Exercise-based cardiac rehabilitation for adults with heart failure

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[Intervention Review]

Exercise-based cardiac rehabilitation for adults with heart failure

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ABSTRACT

Background

Chronic heart failure (HF) is a growing global health challenge. People with HF experience substantial 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 (2014) Cochrane systematic review reported that exercise-based cardiac rehabilitation (CR) compared to no exercise control shows improvement in HRQoL and hospital admission among people with HF, 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 HF with reduced (< 45%) ejection fraction (HFrEF), and women, older people, and those with preserved (≥ 45%) ejection fraction HF (HFpEF) were under-represented; and (2) most trials were undertaken in the hospital/centre-based setting.

Objectives

To determine the effects of exercise-based cardiac rehabilitation on mortality, hospital admission, and health-related quality of life of people with heart failure.

Search methods

We searched the Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, Embase, and three other databases on 29 January 2018. We also checked the bibliographies of systematic reviews and two trial registers.

Selection criteria

We included randomised controlled trials that compared exercise-based CR interventions with six months' or longer follow-up versus a no exercise control that could include usual medical care. The study population comprised adults (> 18 years) with evidence of HF - either HFrEF or HFpEF.

Data collection and analysis

Two review authors independently screened all identified references and rejected those that were clearly ineligible for inclusion in the review. We obtained full papers of potentially relevant trials. Two review authors independently extracted data from the included trials, assessed their risk of bias, and performed GRADE analyses.

Main results

We included 44 trials (5783 participants with HF) with a median of six months' follow-up. For this latest update, we identified 11 new trials (N = 1040), in addition to the previously identified 33 trials. Although the evidence base includes predominantly patients with HFrEF with New York Heart Association classes II and III receiving centre-based exercise-based CR programmes, a growing body of studies include patients with HFpEF and are undertaken in a home-based setting. All included studies included a no formal exercise training intervention comparator. However, a wide range of comparators were seen across studies that included active intervention (i.e. education, psychological intervention) or usual medical care alone. The overall risk of bias of included trials was low or unclear, and we downgraded results using the GRADE tool for all but one outcome.

Cardiac rehabilitation may make little or no difference in all-cause mortality over the short term (≤ one year of follow-up) (27 trials, 28 comparisons (2596 participants): intervention 67/1302 (5.1%) vs control 75/1294 (5.8%); risk ratio (RR) 0.89, 95% confidence interval (CI) 0.66 to 1.21; low-quality GRADE evidence) but may improve all-cause mortality in the long term (> 12 months follow up) (6 trials/comparisons (2845 participants): intervention 244/1418 (17.2%) vs control 280/1427 (19.6%) events): RR 0.88, 95% CI 0.75 to 1.02; high-quality evidence). Researchers provided no data on deaths due to HF. CR probably reduces overall hospital admissions in the short term (up to one year of follow-up) (21 trials, 21 comparisons (2182 participants): (intervention 180/1093 (16.5%) vs control 258/1089 (23.7%); RR 0.70, 95% CI 0.60 to 0.83; moderate-quality evidence, number needed to treat: 14) and may reduce HF-specific hospitalisation (14 trials, 15 comparisons (1114 participants): (intervention 40/562 (7.1%) vs control 61/552 (11.1%) RR 0.59, 95% CI 0.42 to 0.84; low-quality evidence, number needed to treat: 25). After CR, a clinically important improvement in short-term disease-specific health-related quality of life may be evident (Minnesota Living With Heart Failure questionnaire - 17 trials, 18 comparisons (1995 participants): mean difference (MD) -7.11 points, 95% CI -10.49 to -3.73; low-quality evidence). Pooling across all studies, regardless of the HRQoL measure used, shows there may be clinically important improvement with exercise (26 trials, 29 comparisons (3833 participants); standardised mean difference (SMD) -0.60, 95% CI -0.82 to -0.39; I^2 = 87%; Chi^2 = 215.03; low-quality evidence). ExCR effects appeared to be consistent different models of ExCR delivery: centre vs. home-based, exercise dose, exercise only vs. comprehensive programmes, and aerobic training alone vs aerobic plus resistance programmes.

