 years; independence with basic activities of daily living before hospitalisation; achievement of clinical stability allowing study participation; ability to ambulate at least 4 m; planned return home post discharge **Exclusion:**acute coronary syndrome, severe aortic stenosis, end-stage HF requiring advanced therapies or home intravenous inotropic therapy, functional status limited by condition other than HF at the time of enrollment, advanced CKD defined as estimated glomerular filtration rate 20 mL/min/1.73 m^2, terminal illness other than HF, active participation in supervised exercise training before hospitalisation, inability or unwillingness to adhere with the study protocol
Interventions	**Exercise** • Total duration: 12 weeks • Aerobic/resistance/mix: mix • Frequency: 3 sessions/week • Duration: 60 min • Intensity: individually tailored: initially low intensity, rising to 13 ("somewhat hard") on self-reported score • Modality: endurance and strength training • Setting: hospital (supervised) and home (unsupervised) **Other:** components of exercise include static and dynamic balance training (e.g. standing with narrow base of support, standing and reaching); mobility training (e.g. dynamic start and stop, changing direction while walking); functional strength training focused on lower extremities (e.g. chair rise; step-ups); endurance training (sustained walking preferred)

Reeves 2017 *(Continued)*

	Control group/comparison: usual care (regular physician visits with medication adjustments) plus regular contact with study personnel
Outcomes	All-cause hospital admissions
Country and setting	USA, multicentre
Follow-up	6 months
Notes	Exercise was individually tailored and was delivered by trained interventionists in hospital over 12 weeks along with a home exercise prescription (unsupervised low-intensity walking at usual pace for up to 30 min and simple functional strengthening exercises) **Source of funding:** NIH Grants R01AG045551 and R01AG18915; The Claude D. Pepper Older Americans Independence Centre of Wake Forest School of Medicine Winston-Salem, NC, NIH Grant P30AG021332; the Kermit Glenn Phillips II Endowed Chair in Cardiology; Dean's Faculty Achievement, Jefferson Glenn Philips II Endowed Chair in Cardiology; Dean's Faculty Achievement Award, Jefferson College of Health Professions, Philadelphia, PA; and Oristano Family Research Fund

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	"Participants were randomized using a computer-generated list SAS software"
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding (performance bias and detection bias) All outcomes	Low risk	"Follow-up assessments were collected by trained, blinded assessors according to standardized protocols"
Incomplete outcome data (attrition bias)	Unclear risk	Three dropouts from total (N = 24) but no further details or reasons given
Selective reporting (reporting bias)	Unclear risk	Not reported
Groups balanced at baseline?	Low risk	"Baseline characteristics were balanced between the study arms"
Groups received comparable care?	Low risk	Control group received "attention" consisting of at least monthly contact with study personnel via scheduled phone calls and follow-up assessments.
Intention-to-treat analysis?	Low risk	"Intention-to-treat analysis performed for all-cause hospital admissions, with comparisons made using analysis of covariance with heart failure category (ejection fraction <45% or ≥45%)"

Ricca-Mallada 2017

Study characteristics	
Methods	Parallel-group RCT
Participants	**N randomised:** 40 (exercise 20, control 20)

Ricca-Mallada 2017 *(Continued)*

	Diagnosis (% of participants) • Aetiology: ischaemic 53% • NYHA: exercise I 62.5%; II 37.5%; control I 61%; II 39% • LVEF: exercise 32.12 (+- 7.85); control 28.17 (+- 8.06); **Case mix:** as above **Age:** exercise 62.6 (10.8); control 62.2 (10.2) **Male:** 79% **White:** not reported **Inclusion/exclusion criteria** **Inclusion:** aged 18–80 years, sinus rhythm, NYHA Class I-III, and LVEF 40% as documented by echocardiogram **Exclusion:** a history of stroke; extended anterior myocardial scar; revascularisation procedures or recurrent angina within the previous 3 months; orthopaedic impairment; alcohol or drug abuse; implant of pacemaker or cardioverter-defibrillator (AICD); frequent ventricular dysrhythmias, atrial flutter or fibrillation; insulin-dependent DM; severe COPD; severe renal dysfunction; comorbid non-cardiac disease limiting short-term survival; previous enrolment in an exercise programme and an increased propensity for noncompliance
Interventions	**Exercise** • Total duration: 24 weeks (68-74 sessions) • Aerobic/resistance/mix: aerobic • Frequency: 3 days/week • Duration: 1 h • Intensity: 80% maximal HR • Modality: walking (Nordic walking poles); resistance band exercises • Setting: in centre • Other: supervised by a cardiologist **Control:** usual care with no changes to previous physical activity
Outcomes	• Adverse clinical events (temporary or permanent withdrawal from the study protocol due to persistent atrial or ventricular arrhythmias; worsening of CHF symptoms; MI; unstable angina; need for cardiac interventions such as pacemaker, AICD, coronary revascularisation or cardiac transplantation; stroke or transient ischaemic attack and severe peripheral intermittent claudication or death observed during training or follow-up sessions) • LVEF • 6MWT • Stress testing (maximal exercise testing) • QoL (SF-36) • HR variability
Country and setting	Uruguay, single centre
Follow-up	Baseline (prerandomisation) and 24 weeks post-randomisation
Notes	Contacted study authors to seek numerical details of HRQoL (SF-36) not reported in manuscript
Risk of bias	
Bias	**Authors' judgement** **Support for judgement**

Ricca-Mallada 2017 *(Continued)*

Random sequence generation (selection bias)	Unclear risk	Not reported
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding (performance bias and detection bias) All outcomes	Low risk	"A single experienced operator performed the measurements in a blinded manner"
Incomplete outcome data (attrition bias)	Low risk	Exercise 16/20 (80%), control 18/20 (90%), provided outcomes for mortality analysis at follow up.
Selective reporting (reporting bias)	Low risk	All outcomes listed in methods relevant to this review were reported.
Groups balanced at baseline?	Low risk	"Both groups were comparable in terms of baseline demographics, clinical characteristics and comorbidities"
Groups received comparable care?	Low risk	"All patients received an optimal pharmacologic treatment including diuretics, angiotensin converting enzyme inhibitors or angiotensin receptor blockers, and beta-adrenergic blocking agents, and all had been stable on medications for at least 2 months before recruitment"
Intention-to-treat analysis?	Low risk	Although not explicitly stated, it appears an ITT analysis was performed. "There was no patient crossover between groups."

Ryu 2018

Study characteristics	
Methods	Parallel-group RCT
Participants	**N randomised: 47** (2 intervention arms: moderate-intensity home-based CR [MIHE] 20, high-intensity home-based CR 8 [HIME] and control: no home-based exercise 19 [NHE]) **Diagnosis (% of participants)** • Aetiology: not reported • NYHA: I, II, III, IV not reported • LVEF: mean (SD): NHE 30% (8%); MIHE 33% (9%); HIHE 34% (8%) **Case mix:** as above **Age:** mean (SD):61.3 (9.8) years **Male:** 70% **White:** all Korean **Inclusion/exclusion criteria** ***Inclusion:***CHF **Exclusion:** patients with negative and ECG response to cardiopulmonary exercise
Interventions	**Exercise**

Ryu 2018 *(Continued)*

	• Total duration: 52 weeks • Aerobic/resistance/mix: aerobic • Frequency: both groups ≥ 3 days/week • Duration: both groups ≥ 10-30 min • Intensity: moderate or high intensity (not defined) • Modality: MIHE: walking; HIHE: jogging or hill walking • Setting: home-based **Control:** no exercise
Outcomes	• Exercise test • Re-hospitalisation
Country and setting	Korea, single site
Follow-up	1 year
Notes	Data extraction completed with support of Korean translator (Soumeen Jin, MRes biomedical science student)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No details reported
Allocation concealment (selection bias)	Unclear risk	No details reported
Blinding (performance bias and detection bias) All outcomes	Unclear risk	No details reported
Incomplete outcome data (attrition bias)	Low risk	No dropout reported at 1 year (Table 2)
Selective reporting (reporting bias)	Low risk	All outcomes reported in methods also reported in results
Groups balanced at baseline?	Low risk	Table 1 shows no statistically significant differences between groups.
Groups received comparable care?	Unclear risk	Not reported if all 3 groups received usual care
Intention-to-treat analysis?	Low risk	Although term ITT not explicitly used, it appears groups were compared according to initial randomisation

Santa-Clara 2019

Study characteristics	
Methods	Parallel-group RCT

Santa-Clara 2019 *(Continued)*

Participants	**N randomised:** 63 (HIIT 34, control 29) **Diagnosis (% of participants)** • Aetiology: moderate to severe CHF • Ischemic: 39% • Dilated cardiomyopathy: 61% • NYHA: II, III, and IV • LVEF: HIIT 27.0% (SD 6.3), control 25.5% (SD 6.6) **Case mix:** as above **Age:** HIIT 68, (SD 8.9), control 67 (SD 8.2) **Male:** 76% **White:** not reported **Inclusion/exclusion criteria** **Inclusion:** not reported (patients with HF, 2-4 weeks after a CRT implant) **Exclusion:** incapacitating orthopaedic, neurologic, or other limitations to exercise, declining to participate in the study, inability to sign the informed consent, previous treatment with an intravenous inotropic agent within the 30 days prior to implantation, unstable angina pectoris
Interventions	**HIIT** • Total duration: 6 months • Aerobic/resistance/mix: aerobic (interval training) • Frequency: 2 times/week • Duration: 60 min • Intensity: 90%-95% (high intensity) and 60%-70% (moderate intensity) HR reserve • Modality: not reported • Setting: hospital based **Control:** usual care
Outcomes	• Peak VO2 • Percent peak VO2 • Pulse pressure • Rate pulse pressure • LVEF • LVEF volumes • QoL (HeartQoL)*
Country and setting	Portugal, single centre
Follow-up	Baseline (prerandomisation) and 6 months post-randomisation
Notes	Funding from Portuguese Foundation for Science and Technology *Relevant outcomes to this review (also report mortality in the CONSORT)

Risk of bias

Bias	Authors' judgement	Support for judgement

Santa-Clara 2019 *(Continued)*

Random sequence generation (selection bias)	Low risk	"The randomization code was developed with a computer random-number generator to select random permuted blocks"
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding (performance bias and detection bias) All outcomes	Unclear risk	Not reported
Incomplete outcome data (attrition bias)	High risk	HIIT 20/34 (59%), control 17/29 (58%) provided data for analysis
Selective reporting (reporting bias)	Low risk	All outcomes discussed in the methods were reported in the results.
Groups balanced at baseline?	Low risk	"No significant differences were found between the HIIT and CON groups in functional capacity scale or health-related quality of life at baseline." "No significant differences were found between the HIIT and CON groups in any exercise performance parameter at baseline" "No significant differences were found between HIIT and CON groups in any echocardiographic parameter at baseline."
Groups received comparable care?	Low risk	"The CON [control] group was given no specific advice on exercise training and underwent no supervised training."
Intention-to-treat analysis?	Low risk	Whilst both a per-protocol analysis and an ITT analysis were performed, the ITT data are not fully displayed. "Since this study was designed as an efficacy study, we focused initially on a per-protocol analyses, which included the patients in CRT that successfully completed the exercise protocol with attendance rates superior to 80%. Next, we performed an intention-to-treat analysis using all participants that were randomized."

TELEREH-HF 2020

Study characteristics	
Methods	Parallel-group RCT
Participants	**N randomised:** 850 (exercise 425, control 425) **Diagnosis (% of participants)** • Aetiology: ischaemic 65% • NYHA: I 12%; II 68%; III 20%; IV 0% • LVEF: 31% (7) **Case mix:** as above **Age:** exercise 62.6 (10.8); control 62.2 (10.2) **Male:** 88.6% **White:** not reported

TELEREH-HF 2020 *(Continued)*

Inclusion/exclusion criteria

Inclusion

- be of either sex with any aetiology of left ventricular systolic HF as defined in the ESC guidelines
- LVEF ≤ 40% on ECG
- NYHA class I, II or III
- hospitalisation within 6 months prior to randomisation
- be stable clinically (a patient does not need intravenous medication or has not had therapy modified for at least 7 days)
- have no contraindications to undergo cardiopulmonary exercise test
- be able to exercise using the new model of hybrid telerehabilitation

Exclusion

- NYHA class IV
- unstable angina
- unstable clinical status
- a history of acute coronary syndrome within the last forty days in patients with LVEF ≤ 35%
- percutaneous angioplasty within the last 2 weeks
- coronary artery bypass grafting within the last 3 months
- initiation of CRT-P or CRT-D or ICD or PM within the last 6 weeks
- lack of ICD, CRT-P or CRT-D or PM therapy despite the indications for implantation
- according to ESC guidelines
- intracardiac thrombus
- rest HR > 90/min
- tachypnoe > 20 breaths per minute
- symptomatic and/or exercise-induced cardiac arrhythmia or conduction disturbances
- acute myocarditis and/or pericarditis
- valvular or congenital heart disease requiring surgical treatment
- hypertrophic cardiomyopathy
- severe pulmonary disease
- uncontrolled hypertension
- anaemia (haemoglobin < 11.0 g/dL)
- physical disability related to severe musculoskeletal or neurological problems
- recent embolism
- thrombophlebitis
- acute or chronic inflammatory disease
- acute or chronic decompensated non-cardiac diseases (thyreotoxicosis, uncontrolled diabetes)
- active malignant neoplastic diseases with survival prognosis below 2 – 5 years
- orthotropic heart transplant in anamnesis
- presence of an implanted left ventricular assist device or biventricular assist device
- aortic aneurysm
- severe psychiatric disorder
- patient's refusal to participate

Interventions

Exercise

- Total duration: 9 weeks (1 week in hospital, followed by 8 weeks at home)
- Aerobic/resistance/mix: mix
- Frequency: 1 times/day of both aerobic and resistance
- Duration: 15 min increasing to 1 h 15 min/day total
- Intensity: 40%-70% HR
- Modality: walking (Nordic walking poles); resistance band exercises

TELEREH-HF 2020 *(Continued)*

	• Setting: in hospital then home • Other: 3-5 sessions of respiratory muscle training/day, comprehensive intervention "encompassed telecare, telerehabilitation, and remote monitoring of implantable devices" **Control:** usual care
Outcomes	Secondary outcomes assessed at 12-24 months: • all-cause and CV mortality • all-cause, CV and HF hospitalisation
Country and setting	Poland, multicentre (5 sites)
Follow-up	Baseline (prerandomisation) and 9-week and 14-26 months postrandomisation
Notes	Funding from National Centre for Research and Development, Warsaw, Poland 5 relevant publications - see reference for TELEREH-HF 2020

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	“Eligible patients were randomized in a 1:1 ratio (block size of 2, stratified by site)”
Allocation concealment (selection bias)	Low risk	“via a secure web based randomization system (Research Electronic Data Capture [REDCap] housed in the coordinating center). All sites used the same allocation process to ensure uniform randomization. Data were collected in REDCap.”
Blinding (performance bias and detection bias) All outcomes	Low risk	“a clinical end point committee, blinded to treatment allocation, was appointed to adjudicate deaths and hospitalizations.”
Incomplete outcome data (attrition bias)	Low risk	Exercise 425/425 (100%), control 425/425 (100%) provided outcomes for mortality analysis at long-term follow up. Exercise 409/425 (96%), control 409/425 (96%) provided outcomes for hospitalisation analysis at long-term follow up. “Because no patients withdrew informed consent, we were able to obtain complete data for all-cause mortality. Thirty-two participants (3.8%) were lost to follow-up and were censored at the date of last contact. We were able to ascertain mortality status in all patients at study end and hospitalization status in 818 patients (96.2%; 409 in the HCTR arm and 409 in the UC arm)”
Selective reporting (reporting bias)	Low risk	All outcomes described in protocol publication are reported in main trial publications.
Groups balanced at baseline?	Low risk	“Study arms were not significantly different in terms of demographic data, baseline clinical parameters, and treatment”
Groups received comparable care?	Low risk	“All patients, regardless of the treatment group, received recommendations for suitable lifestyle changes and self-management according to guidelines"
Intention-to-treat analysis?	Low risk	“Results were consistent on the modified intent-to-treat population, which excluded patients who did not complete the 9-week intervention period”

Wall 2010

Study characteristics	
Methods	Parallel-group RCT
Participants	**N randomised:** 19 (exercise 9, control 10) **Diagnosis (% of participants)** • Aetiology: not reported • NYHA: mean exercise 2 (SE 0), mean control 2.13 (SE 0.13) • LVEF: ≤ 60% **Case mix:** as above **Age, years:** exercise 69 (SD 4.44), control 70 (SD 4.05) **Male:** 58% **White:** 100% **Inclusion/exclusion criteria** **Inclusion:**diagnosis of NYHA Class I-III congestive HF; EF ≤ 60%; systolic dysfunction; physician approval; ability to complete a minimum of 3 min of a modified Bruce protocol stress test **Exclusion:** failure to meet any of the inclusion criteria; inability to speak English; noticeable cognitive impairment
Interventions	**Exercise** • Total duration: 12 months • Aerobic/resistance/mix: aerobic • Frequency: 3 sessions/week • Duration: > 15 min • Intensity: not reported • Modality: treadmill Lifestyler treadmill provided for 1 year of in-home use; 3 supervised exercise sessions at hospital with CR specialist. Weekly in-home exercise visits with CR specialist, month 1. Monthly in-home exercise visits with CR specialist, months 2-12. Also received comprehensive disease management programme **Setting:** 3 hospital-based; the remainder at home **Other:** not reported **Control group/comparison:** comprehensive disease management by dedicated case manager (participant education on nutrition, medications, and disease management; an oximetry assessment; constant monitoring of symptomatic changes and disease status)
Outcomes	• Disease-specific HRQoL (Chronic Heart Failure Questionnaire) • Mortality
Country and setting	USA, single centre
Follow-up	12 months (after randomisation)
Notes	**Source of funding:** ATPM/CDC/ATSDR Cooperative Agreement No. U50/CCU300860
Risk of bias	

Wall 2010 *(Continued)*

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not reported
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding (performance bias and detection bias) All outcomes	Unclear risk	Not reported
Incomplete outcome data (attrition bias)	Low risk	QUORUM flow diagram report suggests that 19 participants were included in the analysis. 15 participants (79%) completed final follow-up measures at month 12.
Selective reporting (reporting bias)	Low risk	All outcomes described in the methods were reported.
Groups balanced at baseline?	Low risk	Table 3 of the publication suggests there is no difference between the 2 groups (except dyspnoea score).
Groups received comparable care?	Low risk	Both groups received comprehensive disease management.
Intention-to-treat analysis?	Low risk	Although not stated, it is clear from the CONSORT diagram that 2 groups were analysed according to ITT.

Wang 2021

Study characteristics	
Methods	Parallel-group RCT
Participants	**N randomised:** 98 (cardiopulmonary exercise testing 49, control 49) **Diagnosis (% of participants)** • Aetiology: ischaemic 24% • NYHA: 42% I&II, 58% III&IV • LVEF: CPET 29.69 (3.80), control 30.08 (3.71) **Case mix:** as above **Age:** CPET 62.4 (4.6), control 63.0 (4.2) **Male:** 59% **White:** not reported **Inclusion/exclusion criteria** **Inclusion** • The research met the heart function classification (I-III) standard of the NYHA • CHF patients' clinical symptoms were stabe > 30 days • Administered anti-CHF drugs

Wang 2021 *(Continued)*

	• LVEF) score < 45% • Confirmed CHF through ultrasounds and ECGs **Exclusion** • Severe myocardial ischemia, MI, or cardiac pacemaker implantation • Systolic blood pressure ≥ 200 mmHg and diastolic blood pressure ≥ 110 mmHg under a static state • Thrombosis and myocarditis • Pulmonary heart complication, pulmonary hypertension, or severe infections • Unstable diseases of the lower limbs • Cognitive insufficiency or mental illness • Participated in other clinical projects
Interventions	**Cardiac rehabilitation training** • Total duration: 6 months • Aerobic/resistance/mix: aerobic • Frequency: not reported • Duration: 30-60 min • Intensity: 60%-85% HR • Modality: cycling, running • Setting: not reported **Control:** conventional anti-CHF treatment
Outcomes	**Primary** • Heart function • Cardiopulmonary function • Exercise endurance • Comparison of peripheral blood NTproBNP, hscTnT, and CRP levels **Secondary** • MLHFQ • Self-rating anxiety scale (SAS) • Self-rating depression scale (SDS)
Country and setting	China, single centre
Follow-up	Baseline (prerandomisation) and 6 months post-randomisation
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	"The patients were randomly divided into a control group and a CPET group, with 49 cases in each group."
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding (performance bias and detection bias) All outcomes	Unclear risk	Not reported

Wang 2021 *(Continued)*

Incomplete outcome data (attrition bias)	Low risk	CPET 49/49 (100%), control 49/49 (100%) provided data for analysis
Selective reporting (reporting bias)	Low risk	All outcomes discussed in the methods were reported in the results.
Groups balanced at baseline?	Low risk	"There were no significant differences in terms of gender, average age, average course of the disease, BIM, NYHA grade, smoking history, hypertension, diabetes, coronary heart disease, disease type, education, or monthly income between the two groups (all P>0.05)"
Groups received comparable care?	Low risk	"In addition to [usual care], the patients in the CPET group underwent CPET sports rehabilitation training"
Intention-to-treat analysis?	Unclear risk	Not reported

Willenheimer 2001

Study characteristics	
Methods	Parallel-group RCT
Participants	**N randomised:** 54 (exercise 27, control 27) **Diagnosis (% of participants)** • Aetiology: ischaemic 80%, non-ischaemic 20% • NYHA: exercise 2.1 (SD 0.7), control 2.4 (0.7) • LVEF: exercise 35% (SD 12), control 38% (SD 10) **Case mix:** 100%, as above **Age, years:** exercise 64 (SD 5), control 64 (SD 9) **Male:** exercise 73%, control 70% **White:** not reported **Inclusion/exclusion criteria** **Inclusion:** 8 points on Boston heart failure criteria; LVEF 0.45 at the most recent radionuclide or ECG examination (not older than 1 year at inclusion); age 75 years **Exclusion:** change in clinical status or medication (or both) within 4 weeks before inclusion; MI, heart surgery, or coronary angioplasty within 3 months before inclusion; inability to perform a bicycle test; exercise-terminating angina pectoris, ST depressions (> 2 mm in > 1 lead), blood pressure fall (> 0.10 mm Hg), or arrhythmia (e.g. ventricular tachycardia/fibrillation, ventricular extrasystoles, supraventricular tachycardia > 170 bpm) at the most recent maximal exercise test (including the baseline test); pulmonary disease judged to be the main exercise-limiting factor or peak expiratory flow rate < 50% of age- and sex-adjusted reference values, or both; NYHA Class IV; clinically significant aortic stenosis
Interventions	**Exercise** • Total duration: 4 months • Aerobic/resistance/mix: aerobic/interval • Frequency: 2-3 sessions/week • Duration: 15 min/session, increasing to 45 min/session

Willenheimer 2001 *(Continued)*

- Intensity: 80% peak VO_2, or 15 on Borg score
- Modality: cycle ergometry
- Setting: group sessions supervised by physiotherapist

Other: none

Control group/comparison: control participants were asked to not change their degree of physical activity during the active study period. Neither training participants nor controls were instructed regarding physical activity during the 6-month extended follow-up

Outcomes	• HRQoL (Patient's Global Assessment of Quality of Life) • Mortality
Country and setting	Sweden, single centre
Follow-up	10 months (after randomisation)
Notes	**Source of funding:** Swedish Society for Patients With Heart and Lung Diseases

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not reported
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding (performance bias and detection bias) All outcomes	Low risk	Outcome assessors blinded; participants, clinical carers not blinded
Incomplete outcome data (attrition bias)	High risk	Outcomes were available for only 43/54 (80%) participants randomised at 10 months' follow-up. No imputation or sensitivity analysis was undertaken to assess effects of loss to follow-up. Study authors stated that participants available at 10 months' follow-up are representative.
Selective reporting (reporting bias)	Low risk	All outcomes described in the methods were reported in the results.
Groups balanced at baseline?	Low risk	"There was no difference between training (n = 22) and control (n = 27) patients as regards baseline variables"
Groups received comparable care?	Low risk	"No change in medication allowed during study"
Intention-to-treat analysis?	Low risk	Although ITT is not implicit, it appears that groups were analysed according to the original randomised allocation.

Witham 2005

Study characteristics

Methods	Parallel-group RCT

Witham 2005 *(Continued)*

Participants	**N randomised:** 82 (exercise 41, control 41) **Diagnosis (% of participants)** • Aetiology: IHD 66% • NYHA: Class II 56%, Class III 44% • LVEF: not reported **Case mix:** as above **Age, years:** exercise 80 (SD 6), control 81 (SD 4) **Male:** 55% **White:** not reported **Inclusion/exclusion criteria** **Inclusion:** age ≥ 70 years with clinical diagnosis of CHF according to ESC guidelines; NYHA Class II or III symptoms and evidence of LVSD on ECG, contrast ventriculography, or radionuclide ventriculography; evidence of LVSD **Exclusion:** uncontrolled AF, significant aortic stenosis, sustained ventricular tachycardia, recent MI, inability to walk without human assistance, abbreviated mental score < 6 of 10, currently undergoing physiotherapy or rehabilitation
Interventions	**Exercise** • Total duration: 6 months • Aerobic/resistance/mix: mix • Frequency: 2-3 sessions/week • Duration: 20 min • Intensity: Borg 11-13 • Modality: walking and wrist/ankle weights • Setting: 3 months: hospital-based by senior physiotherapist; 3 months: home-based After 3 months of supervised training, participants in the exercise group were asked to continue to perform exercises at home 2 or 3 times/week with the aid of video or audio cassette with demonstrations, instructions, and music. No face-to-face contact was had with the physiotherapist during this period **Other:** not reported **Control group/comparison:** usual medical care
Outcomes	• Disease-specific HRQoL (Guyatt Chronic Heart Failure Questionnaire) • Mortality • Hospitalisation
Country and setting	UK, single centre
Follow-up	6 months (after randomisation)
Notes	**Source of funding:** Grant 2006/918 from The Health Foundation (formerly PPP Health Foundation), London, UK

Risk of bias

Bias	Authors' judgement	Support for judgement

Witham 2005 *(Continued)*

Random sequence generation (selection bias)	Low risk	"A researcher not otherwise connected with the operation of the study prepared cards contained in numbered, sealed envelopes from computer-generated random number tables"
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding (performance bias and detection bias) All outcomes	Low risk	"An experienced research nurse who was blinded to treatment allocation performed all assessments"
Incomplete outcome data (attrition bias)	Low risk	75/82 (91%) and 68/82 (83%) were available at 3 months' and 6 months' follow-up, respectively.
Selective reporting (reporting bias)	Low risk	All outcomes described in the methods were reported in the results.
Groups balanced at baseline?	Low risk	Table 1 of the publication shows that groups were well balanced.
Groups received comparable care?	Low risk	Yes, both groups appear to have received usual medical care; the only difference between groups was the exercise intervention.
Intention-to-treat analysis?	Low risk	It appears from the QUORUM diagram that groups were analysed according to the initial random allocation.

Witham 2012

Study characteristics	
Methods	Parallel-group RCT
Participants	**N randomised:** 107 (exercise 53, control 54) **Diagnosis (% of participants)** • Aetiology: ischaemic 62.6% • NYHA: Class II 79%, Class III 21% • LVEF: not reported **Case mix:** as above **Age, years:** exercise 80.4 (SD 5.8), control 79.5 (SD 4.9) **Male:** exercise 35%; control 37% **White:** 100% **Inclusion/exclusion criteria** **Inclusion:** age ≥ 70 years with confirmed diagnosis of HF due to LVSD (NYHA Class II and III) and history of symptoms and signs of congestive HF **Exclusion:** wheelchair bound, unwilling or unable to give informed consent, aortic stenosis with peak gradient > 30 mmHg, sustained ventricular tachycardia or ventricular fibrillation outside the context of an acute MI, currently (within the past month) with unstable angina or AF with ventricular rate > 100/min

Witham 2012 *(Continued)*

Interventions	**Exercise** • Total duration: 24 weeks • Aerobic/resistance/mix: mix • Frequency: 2 sessions/week • Duration: ≤ 60 min • Intensity: not reported • Modality: home, walking • Setting: hospital and home* **Other:** cognitive and behavioural techniques were incorporated into first 8-week hospital-based rehabilitation; resistance training with elasticised bands **Control group/comparison:** usual medical care (given a booklet with general advice on diet, exercise, and lifestyle); not discouraged from exercising if already in the habit of doing so
Outcomes	• Disease-specific HRQoL (MLWHF questionnaire) • HRQoL (EuroQoL-5D) • Mortality • Hospital admission • Cost
Country and setting	UK, single centre
Follow-up	24 weeks (after randomisation)
Notes	*8 weeks in hospital delivered by experienced physiotherapist, 16-week home-based (telephoned every 2 weeks for 8 weeks by physiotherapists, then monthly for the final 8 weeks) **Source of funding:** Chief Scientist Office (Scottish Government), Grant number CZH/4/426

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	"Using off-site telephone randomization service, randomization was performed without stratification and with block sizes between 8 and 16, depending on the size of each planned exercise class"
Allocation concealment (selection bias)	Low risk	"…the project coordinator passed the participants' details to the research physiotherapist who obtained group allocation, ensuring that the project coordinator remained blind to group assignments"
Blinding (performance bias and detection bias) All outcomes	Unclear risk	Not reported
Incomplete outcome data (attrition bias)	Low risk	89/104 (86%) and 87/104 (83%) were available for follow-up at 8 and 24 weeks, respectively.
Selective reporting (reporting bias)	Low risk	All outcomes described in the methods were reported in the results.
Groups balanced at baseline?	Low risk	Table 1 of the publication suggests no differences between the 2 groups.

Witham 2012 *(Continued)*

Groups received comparable care?	Low risk	It appeared that both groups received the same care, except for the exercise intervention.
Intention-to-treat analysis?	Low risk	Analyses were by ITT.

Yeh 2011

Study characteristics	
Methods	Parallel-group RCT
Participants	**N randomised:** 100 (Tai Chi (exercise) 50, education (control) 50) **Diagnosis (% of participants)** • Aetiology: ischaemic 54%, non-ischaemic 46% • NYHA: Class I 20%, Class II 63%, Class III 17% • LVEF: mean 29% (SD 8%) **Case mix:** 100%, as above **Age, years:** exercise 68.1 (SD 11.9), control 66.6 (SD 12.1) **Male:** 64% **White:** 86% **Inclusion/exclusion criteria:** **Inclusion:**EF ≤ 40% in past 2 years, stable medical regimen, NYHA Class I-III HF **Exclusion:** unstable angina, MI, or major surgery in past 3 months; history of cardiac arrest in past 6 months; history of cardiac re-synchronisation therapy in the past 3 months; unstable serious ventricular arrhythmias; unstable structural valve disease; current participation in conventional CR programme; diagnosis of peripartum cardiomyopathy within preceding 6 months; inability to perform a bicycle stress test; lower extremity amputation or other inability to ambulance owing to condition other than HF; severe cognitive dysfunction (MMSE score ≤ 24); inability to speak English; regular practice of Tai Chi

Interventions	**Exercise**
	
	• Total duration: 12 weeks
	• Aerobic/resistance/mix: aerobic
	• Frequency: 2 sessions/week (for 12 weeks) and encouraged to practice at home at least 3 times/week
	• Duration: 1-h class (30-min warm-up)
	• Intensity: not reported
	• Modality: Tai Chi movements
	  ◦ weeks 2-5: warm-up + raising the power; withdraw and push
	  ◦ weeks 6-9: 1 + grasp sparrow's tail, brush knee twist step
	  ◦ weeks 10-12: 2 + wave hands like clouds
	• Participants were given 45-min instructional videotape that outlined the exercises presented in class as an aid to practice
	• Participants also received the same educational pamphlets used in the education (control) group, with a brief (< 5 min) explanation towards the end of 1 Tai Chi session weekly
	• Setting: centre-based and home-based

Yeh 2011 *(Continued)*

	Other: none reported **Control group/comparison:** educational group ('attention control'): nurse practitioner-led educational session (same duration and frequency as Tai Chi group classes) Participants were asked to not start Tai Chi classes during the study
Outcomes	• HRQoL (MLWHF questionnaire) • mortality • Hospital admission
Country and setting	USA, multisite
Follow-up	12 weeks and 6 months (after randomisation)
Notes	Single-blind **Source of funding:** ROI AT002454 Award from the National Center for Complementary and Alternative Medicine; in part by RR 01032 from the Beth Isreal Deaconess Medical Center General Clinical Research Center from the National Institutes of Health (NIH)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	"The trial uses a permuted block randomization with variable block size to generate treatment assignment"
Allocation concealment (selection bias)	Unclear risk	"Patients who chose to were randomly assigned to receive a 12-week tai chi exercise program or a heart health education program (attention control)"
Blinding (performance bias and detection bias) All outcomes	Low risk	"We masked all the study staff performing all tests to each participant's group allocation"
Incomplete outcome data (attrition bias)	Low risk	Figure 1 of the publication shows 91%-96% complete data across HRQoL and exercise outcomes.
Selective reporting (reporting bias)	Low risk	All outcomes described in the methods were reported in the results.
Groups balanced at baseline?	Low risk	"The 2 groups were generally similar in demographics, clinical classification of heart disease severity, and rates of comorbidities"
Groups received comparable care?	Low risk	Yes, both groups received comprehensive disease management.
Intention-to-treat analysis?	Low risk	All participants were included in the analysis regardless of their attendance.