Authors' conclusions

This updated Cochrane Review provides additional randomised evidence (11 trials) to support the conclusions of the previous version (2014) of this Cochane Review. Compared to no exercise control, CR appears to have no impact on mortality in the short term (< 12 months' follow-up). Low- to moderate-quality evidence shows that CR probably reduces the risk of all-cause hospital admissions and may reduce HF-specific hospital admissions in the short term (up to 12 months). CR may confer a clinically important improvement in health-related quality of life, although we remain uncertain about this because the evidence is of low quality. Future ExCR trials need to continue to consider the recruitment of traditionally less represented HF patient groups including older, female, and HFpEF patients, and alternative CR delivery settings including home- and using technology-based programmes.

PLAIN LANGUAGE SUMMARY

Exercise-based cardiac rehabilitation for heart failure

Background

People with heart failure (HF) experience fatigue and shortness of breath. This negatively affects their activities of daily living and health-related quality of life. They are at increased risk of hospital admission and death.

Study characteristics

We searched the scientific literature for randomised controlled trials (experiments in which two or more interventions, possibly including a control intervention or no intervention, are compared by randomly allocating participants to study groups). We looked at the effectiveness of exercise-based rehabilitation compared with no exercise in adults (over 18 years of age) with heart failure. We considered HF due to reduced ejection fraction (HFrEF) (i.e. the chambers of the heart contract poorly, and, as a result, a smaller volume of

blood is pumped around the body). We also considered HF due to preserved ejection fraction (HFpEF) (i.e. the chambers of the heart contract normally but do not relax efficiently, resulting in a smaller volume of blood pumped around the body). Our search is current to January 2018.

Key results

We found 44 studies that included 5783 people with HF, mainly HFrEF. The findings of this update are broadly consistent with those of the previous (2014) version of this Cochrane Review. They show important benefits of exercise-based rehabilitation that include a probable reduction in the risk of overall hospital admissions in the short term, as well as the potential for reduction in heart failure admissions. The effect of exercise-based rehabilitation on health-related quality of life is uncertain due to very low-quality evidence. Exercise-based rehabilitation may make little or no difference in all-cause mortality in trials with follow-up less than 12 months. Further evidence is needed to better show the effects of exercise rehabilitation among people with HFpEF and the impact of alternative models of delivery, such as home-based programmes.

Quality of evidence

Generally, recent trials have been better reported and are at low to moderate risk of bias. Using the GRADE method, we assessed the quality of evidence to range from high to very low across measured outcomes. Common reasons for downgrading outcomes include that results were inconsistent and/or imprecise.

SUMMARY OF FINDINGS FOR THE MAIN COMPARISON [Explanation]

Exercise-based cardiac rehabilitation compared to usual care for heart failure

Patient or population: adults with heart failure
Setting: hospital-based, community-based, and home-based settings
Intervention: exercise-based cardiac rehabilitation
Comparison: usual care

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 all exercise interventions				
All-cause mortality up to 12 months' follow-up (all studies) **Range: 6 to 12 months**	58 per 1000	52 per 1000 (38 to 70)	RR 0.89 (0.66 to 1.21)	2596 (27 RCTs, 28 comparisons)	⊕⊕◯◯ LOW[a,b]	Overall. exercise-based CR may make little or no difference in all-cause mortality in the short term (up to 12 months) . Six studies had no events in either the intervention arm or the control arm Sensitivity analysis from studies at low risk of bias show similar treatment effects (RR 0.9, 95% CI 0.6 to 1.34; participants = 1651; studies = 16; I^2 = 0%). From these studies, exercise-based cardiac rehabilitation probably makes little or no difference