6MWT: 6-minute walk test; **ACE:** angiotensin-converting enzyme; **ADHF:** acute decompensated heart failure; **AF:** atrial fibrillation; **ARB:** angiotensin II receptor blockers; **BL:** baseline; **BMI:** body mass index; **bpm:** beats/min; **CBT:** cognitive-behavioural therapy; **CHF:** chronic heart failure; **CKD:** chronic kidney disease; **CONSORT:** CONsolidated Standards of Reporting Trials; **COPD:** chronic obstructive pulmonary disease; **CPET:** cardiopulmonary exercise test; **CR:** cardiac rehabilitation; **CRP:** C-reactive protein; **CRT:** cardiac re-synchronisation therapy; **CV:** cardiovascular; **DCM:** dilated cardiomyopathy; **DM:** diabetes mellitus; **DSM-IV:** *Diagnostic and Statistical Manual of Mental Disorders*, 4th Edition; **E/A ratio:** ratio of early (E) to late (A) mitral valve flow velocity; **ECG:** electrocardiogram; **EF:** ejection fraction; EQ-5D: EuroQoL Group Quality of Life Questionnaire based on 5 dimensions; **EQ-5D-3L:** EuroQoL Group Quality of Life Questionnaire based on a 3-level scale; **EHFScBS:** European Heart Failure Self-care Behaviour Scale; **ESC:** European Society of Cardiology; **FEV1:** forced expiratory volume

in the first second; **FVC:** forced vital capacity; **GP:** general practitioner; **HADS:** Hospital Anxiety and Depression Scale; **HAM-D:** Hamilton Depression Rating Scale; **HF:** heart failure; **HFrEF:** heart failure with reduced ejection fraction; **HFmrEF:** heart failure with mildly reduced ejection fraction; **HFPEF:** heart failure with preserved ejection fraction; **HIIT:** high-intensity interval training; **HR:** heart rate; **HRQoL:** health-related quality of life; **ICD:** implantable cardioverter-defibrillator; **IHD:** ischaemic heart disease; **ITT:** intention-to-treat; **KCCQ:** Kansas City Cardiomyopathy Questionnaire; **LASI:** left atrial size index; **LDL:** low-density lipoprotein; **LV:** left ventricular; LVEDD: left ventricular end-diastolic diameter; **LVEDVI:** left ventricular end-diastolic volume index; **LVEF:** left ventricular ejection fraction; **LVMI:** left ventricular mass index; **LVSD:** left ventricular systolic dysfunction; max: maximum; **MDM(P):** multidisciplinary disease management (programme); **MET:** metabolic equivalent; **MFI:** Multidimensional Fatigue Inventory-20; **MI:** myocardial infarction; **MISS:** Minimal Insomnia Symptom Scale; MOS: Medical Outcomes Survey; **Mini:** Mini International Neuropsychiatric Interview; **MLWHF:** Minnesota Living With Heart Failure questionnaire; **MMSE:** Mini Mental State Examination; **MR:** mitral regurgitation; MRI: magnetic resonance imaging; **NIH:** National Institutes of Health; **NIHR:** National Institute for Health Research; **NT-proBNP:** N-terminal prohormone of brain natriuretic peptide; **NYHA:** New York Heart Association; **PVD:** peripheral vascular disease; **QoL:** quality of life; **QUORUM:** Quality of Reporting of Meta-analyses; **RCT:** randomised controlled trial; RPE: rate of perceived exertion; SC: subcutaneous; **SD:** standard deviation; SE: standard error; **SF-36:** Short Form-36; **SPPB:** Short Physical Performance Battery; **STEMI:** ST-elevation myocardial infarction; **VO_2:** oxygen consumption; **WC:** waist circumference

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Abdelbasset 2019	Insufficient follow-up
Abolahrari-Shirazi 2018	Insufficient follow-up
Alonso 2021	Ineligible comparator
Arjunan 2020	Insufficient follow-up
Ayad 2021	Insufficient follow-up
Bahrami 2019	Insufficient follow-up
Bangen 2020	Insufficient follow-up
Bortzova 2018	No response from study author
Brubaker 2020	Insufficient follow-up
Chaveles 2021	Ineligible comparator
Chen 2017	Insufficient follow-up
Chinh 2019	Insufficient follow-up
Davis 2018	Ineligible comparator
Deka 2019	Ineligible comparator
Delgado 2020	Insufficient follow-up
Deng 2020	Ineligible intervention
Galenko 2018a	No response from study author
Galenko 2018b	No response from study author
Gary 2020	Ineligible patient population

Study	Reason for exclusion
Gasser 2021	Ineligible comparator
Gevaert 2021	Ineligible comparator
Guimaraes 2018	Insufficient follow-up
Guimaraes 2021	Insufficient follow-up
Guo 2018	Study author not contactable
Halle 2018	Insufficient follow-up
Hearon 2020	Ineligible comparator
Hieda 2019	Ineligible patient population
Hooglugt 2018	Study author not contactable
Hu 2021	Insufficient follow-up
Hua 2019	Ineligible intervention
Jin 2016	Insufficient follow-up
Jones 2019	Insufficient follow-up
Karaman 2020	Insufficient follow-up
Kim 2016	Insufficient follow-up
Lan 2020	Insufficient follow-up
Li 2020	Ineligible comparator
Limpens 2021	Ineligible comparator
Mendes 2020	Ineligible patient population
Mudge 2011	Insufficient follow-up
Mudge 2018	Ineligible comparator
Murad 2019	Ineligible patient population
Nakaya 2021	Ineligible comparator
Ngengo 2020	Insufficient follow-up
Norman 2020	Ineligible comparator
Omidi 2020	Insufficient follow-up
Orwelius 2020	Insufficient follow-up
Papathanasiou 2017	Ineligible comparator

Study	Reason for exclusion
Papathanasiou 2020	Insufficient follow-up
Pourhabib 2018	Insufficient follow-up
Pourhabib 2019	Insufficient follow-up
Pozehl 2018	Ineligible comparator
Sayegh 2019	Insufficient follow-up
Scuffham 2019	Ineligible comparator
Sengupta 2021	Insufficient follow-up
Sinikova 2019	Ineligible comparaor
Smyrnova 2018	Ineligible intervention
Song 2019	Insufficient follow-up
Spee 2020	Ineligible comparator
Turri-Silva 2021	Insufficient follow-up
Yu 2020	Insufficient follow-up
Zhang 2021	Insufficient follow-up

Characteristics of ongoing studies *[ordered by study ID]*

Bobenko 2019

Study name	Exercise training in patients with a left ventricular assist device (Ex-VAD): rationale and design of a multicentre, prospective, assessor-blinded, randomized, controlled trial
Methods	The objective of the study is to test whether 12 weeks of structured supervised exercise training on top of usual care improves functional capacity in patients with end-stage HF with continuous flow e (LVAD).
Participants	64
Interventions	**Intervention:** exercise training intervention. Structured aerobic endurance/resistance training on top of usual care for 12 weeks (3 x/week) **Control:** usual care

Outcomes	**Primary outcomes**
	
	• Change in maximal exercise capacity (time frame: after 12 weeks of treatment)
	  ○ CPET
	  ○ Peak VO_2
	
	Secondary outcomes

Bobenko 2019 *(Continued)*

- Change in ventilatory efficacy (time frame: after 12 weeks of treatment and 12 weeks of follow-up) cardiopulmonary exercise testing (CPET; VE/VCO2 slope)
- Change in submaximal exercise tolerance (time frame: after 12 weeks of treatment and 12 weeks of follow-up) 6-minute-walk distance (m), anaerobic threshold (VO2 at AT)
- Change in muscle strength (time frame: after 12 weeks of treatment and 12 weeks of follow-up) handgrip (kg)
- Change in body composition (time frame: after 12 weeks of treatment and 12 weeks of follow-up) % fat mass
- Kansas City Cardiomyopathy Questionnaire (KCCQ) (time frame: after 12 weeks of treatment and 12 weeks of follow-up) patient-reported measure of quality of life for patients with heart failure
- 36-Item Short Form Survey (SF-36) (time frame: after 12 weeks of treatment and 12 weeks of follow-up) patient-reported measure of health status
- Patient Health Questionnaire (PHQ-9) (time frame: after 12 weeks of treatment and 12 weeks of follow-up) patient-reported measure of presence and severity of depression
- Change in echocardiographic parameters of cardiac morphology and function at rest and during exercise (time frame: after 12 weeks of treatment and 12 weeks of follow-up) left ventricular ejection fraction (%)
- Change in echocardiographic parameters of cardiac morphology and function at rest and during exercise (time frame: after 12 weeks of treatment and 12 weeks of follow-up) left ventricular end diastolic volume (ml)
- Change in echocardiographic parameters of cardiac morphology and function at rest and during exercise (time frame: after 12 weeks of treatment and 12 weeks of follow-up) left ventricular end diastolic diameters (mm)
- Change in echocardiographic parameters of cardiac morphology and function at rest and during exercise (time frame: after 12 weeks of treatment and 12 weeks of follow-up) tricuspid annular plane systolic excursion (TAPSE; mm)
- Change in markers of neuroendocrine activation (time frame: after 12 weeks of treatment and 12 weeks of follow-up) NT-proBNP (ng/l)
- Change in daily physical activity (time frame: up to 12 weeks of treatment and 12 weeks of follow-up) physical activity diary
- Change in daily physical activity (time frame: up to 12 weeks of treatment and 12 weeks of follow-up) accelerometry

Other outcome measures

- Adherence to exercise training (time frame: up to 12 weeks of treatment) accelerometry

Starting date	2017
Contact information	Frank Edelmann, Charité Universitätsmedizin Berlin, Medizinische Klinik m. S. Kardiologie, Augustenburger Platz 1, 13353 Berlin, Germany
Notes	Clinical Trials.gov Identifier: NCT03369938. Status: completed.

Koifman 2014

Study name	Rehabilitation program in heart failure with preserved ejection fraction
Methods	RCT
Participants	1100 participants
Interventions	Participants will participate in a 6-month CR programme, consisting of structured, 60-minute, bi-weekly exercise training sessions, according to a predefined protocol. Institutional activity will be complemented by 120 min of weekly home exercise prescribed by a CR specialist. Following dis-

Koifman 2014 *(Continued)*

	charge, participants in the comparator arm will return to the outpatient clinics at 2-4 weeks and at 3 and 6 months for consultation. These scheduled consultations will comprise history taking, recording of any new events, physical examination, and recommendations as clinically indicated. Target values for blood pressure and glucose control will be in accordance with current guidelines, and special emphasis will be given to management of fluid retention.
Outcomes	**Primary outcomes:** • combined all-cause mortality • hospitalisations at 12 months' follow-up **Secondary clinical outcomes:** will be collected during 3- and 6-month follow-up visits and will include the following: • blood pressure averages • HbA1C levels • assessment of NYHA class and global clinical assessment, 6MWT, and QoL data as evaluated by the EQ-5D questionnaire • all-cause mortality endpoint (time frame: 12 months after randomisation) • heart failure hospitalisations (time frame: 12 months after randomisation) • number of HF hospitalisations as assessed by HF specialists blinded to participant allocation. Assessment will include medical record and hospital discharge letter review
Starting date	October 2013
Contact information	Edward Koifman, MD, Leviev Heart Center, Chaim Sheba Hospital, Tel Hashomer, Israel 52621
Notes	Clinical Trials.gov Identifier: NCT01914315. Unknown status. Authors contacted 2022 (no response).

Vetrovsky 2017

Study name	Effect of pedometer-based walking intervention on functional capacity and neurohumoral modulation in patients with chronic heart failure with preserved ejection fraction: a multicenter randomized controlled trial
Methods	RCT
Participants	200 physically inactive patients with CHF with preserved EF or mid-range EF
Interventions	The 6-month intervention will consist of an individualised pedometer-based walking programme with weekly step goals, monthly face-to-face sessions with the physician, and monthly telephone calls with the research nurse. The intervention will be based on effective behavioural principles (goal-setting, self-monitoring, personalised feedback).
Outcomes	**Primary outcome:** change in 6MWT at 6 months **Secondary outcomes:** • changes in serum biomarker levels • pulmonary congestion assessed by ultrasound • average daily step count measured by accelerometry • anthropometric measures • symptoms of depression • HRQoL • self-efficacy

Vetrovsky 2017 *(Continued)*

	• MAGGIC risk score
Starting date	April 2017
Contact information	Jan Belohlavek, 2nd Department of Medicine-Department of Cardiovascular Medicine, 1st Faculty of Medicine, Charles University in Prague and General University Hospital in Prague, U Nemocnice 2, 128 00, Prague 2, Czech Republic
Notes	ClinicalTrials.gov identifiers: NCT03041610 (HFrEF), NCT03041376 (HFpEF). Study author contacted July 2022. Reply July 2022; study ongoing and recruitment expected to be finished end of 2022.

Zuazagoitia 2010

Study name	
Methods	RCT
Participants	HF with LVEF < 45%
Interventions	supervised exercise + optimised treatment according to ESC guidelines
Outcomes	**Primary outcome** Change in HRQoL (SF-36 and MLWF)
Starting date	Not known
Contact information	Ana Zuazagoitia, Primary Care Research Unit of Bizkaia, Basque Health Service-Osakidetza, CAIBER, Bilbao, Spain
Notes	Clinical Trials.gov Identifier: NCT01033591. Unknown status. Author contacted July 2022 (no response)

6MWT/D: 6-minute walk test/distance; **ADHF:** acute decompensated heart failure; **AE:** adverse event; **CPET:** cardiopulmonary exercise test; **CR:** cardiac rehabilitation; **EQ-5D:** EuroQoL Group Quality of Life Questionnaire based on 5 dimensions; **EF:** ejection fraction; **EQ-5D-5L:** EuroQoL Group Quality of Life Questionnaire based on 5-level scale; **ET:** exercise training; **HADS:** Hospital Depression and Anxiety Scale; **HbA1C:** glycosylated haemoglobin; **HF:** heart failure; **HFpEF:** heart failure with preserved ejection fraction; **HRQoL:** health-related quality of life; **ISWT:** Incremental Shuttle Walk Test; **LVAD:** left ventricular assist device; **MAGGIC:** Meta-Analysis Global Group in Chronic (Heart Failure); **MLWHF:** Minnesota Living With Heart Failure questionnaire; **NHS:** National Health Service (Uk); **NT-proBNP:** N-terminal prohormone of brain natriuretic peptide; **NYHA:** New York Heart Association; **RCT:** randomised controlled trial; **SAE:** serious adverse event; **SCHFI:** Self-care of Heart Failure Index; **VO_2:** oxygen consumption; **WHO:** World Health Organization.

DATA AND ANALYSES

Comparison 1. Exercise-based rehabilitation versus usual care

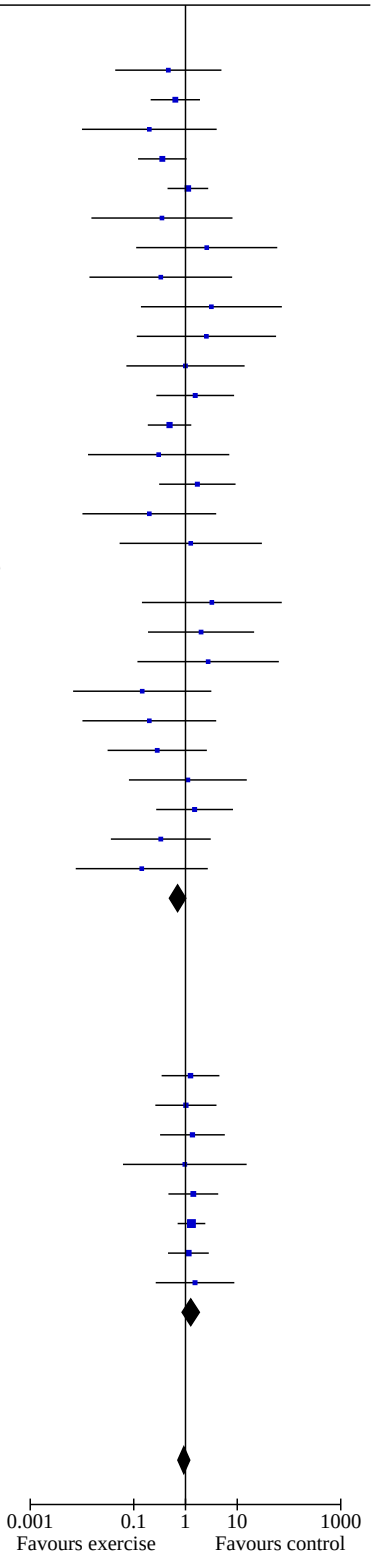
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1.1 All-cause mortality up to 12 months' follow-up	34	3941	Risk Ratio (M-H, Random, 95% CI)	0.93 [0.71, 1.21]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1.1.1 High ROB	26	2498	Risk Ratio (M-H, Random, 95% CI)	0.70 [0.49, 1.01]
1.1.2 Low ROB	8	1443	Risk Ratio (M-H, Random, 95% CI)	1.26 [0.86, 1.85]
1.2 All-cause mortality more than 12 months' follow-up	8	3780	Risk Ratio (M-H, Random, 95% CI)	0.87 [0.72, 1.04]
1.2.1 High ROB	5	400	Risk Ratio (M-H, Random, 95% CI)	0.57 [0.38, 0.87]
1.2.2 Low ROB	3	3380	Risk Ratio (M-H, Random, 95% CI)	0.95 [0.82, 1.11]
1.3 Hospital admissions (all-cause) up to 12 months' follow-up	23	2283	Risk Ratio (M-H, Random, 95% CI)	0.69 [0.56, 0.86]
1.3.1 High ROB	17	1409	Risk Ratio (M-H, Random, 95% CI)	0.64 [0.47, 0.87]
1.3.2 Low ROB	6	874	Risk Ratio (M-H, Random, 95% CI)	0.79 [0.59, 1.07]
1.4 Hospital admissions (all-cause) more than 12 months' follow-up	7	3509	Risk Ratio (M-H, Random, 95% CI)	0.84 [0.70, 1.01]
1.4.1 High ROB	5	361	Risk Ratio (M-H, Random, 95% CI)	0.63 [0.39, 1.03]
1.4.2 Low ROB	2	3148	Risk Ratio (M-H, Random, 95% CI)	0.96 [0.91, 1.01]
1.5 Hospital admissions (heart failure only) up to 12 months' follow-up	10	911	Risk Ratio (M-H, Random, 95% CI)	0.82 [0.49, 1.35]
1.5.1 High ROB	6	369	Risk Ratio (M-H, Random, 95% CI)	0.80 [0.41, 1.56]
1.5.2 Low ROB	4	542	Risk Ratio (M-H, Random, 95% CI)	0.72 [0.25, 2.02]
1.6 Hospital admissions (heart failure only) more than 12 months' follow-up	5	1098	Risk Ratio (M-H, Random, 95% CI)	0.74 [0.50, 1.08]
1.6.1 High ROB	4	280	Risk Ratio (M-H, Random, 95% CI)	0.61 [0.40, 0.94]
1.6.2 Low ROB	1	818	Risk Ratio (M-H, Random, 95% CI)	1.01 [0.80, 1.28]
1.7 Health-related quality of life (MLWHF) up to 12 months' follow-up	21	2699	Mean Difference (IV, Random, 95% CI)	-7.39 [-10.30, -4.47]
1.7.1 High ROB	14	1752	Mean Difference (IV, Random, 95% CI)	-9.59 [-13.11, -6.08]
1.7.2 Low ROB	7	947	Mean Difference (IV, Random, 95% CI)	-3.32 [-8.20, 1.57]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1.8 Health-related quality of life (all scales) up to 12 months' follow-up	33	4769	Std. Mean Difference (IV, Random, 95% CI)	-0.52 [-0.70, -0.34]
1.8.1 High ROB	24	2274	Std. Mean Difference (IV, Random, 95% CI)	-0.61 [-0.84, -0.38]
1.8.2 Low ROB	9	2495	Std. Mean Difference (IV, Random, 95% CI)	-0.28 [-0.51, -0.04]
1.9 Health-related quality of life (MLWHF) more than 12 months' follow-up	3	329	Mean Difference (IV, Random, 95% CI)	-9.49 [-17.48, -1.50]
1.9.1 High ROB	2	217	Mean Difference (IV, Random, 95% CI)	-13.90 [-17.98, -9.82]
1.9.2 Low ROB	1	112	Mean Difference (IV, Random, 95% CI)	-1.60 [-10.26, 7.06]

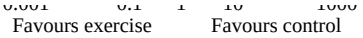
Analysis 1.1. Comparison 1: Exercise-based rehabilitation versus usual care, Outcome 1: All-cause mortality up to 12 months' follow-up

Study or Subgroup	Exercise Events	Exercise Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI
1.1.1 High ROB						
Andryukhin 2010	1	44	2	41	1.3%	0.47 [0.04 , 4.95]
Antonicelli 2016	5	170	8	173	5.8%	0.64 [0.21 , 1.91]
Chen 2018	0	31	2	31	0.8%	0.20 [0.01 , 4.00]
Davidson 2010	4	53	11	52	6.0%	0.36 [0.12 , 1.05]
Dracup 2007	9	87	8	86	8.5%	1.11 [0.45 , 2.75]
Gary 2010 (1)	0	18	1	19	0.7%	0.35 [0.02 , 8.09]
Gary 2010 (2)	1	20	0	17	0.7%	2.57 [0.11 , 59.30]
Giannuzzi 2003	0	45	1	45	0.7%	0.33 [0.01 , 7.97]
Gottlieb 1999	1	17	0	18	0.7%	3.17 [0.14 , 72.80]
Hambrecht 1995	1	12	0	10	0.7%	2.54 [0.11 , 56.25]
Hambrecht 1998	1	10	1	10	1.0%	1.00 [0.07 , 13.87]
Hambrecht 2000	3	36	2	37	2.3%	1.54 [0.27 , 8.69]
Jaarsma 2020	6	305	12	300	7.5%	0.49 [0.19 , 1.29]
Keteyian 1996	0	21	1	19	0.7%	0.30 [0.01 , 7.02]
Lugo 2018	3	23	2	26	2.4%	1.70 [0.31 , 9.27]
Mehani 2013	0	20	2	20	0.8%	0.20 [0.01 , 3.92]
Mueller 2021	1	56	0	23	0.7%	1.26 [0.05 , 29.92]
Mueller 2021	0	55	0	22		Not estimable
Myers 2000	1	12	0	13	0.7%	3.23 [0.14 , 72.46]
Nilsson 2008	2	40	1	40	1.3%	2.00 [0.19 , 21.18]
Norman 2012	1	22	0	20	0.7%	2.74 [0.12 , 63.63]
Pozehl 2008	0	15	1	6	0.7%	0.15 [0.01 , 3.16]
Ricca-Mallada 2017	0	20	2	20	0.8%	0.20 [0.01 , 3.92]
Santa-Clara 2019	1	34	3	29	1.4%	0.28 [0.03 , 2.59]
Wall 2010	1	9	1	10	1.0%	1.11 [0.08 , 15.28]
Willenheimer 2001	3	27	2	27	2.4%	1.50 [0.27 , 8.28]
Witham 2005	1	41	3	41	1.4%	0.33 [0.04 , 3.07]
Yeh 2011	0	50	3	50	0.8%	0.14 [0.01 , 2.70]
Subtotal (95% CI)		**1293**		**1205**	**52.7%**	**0.70 [0.49 , 1.01]**
Total events:	46		69			
Heterogeneity: Tau² = 0.00; Chi² = 16.66, df = 26 (P = 0.92); I² = 0%						
Test for overall effect: Z = 1.89 (P = 0.06)						
1.1.2 Low ROB						
Austin 2005	5	100	4	100	4.2%	1.25 [0.35 , 4.52]
Dalal 2018	4	107	4	109	3.8%	1.02 [0.26 , 3.97]
DANREHAB 2008	4	45	3	46	3.4%	1.36 [0.32 , 5.75]
Du 2018	1	67	1	65	0.9%	0.97 [0.06 , 15.19]
Jolly 2009	7	84	5	85	5.7%	1.42 [0.47 , 4.29]
Kitzman 2021	21	174	16	173	18.5%	1.30 [0.71 , 2.41]
McKelvie 2002	9	90	8	91	8.5%	1.14 [0.46 , 2.82]
Witham 2012	3	53	2	54	2.3%	1.53 [0.27 , 8.78]
Subtotal (95% CI)		**720**		**723**	**47.3%**	**1.26 [0.86 , 1.85]**
Total events:	54		43			
Heterogeneity: Tau² = 0.00; Chi² = 0.29, df = 7 (P = 1.00); I² = 0%						
Test for overall effect: Z = 1.19 (P = 0.24)						
Total (95% CI)		**2013**		**1928**	**100.0%**	**0.93 [0.71 , 1.21]**
Total events:	100		112			
Heterogeneity: Tau² = 0.00; Chi² = 21.71, df = 34 (P = 0.95); I² = 0%						
Test for overall effect: Z = 0.56 (P = 0.58)						
Test for subgroup differences: Chi² = 4.68, df = 1 (P = 0.03), I² = 78.6%						



Analysis 1.1. (Continued)

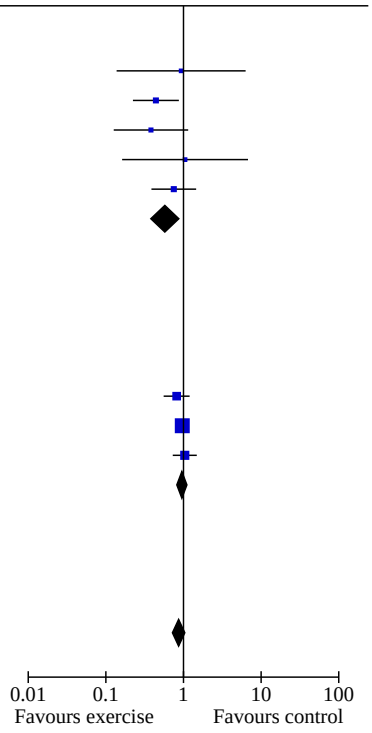
Test for overall effect: Z = 0.56 (P = 0.58)
Test for subgroup differences: Chi² = 4.68, df = 1 (P = 0.03), I² = 78.6%



Footnotes
(1) comprehensive rehabilitation (CBT and exercise)
(2) exercise alone

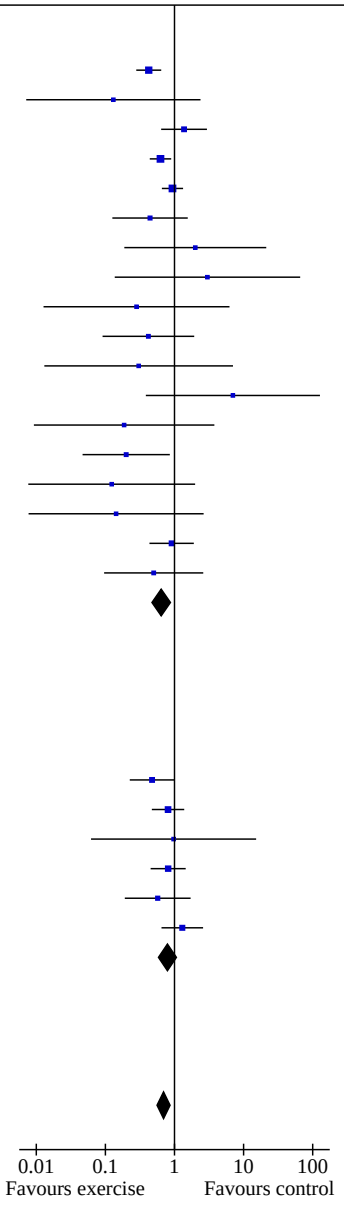
Analysis 1.2. Comparison 1: Exercise-based rehabilitation versus usual care, Outcome 2: All-cause mortality more than 12 months' follow-up

Study or Subgroup	Exercise Events	Exercise Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI
1.2.1 High ROB						
Andryukhin 2010	2	44	2	41	0.9%	0.93 [0.14 , 6.31]
Belardinelli 1999	9	50	20	49	6.6%	0.44 [0.22 , 0.87]
Belardinelli 2012	4	63	10	60	2.7%	0.38 [0.13 , 1.15]
Jónsdóttir 2006	2	21	2	22	1.0%	1.05 [0.16 , 6.77]
Mueller 2007	9	25	12	25	7.0%	0.75 [0.39 , 1.46]
Subtotal (95% CI)		**203**		**197**	**18.1%**	**0.57 [0.38 , 0.87]**
Total events:	26		46			
Heterogeneity: Tau² = 0.00; Chi² = 2.40, df = 4 (P = 0.66); I² = 0%						
Test for overall effect: Z = 2.62 (P = 0.009)						
1.2.2 Low ROB						
Austin 2005	31	100	38	100	17.6%	0.82 [0.56 , 1.20]
HF ACTION 2009	189	1159	198	1171	44.4%	0.96 [0.80 , 1.16]
TELEREH-HF 2020	54	425	52	425	19.8%	1.04 [0.73 , 1.48]
Subtotal (95% CI)		**1684**		**1696**	**81.9%**	**0.95 [0.82 , 1.11]**
Total events:	274		288			
Heterogeneity: Tau² = 0.00; Chi² = 0.87, df = 2 (P = 0.65); I² = 0%						
Test for overall effect: Z = 0.64 (P = 0.53)						
Total (95% CI)		**1887**		**1893**	**100.0%**	**0.87 [0.72 , 1.04]**
Total events:	300		334			
Heterogeneity: Tau² = 0.01; Chi² = 8.29, df = 7 (P = 0.31); I² = 16%						
Test for overall effect: Z = 1.55 (P = 0.12)						
Test for subgroup differences: Chi² = 5.04, df = 1 (P = 0.02), I² = 80.2%						



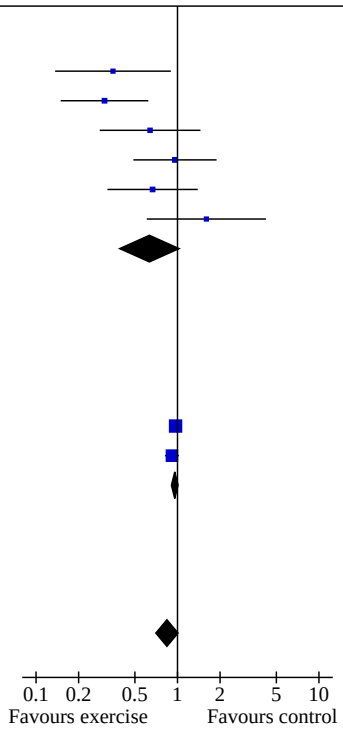
Analysis 1.3. Comparison 1: Exercise-based rehabilitation versus usual care, Outcome 3: Hospital admissions (all-cause) up to 12 months' follow-up

Study or Subgroup	Exercise Events	Exercise Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI
1.3.1 High ROB						
Antonicelli 2016	25	170	60	173	12.2%	0.42 [0.28 , 0.64]
Bocalini 2008	0	22	3	20	0.5%	0.13 [0.01 , 2.38]
Chen 2018	11	31	8	31	5.9%	1.38 [0.64 , 2.95]
Davidson 2010	23	53	36	52	13.9%	0.63 [0.44 , 0.90]
Dracup 2007	35	87	37	86	14.0%	0.94 [0.66 , 1.33]
Giallauria 2008	3	30	7	31	2.6%	0.44 [0.13 , 1.55]
Giannuzzi 2003	2	45	1	45	0.8%	2.00 [0.19 , 21.28]
Gielen 2003	1	10	0	10	0.5%	3.00 [0.14 , 65.90]
Hambrecht 1995	0	12	1	10	0.5%	0.28 [0.01 , 6.25]
Jónsdóttir 2006	2	21	5	22	1.8%	0.42 [0.09 , 1.93]
Keteyian 1996	0	21	1	19	0.5%	0.30 [0.01 , 7.02]
Mehani 2013	3	20	0	20	0.5%	7.00 [0.38 , 127.32]
Passino 2006	0	44	2	41	0.5%	0.19 [0.01 , 3.78]
Ryu 2018	2	20	5	10	2.0%	0.20 [0.05 , 0.86]
Ryu 2018	0	8	4	9	0.6%	0.12 [0.01 , 1.99]
Willenheimer 2001	0	27	3	27	0.5%	0.14 [0.01 , 2.64]
Witham 2005	10	41	11	41	6.2%	0.91 [0.43 , 1.90]
Yeh 2011	2	50	4	50	1.6%	0.50 [0.10 , 2.61]
Subtotal (95% CI)		**712**		**697**	**65.3%**	**0.64 [0.47 , 0.87]**
Total events:	119		188			
Heterogeneity: Tau² = 0.10; Chi² = 25.37, df = 17 (P = 0.09); I² = 33%						
Test for overall effect: Z = 2.82 (P = 0.005)						
1.3.2 Low ROB						
Austin 2005	9	100	19	100	6.2%	0.47 [0.23 , 1.00]
Dalal 2018	19	107	24	109	9.4%	0.81 [0.47 , 1.38]
Du 2018	1	67	1	65	0.6%	0.97 [0.06 , 15.19]
Jolly 2009	16	84	20	85	8.5%	0.81 [0.45 , 1.45]
Lang 2018	4	25	7	25	3.3%	0.57 [0.19 , 1.71]
Witham 2012	14	53	11	54	6.8%	1.30 [0.65 , 2.59]
Subtotal (95% CI)		**436**		**438**	**34.7%**	**0.79 [0.59 , 1.07]**
Total events:	63		82			
Heterogeneity: Tau² = 0.00; Chi² = 4.17, df = 5 (P = 0.53); I² = 0%						
Test for overall effect: Z = 1.54 (P = 0.12)						
Total (95% CI)		**1148**		**1135**	**100.0%**	**0.69 [0.56 , 0.86]**
Total events:	182		270			
Heterogeneity: Tau² = 0.06; Chi² = 30.29, df = 23 (P = 0.14); I² = 24%						
Test for overall effect: Z = 3.30 (P = 0.0010)						
Test for subgroup differences: Chi² = 0.90, df = 1 (P = 0.34), I² = 0%						



Analysis 1.4. Comparison 1: Exercise-based rehabilitation versus usual care, Outcome 4: Hospital admissions (all-cause) more than 12 months' follow-up

Study or Subgroup	Exercise Events	Exercise Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI
1.4.1 High ROB						
Belardinelli 1999	5	50	14	49	3.4%	0.35 [0.14 , 0.90]
Belardinelli 2012	8	63	25	60	5.5%	0.30 [0.15 , 0.62]
Cowie 2014 (1)	6	15	5	8	4.3%	0.64 [0.28 , 1.45]
Cowie 2014 (2)	9	15	5	8	6.0%	0.96 [0.49 , 1.89]
Jónsdóttir 2006	7	21	11	22	5.2%	0.67 [0.32 , 1.39]
Mueller 2007	8	25	5	25	3.2%	1.60 [0.61 , 4.22]
Subtotal (95% CI)		**189**		**172**	**27.7%**	**0.63 [0.39 , 1.03]**
Total events:	43		65			
Heterogeneity: Tau² = 0.20; Chi² = 11.01, df = 5 (P = 0.05); I² = 55%						
Test for overall effect: Z = 1.86 (P = 0.06)						
1.4.2 Low ROB						
HF ACTION 2009	729	1159	760	1171	38.0%	0.97 [0.91 , 1.03]
TELEREH-HF 2020	232	409	254	409	34.3%	0.91 [0.82 , 1.02]
Subtotal (95% CI)		**1568**		**1580**	**72.3%**	**0.96 [0.91 , 1.01]**
Total events:	961		1014			
Heterogeneity: Tau² = 0.00; Chi² = 0.81, df = 1 (P = 0.37); I² = 0%						
Test for overall effect: Z = 1.63 (P = 0.10)						
Total (95% CI)		**1757**		**1752**	**100.0%**	**0.84 [0.70 , 1.01]**
Total events:	1004		1079			
Heterogeneity: Tau² = 0.02; Chi² = 18.17, df = 7 (P = 0.01); I² = 61%						
Test for overall effect: Z = 1.87 (P = 0.06)						
Test for subgroup differences: Chi² = 2.77, df = 1 (P = 0.10), I² = 63.9%						