						in all-cause mortality in the short term. Studies were downgraded due to imprecision (small number of events <300) Overall, exercise-based CR has a tendency towards a slight reduction in all-cause mortality in the medium term (over 12 months) based on the large HF-ACTION study (RR 0.88, 95% CI 0.75 to 1.02; participants = 2845; studies = 6; I^2 = 34%; high-quality evidence as assessed via GRADE)
HF-related mortality	-	-	-	-	-	Studies did not consistently report deaths due to HF nor sudden deaths
Hospital admission up to 12 months' follow-up (all studies) Range: 6 to 12 months	237 per 1000	166 per 1000 (142 to 197)	RR 0.70 (0.60 to 0.83)	2182 (21 RCTs)	⊕⊕⊕◯ MODERATE[c]	Overall exercise-based CR probably improves hospital admissions in the short term (up to 12 months) Sensitivity analysis from studies at low risk of bias was higher (RR 0.74, 95% CI 0.59 to 0.92; participants = 1161; studies = 9; I^2 =0%) Based on low risk of bias studies, exercise-

						based CR may improve hospital admissions in the short term (up to 12 months). Studies were downgraded due to imprecision (small number of events < 300 and confidence intervals including potential for no benefit and important benefit, as 95% CI crosses RR of 0.75) Overall, we are uncertain whether exercise-based CR improves hospital admissions in the medium term (over 12 months) (RR 0.7, 95% CI 0.47 to 1.05; participants = 2691; studies = 6; I^2 = 66%; very low-quality evidence as assessed via GRADE) (see footnotes c, d and e for reasons for downgrade)
Hospital admission heart failure only (all studies) Range: 6 months to 6.2 years	111 per 1000	65 per 1000 (46 to 93)	RR 0.59 (0.42 to 0.84)	1114 (14 RCTs, 15 comparisons)	⊕⊕◯◯ LOW[b,f]	Overall, exercise-based CR may improve hospital admissions for heart failure only in the medium term (over 12 months) Sensitivity analysis from studies at low risk of bias was higher (RR 0.61, 95% CI 0.36 to 1.

						04; participants = 588; studies = 6; I^2 = 10%) Based on low risk of bias studies, exercise-based CR may make little or no difference in hospital admissions for heart failure only. Studies were downgraded due to imprecision (small number of events < 300 and confidence intervals including potential for no benefit and important benefit, as 95% CI crosses RR of 0.75)
Health-related quality of life - MLWHF up to 12 months' follow-up (all studies) **Range: 6 to 12 months**	Mean 18 to 56	MD 7.11 lower (10.49 lower to 3.73 lower)	-	1995 (17 RCTs, 18 comparisons)	⊕⊕◯◯ LOW[f,g]	Overall, exercise-based CR may improve health-related quality of life in the short term (up to 12 months) Sensitivity analysis from studies at low risk of bias was lower (MD 3.38 lower, 95% CI 6.95 lower to 0.19 higher; participants = 1101; studies = 9; I^2 = 71%) Based on low risk of bias studies, exercise-based cardiac rehabilitation may confer little or no benefit for health-

						related quality of life in the short term (up to 12 months) Studies were downgraded due to imprecision (confidence intervals including potential for no benefit and important clinical benefit) and inconsistency (I^2 = 71%) Overall, we are uncertain whether exercise-based CR improves health-related quality of life in the medium term (longer than 12 months) (MD 9. 49 lower, 95% CI 17.48 lower to 1.5 lower; participants = 329; studies = 3; I^2 = 73%; very low-quality evidence as assessed via GRADE) (see footnotes h, i, and j for reasons for downgrade)
Health-related quality of life - MLWHF and other scales up to 12 months' follow-up (all studies) Range: 6 to 30 months	Mean 18 to 71	SMD 0.60 lower (0.82 lower to 0.39 lower)	-	3833 (26 RCTs, 29 comparisons)	⊕⊕◯◯ LOW[f,k]	Overall, exercise-based CR may improve health-related quality of life in the short term (up to 12 months) Sensitivity analysis from studies at low risk of bias was similar (SMD 0.42 lower, 95% CI 0.65 lower to 0.