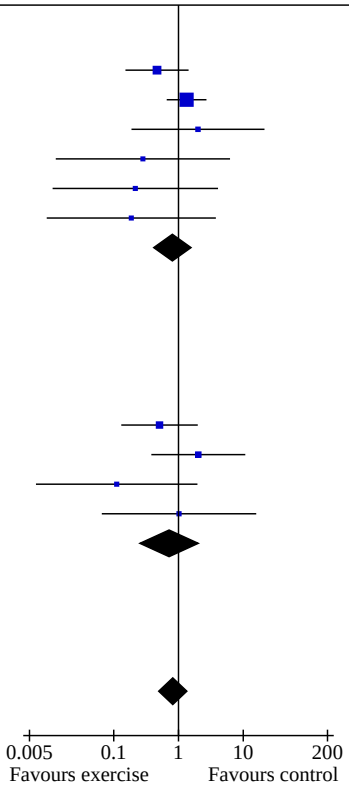
Footnotes

(1) centre (hospital) - based intervention

(2) home - based intervention

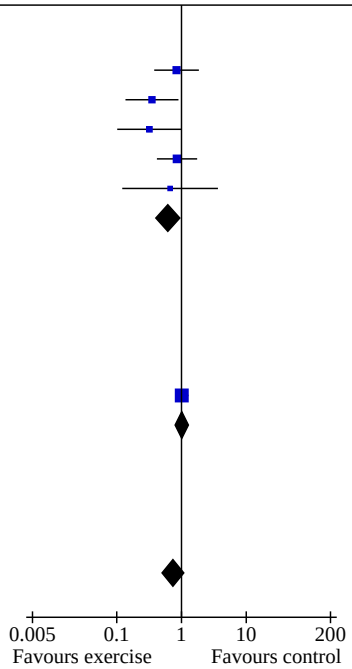
Analysis 1.5. Comparison 1: Exercise-based rehabilitation versus usual care, Outcome 5: Hospital admissions (heart failure only) up to 12 months' follow-up

Study or Subgroup	Exercise Events	Exercise Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI
1.5.1 High ROB						
Andryukhin 2010	4	44	8	41	18.3%	0.47 [0.15 , 1.43]
Chen 2018	12	31	9	31	41.4%	1.33 [0.66 , 2.70]
Giannuzzi 2003	2	45	1	45	4.4%	2.00 [0.19 , 21.28]
Hambrecht 1995	0	12	1	10	2.6%	0.28 [0.01 , 6.25]
Myers 2000	0	12	2	13	2.9%	0.22 [0.01 , 4.08]
Passino 2006	0	44	2	41	2.7%	0.19 [0.01 , 3.78]
Subtotal (95% CI)		**188**		**181**	**72.3%**	**0.80 [0.41 , 1.56]**
Total events:	18		23			
Heterogeneity: Tau² = 0.09; Chi² = 5.67, df = 5 (P = 0.34); I² = 12%						
Test for overall effect: Z = 0.64 (P = 0.52)						
1.5.2 Low ROB						
Dalal 2018	3	107	6	109	12.8%	0.51 [0.13 , 1.98]
Jolly 2009	4	84	2	85	8.6%	2.02 [0.38 , 10.75]
Lang 2018	0	25	4	25	3.0%	0.11 [0.01 , 1.96]
Witham 2012	1	53	1	54	3.3%	1.02 [0.07 , 15.87]
Subtotal (95% CI)		**269**		**273**	**27.7%**	**0.72 [0.25 , 2.02]**
Total events:	8		13			
Heterogeneity: Tau² = 0.16; Chi² = 3.48, df = 3 (P = 0.32); I² = 14%						
Test for overall effect: Z = 0.63 (P = 0.53)						
Total (95% CI)		**457**		**454**	**100.0%**	**0.82 [0.49 , 1.35]**
Total events:	26		36			
Heterogeneity: Tau² = 0.03; Chi² = 9.35, df = 9 (P = 0.41); I² = 4%						
Test for overall effect: Z = 0.80 (P = 0.43)						
Test for subgroup differences: Chi² = 0.03, df = 1 (P = 0.85), I² = 0%						



Analysis 1.6. Comparison 1: Exercise-based rehabilitation versus usual care, Outcome 6: Hospital admissions (heart failure only) more than 12 months' follow-up

Study or Subgroup	Exercise Events	Exercise Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI
1.6.1 High ROB						
Andryukhin 2010	9	44	10	41	15.7%	0.84 [0.38 , 1.85]
Belardinelli 1999	5	50	14	49	12.4%	0.35 [0.14 , 0.90]
Cowie 2014 (1)	3	15	5	8	9.1%	0.32 [0.10 , 1.01]
Cowie 2014 (2)	8	15	5	8	18.0%	0.85 [0.42 , 1.75]
Mueller 2007	2	25	3	25	4.6%	0.67 [0.12 , 3.65]
Subtotal (95% CI)		**149**		**131**	**59.9%**	**0.61 [0.40 , 0.94]**
Total events:	27		37			
Heterogeneity: Tau² = 0.01; Chi² = 4.14, df = 4 (P = 0.39); I² = 3%						
Test for overall effect: Z = 2.24 (P = 0.03)						
1.6.2 Low ROB						
TELEREH-HF 2020	104	409	103	409	40.1%	1.01 [0.80 , 1.28]
Subtotal (95% CI)		**409**		**409**	**40.1%**	**1.01 [0.80 , 1.28]**
Total events:	104		103			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.08 (P = 0.94)						
Total (95% CI)		**558**		**540**	**100.0%**	**0.74 [0.50 , 1.08]**
Total events:	131		140			
Heterogeneity: Tau² = 0.08; Chi² = 8.09, df = 5 (P = 0.15); I² = 38%						
Test for overall effect: Z = 1.55 (P = 0.12)						
Test for subgroup differences: Chi² = 3.99, df = 1 (P = 0.05), I² = 75.0%						



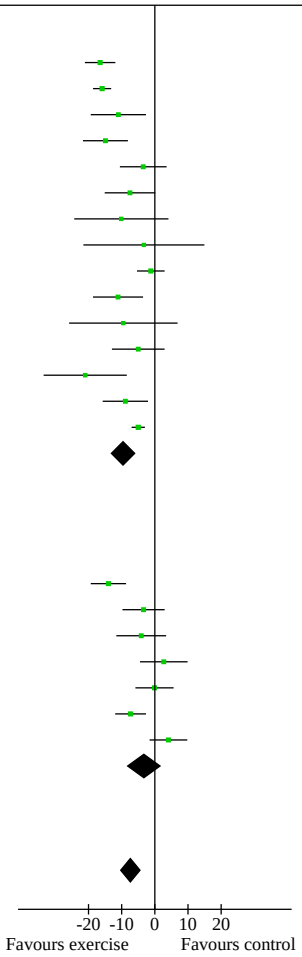
Footnotes

(1) centre (hospital) - based intervention

(2) home-based intervention

Analysis 1.7. Comparison 1: Exercise-based rehabilitation versus usual care, Outcome 7: Health-related quality of life (MLWHF) up to 12 months' follow-up

Study or Subgroup	Exercise Mean	Exercise SD	Exercise Total	Control Mean	Control SD	Control Total	Weight	Mean Difference IV, Random, 95% CI
1.7.1 High ROB								
Andryukhin 2010	44.5	8.9	40	61	11.1	35	5.6%	-16.50 [-21.10 , -11.90]
Antonicelli 2016	28.6	12.3	150	44.5	12.3	163	6.1%	-15.90 [-18.63 , -13.17]
Belardinelli 1999	40	19	48	51	22	46	4.2%	-11.00 [-19.33 , -2.67]
Chen 2018	19.4	12.2	31	34.3	14.4	29	4.8%	-14.90 [-21.68 , -8.12]
Davidson 2010	52.9	15.7	50	56.4	18.3	42	4.7%	-3.50 [-10.54 , 3.54]
Dracup 2007	35.7	23.7	86	43.2	27.3	87	4.5%	-7.50 [-15.12 , 0.12]
Gary 2010 (1)	24.2	16.3	15	34.3	23.6	16	2.5%	-10.10 [-24.30 , 4.10]
Gary 2010 (2)	25.6	19.7	17	28.9	29.9	14	1.8%	-3.30 [-21.55 , 14.95]
Jaarsma 2020	29.96	21.43	228	31.18	23.46	220	5.7%	-1.22 [-5.39 , 2.95]
Koukouvou 2004	34.1	13	16	45.2	9	19	4.5%	-11.10 [-18.65 , -3.55]
Lang 2018	29.2	25.8	22	38.7	30.1	23	2.1%	-9.50 [-25.86 , 6.86]
Nilsson 2008	23	14	35	28	20	37	4.4%	-5.00 [-12.94 , 2.94]
Passino 2006	32	26.5	44	53	32	41	2.9%	-21.00 [-33.54 , -8.46]
Wang 2021	25.36	18.2	49	34.25	16.25	49	4.8%	-8.89 [-15.72 , -2.06]
Yeh 2011	13	4	50	18	6	50	6.3%	-5.00 [-7.00 , -3.00]
Subtotal (95% CI)			**881**			**871**	**64.8%**	**-9.59 [-13.11 , -6.08]**
Heterogeneity: Tau² = 31.63; Chi² = 74.34, df = 14 (P < 0.00001); I² = 81%								
Test for overall effect: Z = 5.35 (P < 0.00001)								
1.7.2 Low ROB								
Austin 2005	22.9	14.7	85	36.9	21.3	94	5.3%	-14.00 [-19.32 , -8.68]
Dalal 2018	24.1	20.9	92	27.5	23.2	93	4.9%	-3.40 [-9.76 , 2.96]
Du 2018	36.9	21.59	67	41	22.4	65	4.5%	-4.10 [-11.61 , 3.41]
Jolly 2009	37.6	21	77	34.9	24.8	80	4.6%	2.70 [-4.48 , 9.88]
McKelvie 2002	-3.4	18.1	57	-3.3	13.9	67	5.1%	-0.10 [-5.86 , 5.66]
Peng 2018	42.32	8.83	42	49.63	12.39	41	5.5%	-7.31 [-11.95 , -2.67]
Witham 2012	15.4	14.8	43	11.3	12.1	44	5.2%	4.10 [-1.59 , 9.79]
Subtotal (95% CI)			**463**			**484**	**35.2%**	**-3.32 [-8.20 , 1.57]**
Heterogeneity: Tau² = 33.87; Chi² = 28.46, df = 6 (P < 0.0001); I² = 79%								
Test for overall effect: Z = 1.33 (P = 0.18)								
Total (95% CI)			**1344**			**1355**	**100.0%**	**-7.39 [-10.30 , -4.47]**
Heterogeneity: Tau² = 34.27; Chi² = 116.79, df = 21 (P < 0.00001); I² = 82%								
Test for overall effect: Z = 4.97 (P < 0.00001)								
Test for subgroup differences: Chi² = 4.18, df = 1 (P = 0.04), I² = 76.1%								



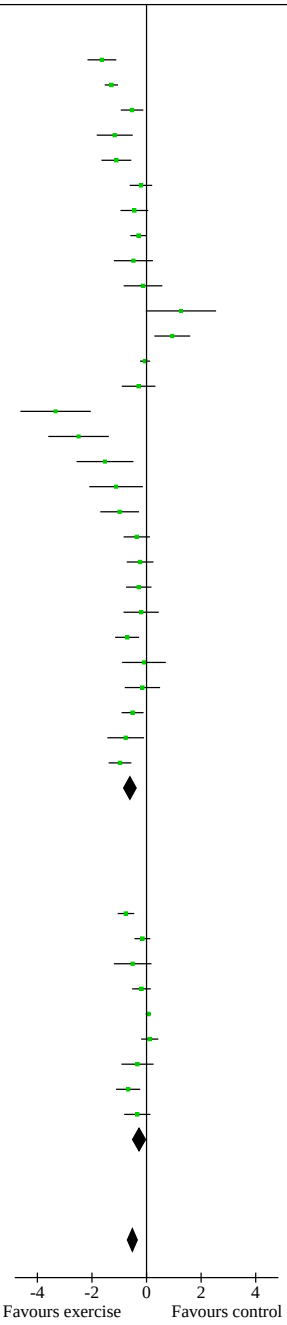
Footnotes

(1) comprehensive rehabilitation (CBT and exercise)

(2) exercise alone

Analysis 1.8. Comparison 1: Exercise-based rehabilitation versus usual care, Outcome 8: Health-related quality of life (all scales) up to 12 months' follow-up

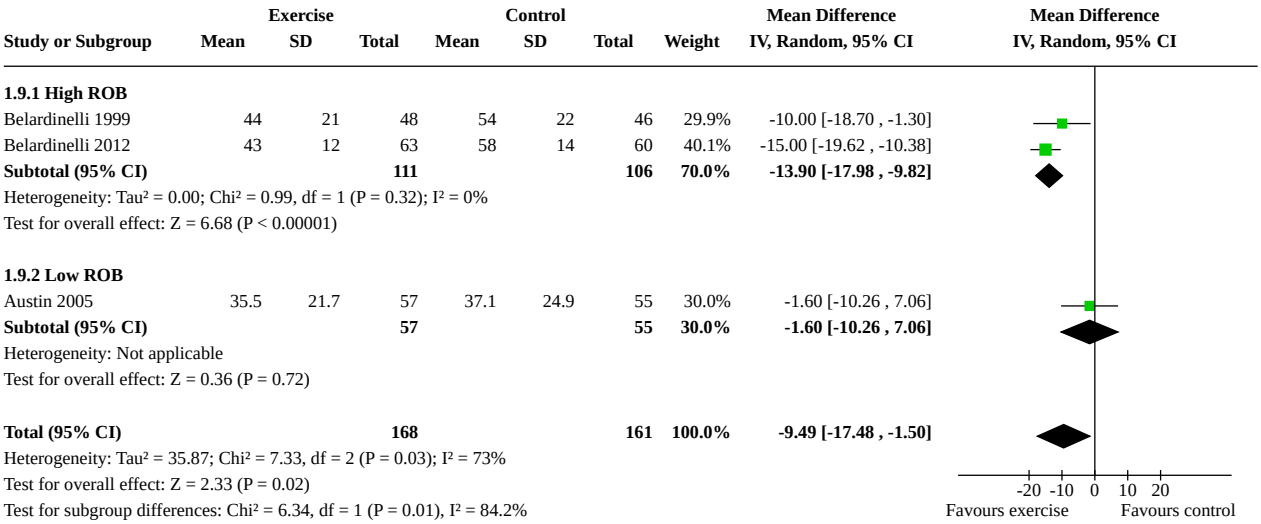
Study or Subgroup	Exercise Mean	Exercise SD	Exercise Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI
1.8.1 High ROB								
Andryukhin 2010	44.5	8.9	40	61	11.1	35	2.7%	-1.64 [-2.16 , -1.11]
Antonicelli 2016	28.6	12.3	150	44.5	12.3	163	3.3%	-1.29 [-1.53 , -1.05]
Belardinelli 1999	40	19	48	51	22	46	3.0%	-0.53 [-0.94 , -0.12]
Bocalini 2008	-87	4	22	-81	6	20	2.4%	-1.17 [-1.83 , -0.51]
Chen 2018	19.4	12.2	31	34.3	14.4	29	2.7%	-1.11 [-1.65 , -0.56]
Davidson 2010	52.9	15.7	50	56.4	18.3	42	3.0%	-0.20 [-0.62 , 0.21]
Dehkordi 2015	-63.34	12.69	30	-58.43	8.67	31	2.8%	-0.45 [-0.96 , 0.06]
Dracup 2007	35.7	23.7	86	43.2	27.3	87	3.2%	-0.29 [-0.59 , 0.01]
Gary 2010 (1)	24.2	16.3	15	34.3	23.6	16	2.3%	-0.48 [-1.20 , 0.23]
Gary 2010 (2)	25.6	19.7	17	28.9	29.9	14	2.3%	-0.13 [-0.84 , 0.58]
Hasanpour-Dehkordi 2020	57.96	5.65	6	50.45	5.34	6	1.3%	1.26 [-0.03 , 2.55]
Hasanpour-Dehkordi 2020	54.65	6	20	48.68	6.41	20	2.4%	0.94 [0.29 , 1.60]
Jaarsma 2020	29.96	21.43	228	31.18	23.46	220	3.4%	-0.05 [-0.24 , 0.13]
Jónsdóttir 2006	-47.55	8.7	21	-44.1	14.04	20	2.5%	-0.29 [-0.91 , 0.32]
Kaltsatou 2014 (3)	-6.5	2.4	18	0.8	1.2	8	1.3%	-3.33 [-4.62 , -2.04]
Kaltsatou 2014 (4)	-5.7	3	16	0.8	1.2	9	1.5%	-2.49 [-3.60 , -1.38]
Klocek 2005 (5)	-109	23.5	14	-71.7	23.5	7	1.6%	-1.52 [-2.57 , -0.48]
Klocek 2005 (6)	-99	23.5	14	-71.7	23.5	7	1.7%	-1.12 [-2.10 , -0.13]
Koukouvou 2004	34.1	13	16	45.2	9	19	2.3%	-0.99 [-1.69 , -0.28]
Mueller 2021	-80	21	47	-72	24	26	2.8%	-0.36 [-0.84 , 0.12]
Mueller 2021	-77	19	45	-72	24	25	2.8%	-0.24 [-0.73 , 0.25]
Nilsson 2008	23	14	35	28	20	37	2.9%	-0.29 [-0.75 , 0.18]
Norman 2012	-81	18.2	19	-77.9	11.6	18	2.5%	-0.20 [-0.84 , 0.45]
Passino 2006	32	26.5	44	53	32	41	2.9%	-0.71 [-1.15 , -0.27]
Reeves 2017	-65	19	12	-63	22	12	2.1%	-0.09 [-0.89 , 0.71]
Santa-Clara 2019	-1.9	0.45	20	-1.8	0.82	17	2.4%	-0.15 [-0.80 , 0.50]
Wang 2021	25.36	18.2	49	34.25	16.25	49	3.0%	-0.51 [-0.91 , -0.11]
Willenheimer 2001	-0.7	0.8	20	0	1	17	2.4%	-0.76 [-1.44 , -0.09]
Yeh 2011	13	4	50	18	6	50	3.0%	-0.97 [-1.39 , -0.56]
Subtotal (95% CI)			**1183**			**1091**	**72.9%**	**-0.61 [-0.84 , -0.38]**
Heterogeneity: Tau² = 0.30; Chi² = 169.24, df = 28 (P < 0.00001); I² = 83%								
Test for overall effect: Z = 5.20 (P < 0.00001)								
1.8.2 Low ROB								
Austin 2005	22.9	14.7	85	36.9	21.3	94	3.2%	-0.76 [-1.06 , -0.45]
Dalal 2018	24.1	20.9	92	27.5	23.2	93	3.3%	-0.15 [-0.44 , 0.14]
DANREHAB 2008	-42.7	9.1	19	-37.4	11.4	15	2.4%	-0.51 [-1.20 , 0.18]
Du 2018	36.9	21.59	67	41	22.4	65	3.2%	-0.19 [-0.53 , 0.16]
HF ACTION 2009	72.8	20.4	828	71.4	21.3	784	3.5%	0.07 [-0.03 , 0.16]
Jolly 2009	37.6	21	77	34.9	24.8	80	3.2%	0.12 [-0.20 , 0.43]
Lang 2018	29.2	25.8	22	38.7	30.1	23	2.6%	-0.33 [-0.92 , 0.26]
Peng 2018	42.32	8.83	42	49.63	12.39	41	2.9%	-0.67 [-1.12 , -0.23]
Witham 2005	-69	13	36	-65	10	32	2.8%	-0.34 [-0.82 , 0.14]
Subtotal (95% CI)			**1268**			**1227**	**27.1%**	**-0.28 [-0.51 , -0.04]**
Heterogeneity: Tau² = 0.09; Chi² = 39.87, df = 8 (P < 0.00001); I² = 80%								
Test for overall effect: Z = 2.27 (P = 0.02)								
Total (95% CI)			**2451**			**2318**	**100.0%**	**-0.52 [-0.70 , -0.34]**
Heterogeneity: Tau² = 0.24; Chi² = 269.51, df = 37 (P < 0.00001); I² = 86%								
Test for overall effect: Z = 5.63 (P < 0.00001)								
Test for subgroup differences: Chi² = 3.95, df = 1 (P = 0.05), I² = 74.7%								



Footnotes

(1) comprehensive (CBT and exercise)
(2) exercise alone
(3) dance
(4) formal exercise
(5) constant exercise
(6) progressive exercise

Analysis 1.9. Comparison 1: Exercise-based rehabilitation versus usual care, Outcome 9: Health-related quality of life (MLWHF) more than 12 months' follow-up



ADDITIONAL TABLES

Table 1. Health-related quality of life (HRQoL)

Study	Follow-up	Measure	Outcome values (or change from baseline) at follow-up Control vs ExCR (Mean (SD)); between-group P value	Between-group difference
Andryukhin 2010	6 months	MLWHF Total	61 (11.1) vs 44.5 (8.9); P < 0.001[a]	ExCR > control
		MLWHF Emotional	6 (3) vs 13 (3.7); P < 0.001[a]	ExCR > control
		MLWHF Physical	26 (5.2) vs 18 (4.4); P < 0.001[a]	ExCR > control
Antonicelli 2016	6 months	MLWHF Total	44.5 (12.3) vs 28.6 (12.3); P < 0.001	ExCR > control
Austin 2005	6 months	MLWHF Physical	20.4 (12.2) vs 12.6 (9.7); P < 0.0001[a]	ExCR > control
		MLWHF Emotional	8.0 (7.1) vs 4.4 (10.4); P < 0.01[a]	ExCR > control
		MLWHF Total	36.9 (24.0) vs 22.9 (17.8); P < 0.001[a]	ExCR > control
		EQ-5D	0.58 (0.19) vs 0.70 (0.16); P < 0.0001[a]	ExCR > control
	5 years	MLWHF Physical	19.3 (23.5) vs 18.3 (11.2); P = 0.66[a]	ExCR = control
		MLWHF Emotional	7.6 (7.1) vs 7.4 (6.5); P = 0.88[a]	ExCR = control
		MLWHF Total	37.1 (24.9) vs 35.5 (21.7); P = 0.72[a]	ExCR = control
		EQ-5D	0.58 (0.22) vs 0.64 (0.19); P = 0.12[a]	ExCR = control
Belardinelli 1999	2 months	MLWHF Total	52 (29) vs 40 (19); P < 0.001	ExCR > control
	15 months		52 (20) vs 39 (20); P < 0.001	ExCR > control

Table 1. Health-related quality of life (HRQoL) *(Continued)*

	29 months		54 (22) vs 44 (21); P < 0.001	ExCR > control
Belardinelli 2012	10 years	MWLHF Total	58 (14) vs 43 (12); P < 0.001	ExCR > control
Bocalini 2008	6 months	WHOQoL	2 (1) vs 23 (4); P < 0.0001[a]	ExCR > control
		Physical	1 (1) vs 20 (2); P < 0.0001[a]	ExCR > control
		Psychological	3 (2) vs 16 (1); P < 0.0001[a]	ExCR > control
		Social	2 (1) vs 15 (2); P < 0.0001[a]	ExCR > control
		Environmental		
Chen 2018	6 months	Physical (SPPB)	8.9 (2.3) vs 10.0 (2.1); P = 0.059	ExCR = control
		MLWHF Total	34.3 (14.4) vs 19.4 (12.2); P < 0.001	ExCR > control
Dalal 2018	12 months	MLWHF Total	27.5 (23.2) vs 24.1 (20.9); P = 0.025	ExCR > control
		Physical	14.5 (11.8) vs 12.2 (10.8); P = 0.016	ExCR > control
		Emotional	5.5 (6.4) vs 5.1 (5.8); P = 0.273	ExCR = control
		Heart QoL Global	1.9 (0.9) vs 1.9 (0.9); P = 0.823	ExCR = control
		Heart QoL Physical	1.7 (0.9) vs 1.8 (0.9); P = 0.869	ExCR = control
		Heart QoL Emotional	2.3 (0.8) vs 2.3 (0.8); P = 0.683	ExCR = control
		EQ-5D-3L	0.739 (0.263) vs 0.752 (0.240); P = 0.487	ExCR = control
DANREHAB 2008	12 months	SF-36 PCS	37.4 (11.4) vs 42.7 (9.1)[a]; P = 0.14	ExCR = control
		SF-36MCS	50.5 (10.0) vs 49.7 (8.8)[a]; P = 0.81	ExCR = control
Davidson 2010	12 months	MLWHF Total	56.4 (18.3) vs 52.9 (15.7); P = 0.33	ExCR = control
Dracup 2007	6 months	MLWHF Physical	19.4 (11.5) vs 16.1 (10.0); P = 0.04[a]	ExCR > control
		MLWHF Emotional	10.5 (7.4) vs 7.8 (6.6); P = 0.01[a]	ExCR > control
		MLWHF Total	43.2 (26.5) vs 35.7 (23.7); P = 0.05	ExCR > control
Du 2018	6 months	MLWHF Total	41 (22.4) vs 36.9 (21.59); P = 0.535	ExCR = control
		SF-36	54.5 (25.31) vs 53.9 (22.78); P = 0.697	ExCR = control
Gary 2010 **Comp**	6 months	MLWHF Total	34.3 (23.6) vs 24.2 (16.3); P = 0.18[a]	ExCR = control
Gary 2010 **Exer**	6 months	MLWHF Total	28.9 (29.9) vs 25.6 (19.7); P = 0.71[a]	ExCR = control
Dehkordi 2015	6 months	MacNew	58.43 (8.67) vs 63.34 (12.69); P < 0.05	ExCR > control
Hasan-pour-Dehkordi 2020 **CHF II**	6 months	SF-36 Physical functioning	52.65 (5.72) vs 56.76 (4.89); P = 0.205[a]	ExCR = control
		SF-36 Role-physical	49.32 (4.65) vs 55.66 (5.12); P = 0.051[a]	ExCR = control
		SF-36 Bodily	67.35 (6.12) vs 63.44 (5.47); P = 0.273[a]	ExCR = control
		SF-36 General	57.34 (3.76) vs 66.36 (7.89); P = 0.039[a]	ExCR = control
			51.35 (3.66) vs 63.71 (7.67); P = 0.009[a]	ExCR > control
			66.34 (6.45) vs 74.39 (4.54); P = 0.037[a]	ExCR > control
			52.34 (3.44) vs 58.43 (8.45); P = 0.153[a]	ExCR > control

Table 1. Health-related quality of life (HRQoL) *(Continued)*

		SF-36 Energy	55.55 (5.58) vs 67.33 (5.66); P < 0.005[a]	ExCR > control
		SF-36 Social functioning	6.45 (1.4) vs 2.1 (1.21); P < 0.000[a]	ExCR > control
		SF-36 Role-emotional	50.45 (5.34) vs 57.96 (5.65); P0.042[a]	ExCR = control
		SF-36 Mental		ExCR > control
		SF-36 Fatigue		ExCR < control
		SF-36 Total		ExCR > control
Hasanpour-Dehkordi 2020 **CHF III**	6 months	SF-36 Physical functioning	43.43 (4.66) vs 52.34 (3.43); P < 0.000[a]	ExCR > control
		SF-36 Role-physical	47.34 (4.98) vs 52.32 (7.45); P = 0.018[a]	ExCR > control
		SF-36 Bodily	67.34 (4.29) vs 58.87 (6.99); P < 0.000[a]	ExCR < control
		SF-36 General	52.47 (7.34) vs 61.44 (4.35); P < 0.000[a]	ExCR > control
		SF-36 Energy	45.89 (4.66) vs 56.34 (8.84); P < 0.000[a]	ExCR > control
		SF-36 Social functioning	60.56 (7.34) vs 68.11 (6.76); P = 0.002[a]	ExCR > control
		SF-36 Role-emotional	49.44 (4.51) vs 54.98 (7.61); P = 0.009[a]	ExCR > control
		SF-36 Mental	55.89 (5.66) vs 66.78 (7.56); P < 0.000[a]	ExCR < control
		SF-36 Fatigue	7.87 (2.12) vs 2.7 (1.3); P < 0.000[a]	ExCR > control
		SF-36 Total	48.68 (6.41) vs 54.65 (6.0); P = 0.004[a]	
Gottlieb 1999	6 months	MLWHF Total	NR (NR) vs 22 (20); NR	NR
		MOS PF	NR (NR) vs 68 (28); NR	NR
		MOS RL	NR (NR) vs 50 (42); NR	NR
		MOS GH	NR (NR) vs 361 (224); NR	NR
HF ACTION 2009	12 months	KCCQ[b]	71.4 (21.3) vs 72.8 (20.4)	ExCR > control[c]
Jaarsma 2020	6 months	MLWHF Total	28.9567 (20.75924) vs 29.5789 (21.84543); P = 0.755[a]	ExCR = control
		MLWHF Physical	29.9605 (21.42959) vs 31.1773(23.46338); P = 0.567[a]	ExCR = control
		MLWHF Emotional	12.0087 (9.28767) vs 12.4211(9.63053); P = 0.641[a]	ExCR = control
	12 months	MLWHF Total	13.3333(9.76704) vs 13.9773 (10.38415); P = 0.500[a]	ExCR = control
		MLWHF Physical	5.961 (5.72965) vs 6.1754 (6.45724); P = 0.707[a]	ExCR = control
		MLWHF Emotional	6.4693 (6.23716) vs 6.5864 (6.50513); P = 0.846[a]	ExCR = control
Jolly 2009	6 months	MLWHF Total	34.5 (24.0) vs 36.3 (24.1); P = 0.30	ExCR = control

Table 1. Health-related quality of life (HRQoL) *(Continued)*

		EQ-5D	0.62 (0.32) vs 0.66 (0.24); P = 0.004	ExCR > control
	12 months	MLWHF Total	34.9 (24.8) vs 37.6 (21.0); P = 0.80	ExCR = control
		EQ-5D	0.69 (0.28) vs 0.68 (0.21); P = 0.07	ExCR = control
Jónsdóttir 2006	6 months	Icelandic quality of life questionnaire	4.10 (14.04) vs 47.55 (8.7); P = 0.34	ExCR = control
Kaltsatou 2014 **(Dance)**	8 months	SF-36 (physical)[b]	−0.6 (0.9) vs 3.3 (1.6); P < 0.05	ExCR > control
		SF-36 (mental)[b]	−0.2 (0.5) vs 3.1 (1.3); P < 0.05	ExCR > control
		SF-36 (total)[b]	−0.8 (1.2) vs 6.5 (2.4); P < 0.05	ExCR > control
Kaltsatou 2014 **(ExCR)**	8 months	SF-36 (physical)[b]	−0.6 (0.9) vs 2.9 (1.5); P < 0.05	ExCR > control
		SF-36 (mental)[b]	−0.2 (0.5) vs 2.7 (2.2); P < 0.05	ExCR > control
		SF-36 (Total)[b]	−0.8 (1.2) vs 5.7 (3.0); P < 0.05	ExCR > control
Klocek 2005 **(Const or Prog)**	6.5 months	PGWB total	99.0 vs 109.0 (training grp A) vs 71.7 (training grp B); P < 0.01	ExCR > control
Koukouvou 2004	6 months	MLWHF total	34.1 (13.0) vs 45.1 (9.9); P = 0.05[a]	ExCR > control
		Spritzer QLI total	7.1 (1.1) vs 9.1 (1.1); P < 0.0001[a]	ExCR > control
Lang 2018	6 months	MLWHF total	29.2 (25.8) vs 38.7 (30.1); P > 0.05	ExCR = control
		Heart-QoL	2.0 (1.0) vs 1.9 (1.0); P > 0.05	ExCR = control
		EQ-5D-5L	0.65 (0.31) vs 0.55 (0.29); P > 0.05	ExCR = control
Lugo 2018	6 months	SF-36 Body pain	8.05 (−3.77 to 19.87)	ExCR = control
		SF-36 Change of health	−7.98 (−18.8 to 2.92)	ExCR = control
		SF-36 Emotional wellbeing	3.56 (−11.22 to 18.34)	ExCR = control
		SF-36 Physical well-being	8.68 (−8.31 to 25.66)	ExCR = control
		SF-36 Physical function	4.65 (−4.54 to 13.84)	ExCR = control
		SF-36 Social function	1.89 (−6.46 to 10.26)	ExCR = control
		SF-36 Mental health	−4.62 (−14.94 to 5.69)	ExCR = control
		SF-36 Vitality	−3.02 (−13.94 to 7.89)	ExCR = control
		SF-36 General health	4.41 (−7.48 to 16.3)	ExCR = control
McKelvie 2002	12 months	MLWHF total[b]	−3.3 (13.9) vs −3.4 (18.1); P = 0.98	ExCR = control
Mueller 2021 **HIIT**	12 months	KCCQ Total	1.0 (−7.2 to 9.2)	ExCR = control
			−2 (−9 to 5)	ExCR = control

Table 1. Health-related quality of life (HRQoL) *(Continued)*

		KCCQ Physical limitation	10 (2 to 19)	ExCR > control
		KCCQ Symptom stability	0 (−7 to 7)	ExCR = control
		KCCQ Symptom frequency	1 (−7 to 8)	ExCR = control
		KCCQ Symptom burden	0 (−6 to 7)	ExCR = control
		KCCQ Total symptom	8 (−2 to 19)	ExCR = control
		KCCQ Self-efficacy	4 (−3 to 12)	ExCR = control
		KCCQ QOL	0 (−9 to 9)	ExCR = control
		KCCQ Social limitation	0 (−5 to 6)	ExCR = control
		KCCQ Overall summary	−1 (−7 to 5)	ExCR = control
		KCCQ Clinical summary		
Mueller 2021 **MCT**	12 months	KCCQ Total	1.0 (−7.2 to 9.2)	ExCR = control
		KCCQ Physical limitation	2 (−5 to 9)	ExCR = control
		KCCQ Symptom stability	10 (0 to 20)	ExCR = control
		KCCQ Symptom frequency	1 (−6 to 9)	ExCR = control
		KCCQ Symptom burden	7 (0 to 20)	ExCR = control
		KCCQ Total symptom	4 (−2 to 11)	ExCR = control
		KCCQ Self-efficacy	8 (−2 to 17)	ExCR = control
		KCCQ QOL	11 (2 to 19)	ExCR > control
		KCCQ Social limitation	2 (−8 to 11)	ExCR = control
		KCCQ Overall summary	4 (−2 to 11)	ExCR = control
		KCCQ Clinical summary	3 (−3 to 9)	ExCR = control
Nilsson 2008	12 months	MLWHF Total	28 (20) vs 22 (12); P = 0.003	ExCR > control
Norman 2012	6 months	KCCQ	77.9 (11.6) vs 81.0 (18.2); P = 0.78	ExCR = control
Passino 2006	9.75 months	MLWHF Total	53 (32) vs 32 (26.5); P < 0.0001[a]	ExCR > control
Peng 2018	6 months	MLWHF Total	42.32 (8.83) vs 49.63 (12.39); P <0.01	ExCR > control

Table 1. Health-related quality of life (HRQoL) *(Continued)*

Santa-Clara 2019	6 months	HeartQoL	1.9 (0.45) vs 1.8 (0.82); P = 0.879	ExCR = control
Wang 2021	6 months	MLWHF	25.36 (18.2) vs 34.25 (16.25); P = 0.012	ExCR = control
Willenheimer 2001	10 months	PGAQoL	0 (1) vs 0.7 (0.9); P = 0.023	ExCR > control
Witham 2005	6 months	GCHFQ	69 (13) vs 65 (10); P = 0.48	ExCR = control
Witham 2012[d]	6 months	MLWHF Total	15.4 (14.8) vs 11.3 (12.1); P > 0.05	ExCR = control
Yeh 2011	12 months	MLWHF Total	18 (6) vs 13 (4); P < 0.0001	ExCR > control

ExCR = control: no statistically significant difference (P > 0.05) in HRQoL between exercise and control groups at follow-up.