			19 lower; participants = 3181; studies = 16; I^2 = 84%) Based on low risk of bias studies, exercise-based cardiac rehabilitation probably improves health-related quality of life in the short term (up to 12 months). Studies were downgraded due to inconsistency (I^2 = 84%)

*__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; CR: cardiac rehabilitation; HF: heart failure; MD: mean difference; MLWHF: Minnesota Living With Heart Failure questionnaire; OR: odds ratio; 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] Some concerns with random sequence generation and allocation concealment; bias likely - therefore quality of evidence downgraded by one level.
[b] Imprecise due to small numbers of events (< 300) (Ryan 2016); therefore quality of evidence downgraded by one level.
[c] Some concerns with random sequence generation, allocation concealment, and groups balanced at baseline; bias likely - therefore quality of evidence downgraded by one level.
[d] Inconsistent directions of effect and substantial statistical heterogeneity (I^2 = 66%); therefore quality of evidence downgraded by one level.
[e] Imprecise due to confidence intervals, including potential for no benefit and important benefit, as 95% CI crosses RR of 0.75; therefore quality of evidence downgraded by one level.
[f] Some concerns with random sequence generation, allocation concealment, and blinding of outcome assessment; bias likely - therefore quality of evidence downgraded by one level.

[g]Inconsistency with considerable statistical heterogeneity (I^2 = 82%); therefore quality of evidence downgraded by one level.
[h]Some concerns with random sequence generation, allocation concealment, blinding of outcome assessment, intention-to-treat analysis, and groups not receiving the same intervention; bias likely - therefore quality of evidence downgraded by two levels.
[i]Inconsistency with substantial statistical heterogeneity (I^2 = 73%); therefore quality of evidence downgraded by one level.
[j]Imprecise due to small number of participants (< 400) (Ryan 2016); therefore quality of evidence downgraded by one level.
[k]Inconsistency with considerable statistical heterogeneity (I^2 = 86%); therefore quality of evidence downgraded by one level.

BACKGROUND

Description of the condition

Chronic heart failure (HF) is a growing global health challenge (Braunwald 2015; Ziaeian 2016), with increasing prevalence as reported in Braunwald 2015 and an annual economic burden predicted to grow to more than USD108 billion per annum as the population ages (Cook 2014). Unplanned hospital admissions are a key driver of the cost of HF (Cook 2014).

Patients with HF experience substantial burden that includes exercise intolerance, poor health-related quality of life (HRQoL), mortality, increased hospital admissions, and higher healthcare costs (Braunwald 2015; Ziaeian 2016). With important gains in mortality achieved over the past decade through pharmacological and device therapy in patients with HF with reduced ejection fraction (HFrEF) (Braunwald 2015), the focus is increasingly shifting towards HRQoL (Calvert 2007).

Heart failure has two main subcategories: HF with impaired left ventricular contraction, which results in a reduced ejection fraction (< 45% to 50%), known as HF with reduced ejection fraction (HFrEF) (ACCF/AHA 2013); and HF with preserved ejection fraction (HFpEF), with an ejection fraction greater than 45% to 50% (Dunley 2017; Lam 2011). Whilst epidemiological data show that approximately half of all patients with HF 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. No large-scale randomised trials have demonstrated treatment benefits that alter the natural course of HFpEF, or that lower mortality (Holland 2011; Komajda 2017).

Description of the intervention

The British Association for Cardiovascular Prevention and Rehabilitation (BACPR) defines cardiac rehabilitation (CR) 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 CR is exercise training (Piepoli 1998; Piepoli 2015), CR programmes should be comprehensive and should provide risk factor and lifestyle education on risk factor management plus counselling and psychological support (Corra 2005).

Based on current evidence on clinical outcomes and costs, national and international guidelines on the management of HF, 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, consistently recommend CR as an effective and safe intervention (ACCF/AHA 2013; ESC 2016; NICE 2018). However, surveys in the United States and Europe have shown that the current uptake of CR for HF remains suboptimal, with less than 20% of HF patients receiving rehabilitation (Bjarnason-Wehrens 2010; Golwala 2015). To improve access to and uptake of CR for HF, there have been calls for alternative models to centre-based CR, including home-based and technology-based provisions (Dalal 2015).