ExCR > control: statistically significant (P ≤ 0.05) higher HRQoL in exercise group compared to control group at follow-up.

ExCR < control: statistically significant (P ≤ 0.05) lower HRQoL in exercise group versus control group at follow-up.

EQ-5D: EuroQoL Group Quality of Life Questionnaire based on 5 dimensions; **EQ-5D-3L:** EuroQoL Group Quality of Life Questionnaire based on 3-level scale; **ExCR:** exercise for cardiac rehabilitation; **GCHFQ:** Guyatt Chronic Heart Failure Questionnaire; **GH:** general health; **KCCQ:** Kansas City Cardiomyopathy Questionnaire; **MacNew:** MacNew Heart Disease Health-Related Quality of Life questionnaire; **MCS:** Mental Component Score; **MLWHF:** Minnesota Living With Heart Failure questionnaire; **MOS:** Medical Survey Outcome; **NR:** not reported; **PCS:** Physical Component Score; **PF:** Physical functioning; **PGAQoL:** Patient's Global Assessment of Quality of Life; **PGWB:** Psychological General Well-Being index; **QLI**: quality of life index; **QoL:** quality of life; **RL:** role limitation; **SF-36:** Short Form-36; **SPPB:** Short Physical Performance Battery; **WHOQoL**: World Health Organization Quality of Life questionnaire

[a]P values: calculated by the review authors.
[b]Change in outcome from baseline.
[c]We have calculated the between P value for this trial based on individual participant data.
[d]Data obtained from study authors.

Table 2. Costs and cost-effectiveness

Study	Georgiou 2001	HF ACTION 2009	Witham 2012	Cowie 2014 (centre and home)	Dalal 2018	Lang 2018	Dalal 2021
Year of costs	1998	2008	2010	2013/2014	2016	2016	2015
Country	USA	USA	UK	UK	UK	UK	UK
Currency	USD	USD	GBP	GBP	GBP	GBP	GBP
Intervention cost							
Mean costs/patient	4563	6483 (SD 4884)	474.75	Not reported	418.39	362.61	418
Costs considered	Staffing, space rental, equipment, patients' lost wages	Staffing, patient time, travel, parking	Staffing, equipment, staff and patient travel	Staffing, equipment, consumables* (*home training only)	Primary and secondary care, social care, drugs, NHS and intervention costs	Staffing, equipment, staff travel	?
Cost-effectiveness							
Follow-up period	15.5 years	Mean 2.5 years	6 months	5 years	NR	NR	38 months
Total mean healthcare cost/patient (exercise)	5282*	57,338 (SD 81,343)+	1888.24 (SD 3111)	221.58 (hospital) and 196.53 (home)	NR	NR	15,452
Total mean healthcare costs per patient (control)	2055*	56,177 (SD 92,749)+	1943.93 (SD 4551)	Not calculated	NR	NR	15,051
Incremental healthcare costs	3227*	1161 (95% CI −6205 to 8404)	−447.85 (95% CI −1696.00 to 931.00)	NR	NR	NR	400
Additional healthcare costs considered	Hospitalisations	Medication, procedures, outpatient visits, emergency visits, hospitalisations, tests	Inpatient and outpatient admissions, primary care contacts, medication	NR	NR	NR	NR

Table 2. Costs and cost-effectiveness *(Continued)*

Mean healthcare benefit (exercise)	10.24 life-years	2.02 QALYs (SD 1.00)	NR	NR	0.74 QALYs (SD 0.22)	NR	4.24 QUALYs
Mean healthcare benefit (control)	7.96 life-years	1.99 QALYs (SD 1.01)	NR	NR	0.76 QALYs (SD 0.21)	NR	4.47 QUALYs
Incremental mean healthcare benefit	1.82 life-years	0.03 (95% CI −0.06 to 0.11)	NR	NR	NR	NR	0.23 QUALYs
Incremental cost-effectiveness ratio	1773 per life-year saved	NR	NR	NR	NR	NR	GBP 1721 per QALY

CI: confidence interval; **GBP:** GB Pounds; **NR:** not reported; **QALY:** quality-adjusted life year; **SD:** standard deviation; **USD:** US Dollars

Table 3. Univariate meta-regression

	All-cause mortality P value	All-cause hospitalisations P value	HF-related hospitalisation P value	HRQoL (MLWHF only) P value	HRQoL (all scales) P value
Type of rehabilitation (exercise only vs comprehensive)	0.832	0.253	0.630	0.437	0.880
Type of exercise (aerobic training alone vs aerobic plus resistance training)	0.309	0.407	0.052	0.621	0.199
Exercise dose (number of weeks × number of sessions/week × average duration of session in hours)	0.102	0.218	0.496	0.702	0.551
Exercise setting (hospital only, home only, both hospital and home)	0.427	0.321	0.284	0.848	0.750
Single vs multi-centre	0.372	0.966	0.213	0.046	0.750
Publication date	0.453	0.364	0.043	0.846	0.756
Continent (North America vs. Europe vs. Other)	0.050	0.822	0.783	0.158	0.665
Risk of bias	0.050	0.240	0.070	0.030	0.080
Follow up (months)	0.698	0.097	0.770	0.128	0.747
Sample size	0.712	0.939	0.297	0.297	0.220

HRQoL: health-related quality of life; **MLWHF:** Minnesota Living With Heart Failure questionnaire

Table 4. Trial-level subgroup analysis

Study (report/year)	Outcome(s)	Subgroup(s)	Results (P value)	Data analysis methods	Predefined?
HF ACTION 2009 **(O'Connor 2009)**	Composite primary endpoint of all-cause mortality or hospitalisation, median follow-up 30 months	Age (≤ 70 years vs > 70 years), gender (male vs female), race (white vs non-white), HF aetiology (ischaemic vs non-ischaemic), baseline LVEF (≤ 25% vs > 25%), baseline NHYA (II vs III/IV), previous re-vascularisation, history of MI, on ACE or beta	"There was no significant interaction of exercise training with any of the factors defining these subgroups" (P > 0.05)	Interaction test on hazard ratio	Yes

Table 4. Trial-level subgroup analysis *(Continued)*

		blocker at baseline			
HF ACTION 2009 **(Flynn 2009)**	KCCQ) overall score up to 36 months	Age, LVEF (≤ 25% or > 25%), previous revascularisation (coronary artery bypass graft surgery or percutaneous coronary intervention, or no previous revascularisation), history of MI, and KCCQ overall summary score at baseline (0-50, 50-75, or 75-100)	No significant subgroup interactions (P > 0.05)	Interaction test	Yes
HF ACTION 2009 **(Keteyian 2012)**	All-cause mortality or hospitalisation and cardiovascular mortality or HF hospitalisation, median follow-up 28.2 months	Exercise volume defined as MET-h/week (i.e. product of exercise intensity (where 1 MET is 3.5 mL VO_2/kg/min) and hours of exercise/week)	Exercise volume was linear logarithmic predictor (P = 0.03) for all-cause mortality or hospitalisation. For cardiovascular mortality or HF hospitalisation, exercise volume was a significant (P < 0.001) linear and logarithmic predictor Moderate exercise volumes of 3-5 MET-hours and 5-7 MET-hours/week were associated with reductions in subsequent risk that exceeded 30%	Regression-based methods (based only on exercise group data)	Post hoc
HF ACTION 2009 **(Pina 2013)**	KCCQ	Haemoglobin	…interaction…by Hgb by exercise training were not significant for the overall summary scale (P = 0.65 for the jump of baseline to 3 months, P = 0.56 for the slope of 3 months to the end of the study). Results for KCCQ subscales were similar to results for the overall summary scale; none of the 3-way interaction terms were statistically significant.	Interaction test	Post hoc
HF ACTION 2009 **(Mentz 2013)**	Mortality/hospitalisation, mortality, and CV mortality/HF hospitalisation	COPD	No evidence to suggest an interaction between exercise training and COPD status for any of the clinical endpoints (all P < 0.15)	Interaction test	Post hoc
HF ACTION 2009 **(Mentz 2013)**	Mortality/hospitalisation, mortality, and CV mortality/HF hospitalisation/exercise capacity/HRQoL	Race (white/black/other)	No interaction between race and assignment to exercise training on clinical outcomes. However, there was evidence for an interaction between black race and exercise training for change in 6-MWD. No other exercise or health status variable demonstrated a statistically significant interaction with race and exercise training.	Interaction test	Post hoc

Table 4. Trial-level subgroup analysis *(Continued)*

HF ACTION 2009 **(Zeitler 2015)**	All-cause death or hospitalisation	Ventricular pacing status	Interaction tests for reduction in all-cause death and device type (P < 0.33) and reduction in CV death or CV hospitalisation (P < 0.19) did not meet statistical significance	Interaction test	Post hoc
HF ACTION 2009 **(Banks 2016)**	6-MWD and peak VO_2	DM	No evidence of an interaction between DM and exercise training on any clinical outcomes	Interaction test	Post hoc
HF ACTION 2009 **(Parikh 2016)**	KCCQ and exercise capacity	AP	Evidence of an interaction between baseline AP and exercise training and change in peak VO_2 (interaction P < 0.019) but not with change in HRQoL or change in 6MWD (interaction P > 0.1). Exercise training (vs usual care) was associated with greater peak VO_2 improvement in patients with AP (treatment effect + 1.25 mL/kg/min, 95% CI 0.64 to 1.85) than in patients without AP (treatment effect = 0.45 mL/kg/min, 95% CI 0.18 to 0.72)	Interaction test	Post hoc
HF ACTION 2009 **(Luo 2017)**	Mortality/hospitalisation, mortality, and CV mortality/HF hospitalisation/exercise capacity/HRQoL	AF	No significant interactions between baseline AF status and randomisation group for change in QoL and functional capacity from baseline to 3 months. No evidence of a differential effect of exercise training based on events and AF status (all interactions P > 0.10)	Interaction test	Post hoc
HF ACTION 2009 **(Verma 2017)**	Mortality/hospitalisation, mortality, and CV mortality/HF hospitalisation/exercise capacity/HRQoL	Having a partner, SES (education beyond high school, income USD25,000, and employed)	No interaction between any of the partner status or SES variables and exercise training for outcomes (all P > 0.5)	Interaction test	Post hoc
Dalal 2018	MLWHF, follow-up 12 months	Baseline NT-proBNP level, presence of caregiver, recruitment site, duration of HF	"We found no evidence of a significant subgroup treatment interaction on the primary outcome at 12 months by NT-pro-BNP level, presence of caregiver, recruitment site, or duration of HF"	Interaction test	Yes
TELEREH-HF 2020 **(Piotrowicz 2019)**	All-cause mortality at 26 months, all-cause hospitalisation at 26 months	Age, gender, NYHA class, Peak VO_2,	"There were no statistically significant differences on the percentage of days alive and out of the hospital, all-cause mortality, or all-cause hospitalizations in prespecified subgroups (age, sex, peak VO2, patients in NYHA classes I-II vs those in NYHA class III, and patients with vs without cieds [cardiac implantable electrical devices] with the exception of the effect of site. Interaction P values for the effect of a site were nonsignificant for all-cause mor-	Interaction test	Yes

Table 4. Trial-level subgroup analysis *(Continued)*

			tality and significant for all-cause hospitalisation"		
Jaarsma 2020	6MWD	Age, gender, NHYA class, HFrEF/HFpEF, depression. anxiety, NT-proBNP, grandchildren, comorbid stroke, comorbid diabetes, comorbid impairment	"There was no statistically significant interaction of the intervention with age, gender, NYHA classification, HFrEF/HFpEF, depression, anxiety, NT-proBNP, having grandchildren, comorbid diabetes and cognitive impairment. Only comorbid history of stroke showed a significant interaction with the treatment effect over time with the likelihood ratio test, showing that patients without a history of stroke improved more as a result of exergaming than patients who had a history of stroke."	Interaction test	Yes (predefined in protocol but other variables included retrospectively)

6MWD: 6-minute walking distance; **ACE:** angiotensin-converting enzyme; **AF:** atrial fibrillation; **AP:** angina pectoris; **CI:** confidence interval; **COPD:** chronic obstructive pulmonary disease; **CV:** cardiovascular; **DM:** diabetes mellitus; **HF:** heart failure; **HFpEF:** heart failure with preserved ejection fraction; **HFrEF:** heart failure with reduced ejection fraction; **HRQoL:** health-related quality of life; **KCCQ:** Kansas City Cardiomyopathy Questionnaire; **LVEF:** left ventricular ejection fraction; **MET:** metabolic equivalent; **MI:** myocardial infarction; **MLWHF:** Minnesota Living With Heart Failure questionnaire; **NTproBNP:** N-terminal prohormone of brain natriuretic peptide; **NYHA:** New York Heart Association; **QoL:** quality of life; **SES:** socioeconomic status; **VO_2:** oxygen uptake

APPENDICES

Appendix 1. Search strategy

Cochrane Central Register of Controlled Trials (CENTRAL; 2021, Issue 12)

([mh "Heart Failure"] or ((Heart and Failure) OR HFNEF or HFPEF or HFREF or "HF NEF" or "HF PEF" or "HF REF" OR Left Ventricular Failure OR LVF):ti,ab) AND ([mh ^"Rehabilitation Centers"] OR [mh "Exercise Therapy"] OR [mh ^Sports] OR [mh "Physical Exertion"] OR [mh Exercise] OR [mh Rehabilitation] OR [mh ^"Patient Education as Topic"] OR [mh "Self Care"] OR [mh "Ambulatory Care"] OR [mh Psychotherapy] OR [mh "Mind-Body Therapies"] OR [mh Counseling] OR [mh "Cognitive Therapy"] OR [mh "Behavior Therapy"] OR [mh "Stress, Psychological"] OR [mh Meditation] OR [mh ^Anxiety] OR [mh Psychopathology] OR [mh "Autogenic Training"] OR [mh "Health Education"] OR (rehabilitat*):ti,ab or (physical* near (fit* or train* or therap* or activit*)):ti,ab or ((train*) near (strength* or aerobic or exercise*)):ti,ab or ((exercise* or fitness) near/3 (treatment or intervent* or program*)):ti,ab or (patient* near/3 educat*):ti,ab or (psychotherap* or relax* or meditat* or CBT or hypnotherap* or psycho-educat* or psychoeducat* or psychopathol* or autogenic* or distress* or psychosocial* or psycho-social or heart manual):ti,ab or ((lifestyle or life-style) near/3 (intervent* or program* or treatment*)):ti,ab or (psycholog* near intervent*):ti,ab or ((Mind or Body) and (Relaxation Techniques)):ti,ab or (counseling or counselling):ti,ab or ((behavio*r*) near/4 (modif* or therap* or rehab* or change)):ti,ab or (stress near manage*):ti,ab or (cognitive* near therap*):ti,ab or ((manage*) near (anxiety or depres*)):ti,ab or (goal near/3 (setting)):ti,ab or (motivat* near (interv*)):ti,ab or (self near (manage* or care or motivat*)):ti,ab or (nutrition or diet or health near (education)):ti,ab)

Publication Year from 2018 to 2021, in Trials

MEDLINE (Ovid, 1946 to 10 December 2021)

1 exp Heart Failure/ or ((heart adj5 failure) or HFNEF or HFPEF or HFREF or "HF NEF" or "HF PEF" or "HF REF" or Left Ventricular Failure or LVF).ti,ab.

2 *Rehabilitation Centers/ or exp Exercise Therapy/ or exp Sports/ or *Rehabilitation/ or exp Exercise/ or Patient Education as Topic/ or *Self Care/ or *Ambulatory Care/ or exp Psychotherapy/ or exp Relaxation Therapy/ or exp Mind-Body Therapies/ or exp Counseling/ or exp Cognitive Therapy/ or exp Behavior Therapy/ or *Stress, Psychological/ or *Meditation/ or exp Anxiety/ or Psychopathology/ or exp Health Education/ or Autogenic Training/ or Physical Exertion/ or exertion.ti,ab. or rehabilitat$5.ti,ab. or (physical$4 adj5 (fit or fitness or train $5 or therap$5 or activit$5)).ti,ab. or (train$5 adj5 (strength$3 or aerobic or exercise$4)).ti,ab. or ((exercise$4 or fitness) adj5 (treatment or intervent$4 or programs$2 or therapy)).ti,ab. or (patient$2 adj5 educat$4).ti,ab. or ((lifestyle or life-style) adj5 (intervent$5 or program $2 or treatment$2)).ti,ab. or (self adj5 (manage$5 or care or motivate$5)).ti,ab. or psychotherap$2.ti,ab. or (psycholog$5 adj5 intervent $5).ti,ab. or relax$6.ti,ab. or (counselling or counseling).ti,ab. or ((behavior$4 or behaviour$4) adj5 (modify or modificat$4 or therap$2

or change)).ti,ab. or (stress adj5 management).ti,ab. or (cognitive adj5 therap$2).ti,ab. or meditat$4.ti,ab. or (manage$5 adj5 (anxiety or depress$5)).ti,ab. or CBT.ti,ab. or hypnotherap$5.ti,ab. or (goal adj5 setting).ti,ab. or (goal$2 adj5 setting).ti,ab. or (psycho-educat$5 or psychoeducat$5).ti,ab. or (motivat$5 adj5 (intervention or interv$3)).ti,ab. or psychopathol$4.ti,ab. or psychosocial$4.ti,ab. or distress $4.ti,ab. or (health adj5 education).ti,ab. or (heart adj5 manual).ti,ab. or autogenic$5.ti,ab.

3 randomized controlled trial/ or controlled clinical trial/ or Random Allocation/ or Double-Blind Method/ or single-blind method/ or exp Research Design/ or exp clinical trial/ or (randomized controlled trial or controlled clinical trial or Clinical Trial).pt. or (random$ or placebo $).ti,ab. or ((singl$3 or doubl$3 or tripl$3 or trebl$3) adj5 (blind$3 or mask$3)).ti,ab. or (clinic$3 adj trial$2).ti,ab.

4 1 and 2 and 3

5 (Animals not Humans).sh.

6 4 not 5

7 limit 6 to ed=20180129-20211231

8 limit 6 to dt=20180129-20211231

9 7 or 8

Embase (Ovid, 1980 to 2021 week 49)

1 exp congestive heart failure/ or ((heart adj5 failure) or HFNEF or HFPEF or HFREF or "HF NEF" or "HF PEF" or "HF REF" or Left Ventricular Failure or LVF).ti,ab.

2 *Psychotherapy/ or relaxation training/ or *counselling/ or stress management/ or *Mediation/ or exp psychosocial care/ or exp psychosocial rehabilitation/ or exp health education/ or autogenic training/ or *Rehabilitation/ or rehabilitation center/ or exp Sport/ or exp Kinesiotherapy/ or exp Physiotherapy/ or patient education/ or exp self care/ or exp ambulatory care/ or psychosocial care/ or psychosocial rehabilitation/ or exp health education/ or autogenic training/ or psychosocial care/ or psychosocial rehabilitation/ or exp health education/ or psychotherapy$2.ti,ab. or (psycholog$5 adj5 intervent$5).ti,ab. or relax$6.ti,ab. or (counselling or counseling).ti,ab. or ((behavior$4 or behaviour$4) adj5 (modify or modificat$4 or therap$2 or change)).ti,ab. or (stress adj5 management).ti,ab. or meditat $5.ti,ab. or (manage$5 adj5 (anxiety or depress$5)).ti,ab. or CBT.ti,ab. or hypnotherap$2.ti,ab. or (goal$2 adj5 setting).ti,ab. or (psycho-educat$5 or psychoeducat$5).ti,ab. or (motivat$5 adj5 intervent$6).ti,ab. or psychosocial.ti,ab. or (health adj5 education).ti,ab. or (heart adj5 manual).ti,ab. or autogenic.ti,ab. or rehabil$.ti,ab. or exp Exercise/ or (physical$4 adj5 (fit or fitness or train$5 or therap$5 or activit $5)).ti,ab. or (train$5 adj5 (strength$3 or aerobic or exercise$4)).ti,ab. or ((exercise$4 or fitness) adj5 (treatment or intervent$4 or programs $2 or therapy)).ti,ab. or (aerobic$4 adj5 exercise$4).ti,ab. or (kinesiotherapy or physiotherapy).ti,ab. or (patient$2 adj5 educat$4).ti,ab. or ((((lifestyle or life) adj1 style) or life-style) adj5 (intervent$5 or program$2 or treatment$2)).ti,ab. or (self adj5 (manage$5 or care or motivate$5)).ti,ab. or (psycho-educat$5 or psychoeducat$5).ti,ab. or (motivat$5 adj5 intervent$6).ti,ab. or psychosocial.ti,ab. or (health adj5 education).ti,ab. or (heart adj5 manual).ti,ab. or autogenic$5.ti,ab. or (psycho-educat$5 or psychoeducat$5).ti,ab. or (motivat$5 adj5 intervent$6).ti,ab. or psychosocial.ti,ab. or (health adj5 education).ti,ab. or (heart adj5 manual).ti,ab.

3 randomized controlled trial/ or (random$ or placebo$).ti,ab. or ((singl$4 or doubl$4 or tripl$4 or trebl$4) adj5 (blind$4 or mask$4)).ti,ab. or (controlled adj1 clinical adj1 trial).ti,ab.

4 1 and 2 and 3

5 (animal$ not human$).sh,hw.

6 4 not 5

7 limit 6 to em=201806-202129

8 limit 7 to (conference abstracts or embase)

CINAHL (EBSCO, 1937 to 13 December 2021)

S1 (MH "Heart Failure+") OR TI heart N5 failure OR AB heart N5 failure OR TI (HFNEF or HFPEF or HFREF or "HF NEF" or "HF PEF" or "HF REF" or Left Ventricular Failure OR LVF) OR AB (HFNEF or HFPEF or HFREF or "HF NEF" or "HF PEF" or "HF REF" or Left Ventricular Failure OR LVF)

S2 ((MM "Rehabilitation") OR (MM "Sports") OR (MM "Physical Activity") OR (MH "Muscle Strengthening+") OR (MH "Aerobic Exercises+") OR (MH "Physical Fitness+") OR (MH "Patient Education+") OR (MH "Therapeutic Exercise+") OR (MH "Self Care+") OR (MM "Ambulatory Care") OR (MH "Psychotherapy+") OR (MH "Relaxation Techniques+") OR (MH "Counseling+") OR (MM "Stress Management") OR (MM "Meditation") OR (MH "Anxiety+") OR (MH "Health Education+")) OR TI (rehabilitat* OR (physical* N5 fit) or (physical N5 fitness) or (physical N5 train*) or (physical N5 therap*) or (physical N5 activit*) OR (train N5 strength) or (train N5 aerobic) or (train N5 exercis*) OR (exercise N5 treatment) or (fitness N5 treatment) or (exercise N5 intervent*) or (fitness N5 intervent*) or (exercise N5 program*) or (fitness N5 program) or (exercise N5

therapy) or (fitness N5 therapy) OR (patient* N5 educat*) OR (lifestyle N5 intervent*) or (life-style N5 intervent*) or (lifestyle N5 program*) or (life-style N5 program*) or (lifestyle N5 treatment) or (life-style N5 treatment) OR (self N5 manage*) or (self N5 care) or (self N5 motivat*) OR aerobic OR (resistance W1 train*) OR (muscle W1 strength*) OR (resistance W1 train*) OR (muscle W1 strength*) OR psychotherap* OR (psycholog* N5 intervent*) OR relax* OR counselling or counseling OR (behavio?r* N5 modify) or (behavio?r* N5 modificat*) or (behavio?r* N5 therap*) or (behavio?r* N5 change) OR (stress N5 manag*) OR (cognitive N5 therap*) OR (manage* N5 anxiety) or (manage* N5 depress*) OR (goal* N5 setting) OR (motivat* N5 interv*) or (motivate* N5 intervent*) OR (health N5 educat*) OR (heart W1 manual) OR meditat* OR CBT OR hypnotherap* OR psychosocial* OR autogenic* OR psycho-educat* or psychoeducat*) OR AB (rehabilitat* OR (physical* N5 fit) or (physical N5 fitness) or (physical N5 train*) or (physical N5 therap*) or (physical N5 activit*) OR (train N5 strength) or (train N5 aerobic) or (train N5 exercis*) OR (exercise N5 treatment) or (fitness N5 treatment) or (exercise N5 intervent*) or (fitness N5 intervent*) or (exercise N5 program*) or (fitness N5 program) or (exercise N5 therapy) or (fitness N5 therapy) OR (patient* N5 educat*) OR (lifestyle N5 intervent*) or (life-style N5 intervent*) or (lifestyle N5 program*) or (life-style N5 program*) or (lifestyle N5 treatment) or (life-style N5 treatment) OR (self N5 manage*) or (self N5 care) or (self N5 motivat*) OR aerobic OR (resistance W1 train*) OR (muscle W1 strength*) OR (resistance W1 train*) OR (muscle W1 strength*) OR psychotherap* OR (psycholog* N5 intervent*) OR relax* OR counselling or counseling OR (behavio?r* N5 modify) or (behavio?r* N5 modificat*) or (behavio?r* N5 therap*) or (behavio?r* N5 change) OR (stress N5 manag*) OR (cognitive N5 therap*) OR (manage* N5 anxiety) or (manage* N5 depress*) OR (goal* N5 setting) OR (motivat* N5 interv*) or (motivate* N5 intervent*) OR (health N5 educat*) OR (heart W1 manual) OR meditat* OR CBT OR hypnotherap* OR psychosocial* OR autogenic* OR psycho-educat* or psychoeducat*)

S3 PT CLINICAL TRIAL OR (MH "Clinical Trials+") OR TI (random* or placebo* OR (singl* or double* or triple* or treble* and (blind* or mask*)) OR (controlled w1 clinical w1 trials)) OR AB (random* or placebo* OR (singl* or double* or triple* or treble* and (blind* or mask*)) OR (controlled w1 clinical w1 trials))

S4 S1 AND S2 AND S3

Limiters - Exclude MEDLINE records

S5 EM 201801-

S6 S4 AND S5

PsycINFO (Ovid, 1806 to December week 5 2021)

1 ((heart adj5 failure) or HFNEF or HFPEF or HFREF or "HF NEF" or "HF PEF" or "HF REF" or Left Ventricular Failure or LVF).ti,ab.

2 exp Physical Activity/ or exp Sports/ or *Physical Education/ or exp Health Behavior/ or *Physical Fitness/ or exp Client Education/ or exp Health Promotion/ or exp Outpatient Treatment/ or exp Psychotherapy/ or exp Treatment/ or exp Counseling/ or exp Coping Behavior/ or *Meditation/ or *Autogenic Training/ or exp Health Education/ or (physical adj1 education).ti,ab. or exertion$6.ti,ab. or rehabilitat$6.ti,ab. or (physical adj5 (fit$5 or train$5 or therap$5 or activit$4)).ti,ab. or (train$4 adj5 (strength$4 or aerobic or exercise$2)).ti,ab. or ((exercise $3 or fitness) adj5 (treatment or intervent$4 or program$4 or therap$2)).ti,ab. or patient with education.ti,ab. or ((lifestyle or life-style) adj5 (intervent$5 or program$2 or treatment$2)).ti,ab. or psychotherapy$2.ti,ab. or (psycholog$4 adj5 intervent$5).ti,ab. or relax$6.ti,ab. or (counselling or counseling).ti,ab. or ((behavior or behaviour) adj5 (modif$5 or therap$5 or rehabilit5 or change)).ti,ab. or (stress adj5 management).ti,ab. or meditat$5.ti,ab. or (manage$5 adj5 (anxiety or depress$5)).ti,ab. or ((cbt or cognitive$2) adj5 therap$3).ti,ab. or hypnotherap$3.ti,ab. or (psycho-educat$6 or psychoeducat$6).ti,ab. or (motivat$5 adj5 intervent$5).ti,ab. or (self adj5 manag$6).ti,ab. or autogenic$3.ti,ab. or (goal adj5 setting).ti,ab. or (health adj5 education).ti,ab. or (heart adj1 manual).ti,ab.

3 (random$5 or placebo$5 or ((single$4 or double$4 or triple$4) and (blind$4 or mask or sham$4 or dummy)) or RCT).ti,ab.

4 1 and 2 and 3

5 limit 4 to up=20180129-20211231

Web of Science (Thomson Reuters, 1900 to 13 December 2021)

(heart SAME failure) OR HFNEF or HFPEF or HFREF or "HF NEF" or "HF PEF" or "HF REF" OR Left Ventricular Failure OR LVF (Topic) and rehab* or educat* (Topic) and random* or placebo* or ((singl* or doubl* or tripl* or trebl*) SAME (blind* or mask*)) or "clinic* trial*" (Topic)

Publication dates 2018-01-01 – 2021-12-13

Editions = A&HCI, CPCI-SSH, CPCI-S, SCI-EXPANDED, SSCI

WHAT'S NEW

Date	Event	Description
7 March 2024	New search has been performed	Searches were updated on 13 December 2021.
7 March 2024	New citation required but conclusions have not changed	16 new studies (27 publications) were included in this update. Review conclusions remain broadly unchanged.

HISTORY

Protocol first published: Issue 4, 2001
Review first published: Issue 3, 2004

Date	Event	Description
1 June 2018	New citation required but conclusions have not changed	Eleven new studies (29 publications) were included in the update. The study population included adults with evidence of HF - either HFrEF or HFpEF. We based our search strategy on the January 2013 search strategy, which was made to reflect more recent use of the terms 'HFpEF' and 'HFrEF'. The search for this current review update was updated from the 2013 search (January 2013 to 29 January 2018), with date limits applied to our latest search to identify only those records that have been newly added to the databases since the last search. Review conclusions remain unchanged
31 May 2018	New search has been performed	We updated this review with trials identified by the update search, which we ran on 29 January 2018
1 November 2013	New citation required but conclusions have not changed	For this review update, we identified 14 additional trials. Whilst conclusions of the review have not changed, this update provides a broader body of evidence of the benefits of exercise-based interventions, which includes patients with HFpEF and delivery in a home-based setting
14 February 2013	New search has been performed	Searches were updated
18 May 2004	New citation required and conclusions have changed	Substantive amendments were made

CONTRIBUTIONS OF AUTHORS

Cal Molloy (CM) and Ify Mordi (IM) undertook study selection, data extraction, assessment of risk of bias, and data analysis, including meta-analysis. Rod Taylor (RST) checked the data extraction and risk of bias assessment. CM and Linda Long (LL) undertook GRADE assessment and with RST as arbiter, they updated the summary of findings table.

Rod Taylor (RST) led the update of the review, contributed to drafting of the review update text and responding to peer reviewers, and undertook meta-regression analysis. CM and RST wrote the first draft of the review update and responded to peer reviewers.

All authors reviewed the updated review text and approved the final submitted version.

DECLARATIONS OF INTEREST

Rod Taylor*: no relevant interests; former Editor for the Cochrane Heart Group (closed March 2023), with no role in the editorial decision-making of this review update.

Cal Molloy: none known

Linda Long: none known

Ify Mordi: no relevant interests; site PI for REACH-HFpEF trial at Ninewells Hospital (led by Rod Taylor), funded by NIHR

Charlene Bridges: no relevant interests; former Information Specialist for the Cochrane Heart Group (closed March 2023), with no role in the editorial decision-making of this review update.

Viral Segar: no relevant interests; Cardiology fellow, Guy's and St Thomas' Hospital, London, UK

Edward Davies: none known

Andrew Coats: no relevant interests; published opinions/review articles about exercise

Karen Rees: no relevant interests; former Editor for the Cochrane Heart Group (closed March 2023), with no role in the editorial decision-making of this review update

Sally Singh: no relevant interests; health professional at the University of Leicester; co-applicant (not a recruiting site) University Hospitals of Leicester NHS Trust for a study that is eligible for inclusion in the work, funded by NIHR

Hasnain Dalal*: no relevant interests; published BMJ Clinical Reviews in 2015 and 2021 on Cardiac Rehabilitation; chief investigator for the Cornwall Heart Attack Rehabilitation Management Study (CHARMS); Dalal HM, Evans PH, Campbell JL, Taylor RS, Watt A, Read KL, et al. Home-based versus hospital-based rehabilitation after myocardial infarction: a randomized trial with preference arms - Cornwall Heart Attack Rehabilitation Management Study (CHARMS). International Journal of Cardiology 2007;119(2):202-11. Taylor RS, Watt A, Dalal HM, Evans PH, Campbell JL, Read KL, et al. Home-based cardiac rehabilitation versus hospital-based rehabilitation: a cost-effectiveness analysis. International Journal of Cardiology 2007;119(2):196-201; funded by National Institute for Health Research (NIHR) Programme Grants for Applied Research (RP-PG-1210-12004).

*RT and HD are co-lead investigators on an ongoing National Institute for Health Research (NIHR) Programme Grants for Applied Research-funded study - Rehabilitation Enablement in Chronic Heart Failure (REACH-HF) - to develop and evaluate the costs and outcomes of a home-based self-help heart failure exercise rehabilitation manual (RP-PG-1210-12004). Several review authors are also authors of included studies – Dalal 2018; Jolly 2009; Lang 2018. They did not extract data from their own studies. Instead, another author extracted these data and checked the interpretation against the study report.

SOURCES OF SUPPORT

Internal sources

- No internal sources of support, Other

  None

External sources

- No external sources of support, Other

  None

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

We have updated this review compared to the protocol in terms of specification of outcomes. We have changed 'must report outcome' to 'must have intended to assess outcomes of interest'; also, sudden death is no longer an outcome of interest.

Since the update in 2014, we have broadened the inclusion criteria from chronic systolic heart failure to general heart failure.

In 2019, following editorial discussion, the review title was updated to include the term 'adults'. Health-related quality of life, as assessed by a validated measurement tool, was amended from a secondary to a primary outcome measure.

INDEX TERMS

Medical Subject Headings (MeSH)

*Cardiac Rehabilitation [methods]; Exercise; Exercise Therapy; *Heart Failure; Quality of Life

MeSH check words

Humans