How the intervention might work

Exercise-based CR might benefit patients with HF through a variety of mechanisms. First, for people with an ischaemic cause of HF, 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, HF 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 HF has been shown to stimulate vasodilation in the skeletal muscle vasculature (Hambrecht 1998).

Why it is important to do this review

This is an update of a Cochrane review published in 2014. The first Cochrane systematic review of exercise-based CR for HF 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 updated 2010 Cochrane Review focussed 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 randomised trials (3647 participants) showed no difference between exercise and control in either short-term or long-term all-cause mortality, a reduction in HF-related hospitalisations (risk ratio (RR) 0.72, 95% confidence interval (CI) 0.52 to 0.99), and improvement in patient-reported HRQoL (standard-

ised 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 2014 review of 33 RCTs (4740 participants) presented findings consistent with the previous (2010) version and concluded that exercise-based CR reduced the risk of hospital admission due to HF and led to improvements in HRQoL compared with no exercise. To continue to promote international access and uptake of CR for HF, the current evidence base must be updated to reflect recent trials that are increasingly testing alternative models to centre-based CR, such as home- and technology-based programmes (Dalal 2015).

By gathering additional RCT evidence provided since the 2014 Cochrane review, and by performing a GRADE analysis, authors of this review update sought to reassess the effectiveness of exercise-based CR in terms of mortality, hospital admissions, morbidity, and HRQoL of people with HF compared with no exercise training, regardless of setting.

OBJECTIVES

To determine the effects of exercise-based cardiac rehabilitation on mortality, hospital admission, and health-related quality of life of people with heart failure.

METHODS

Criteria for considering studies for this review

Types of studies

We included RCTs of a parallel-group or cross-over 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 policy makers.

Types of participants

We included adults aged 18 years or older with HF. We excluded trials that focussed on participants who had received exercise-based CR, as previous participant exposure to the intervention may confound the interpretation of trials. However, if the trial population consisted primarily of new CR patients who predominantly had HF, we included the trial.

Types of interventions

We included exercise-based interventions given alone or as a component of comprehensive CR (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

To be included, the study must have intended to assess one or more of the following outcomes. 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
- HF mortality
- Number of participants who experienced an all-cause hospital admission
- Number of participants who experienced an HF-related hospital admission

These event outcomes reflect both potential efficacy and harm.

Secondary outcomes

- HRQoL assessed by a validated outcome measure (e.g. 36-item Short Form (SF-36), Minnesota Living With Heart Failure (MLWHF) questionnaire)
- Costs and cost-effectiveness

Search methods for identification of studies

To update searches from the previous Cochrane Review, we searched the Cochrane Central Register of Controlled Trials (CENTRAL), in the Cochrane Library, from January 2013 to 29 January 2018. We also searched MEDLINE, Embase, the Cumulative Index to Nursing and Allied Health Literature (CINAHL), and PsycINFO (January 2013 to 30 January 2018), without language restrictions. We checked Web of Science and bibliographies of systematic reviews. We examined trial registers (World Health Organization (WHO) International Clinical Trials Registry Platform (ICTRP) and Clinicaltrials.gov) twice, on 14 March 2018, and again on 4 October 2018.

Electronic searches

For this update, we reran searches of the following databases on 29 January 2018 (search strategies presented in Appendix 1).

- CENTRAL, in the Cochrane Library (2017, Issue 12 of 12).
- Epub Ahead of Print, In-Process & Other Non-Indexed Citations, MEDLINE Daily, and MEDLINE (Ovid, 1946 to 29 January 2018).
- Embase (Ovid, 1980 to 2018 week 5).
- CINAHL (EBSCO, 1937 to 29 January 2018).
- PsycINFO (Ovid, 1806 to January week 4 2018).
- Web of Science: Science Citation Index - Expanded (SCI-EXPANDED), Social Sciences CItation Index (SSCI), Arts and Humanities Citation Index (A&HCI), Conference Proceedings Citation Index - Science (CPCI-S), Conference Proceedings Citation Index - Social Science and Humanities (CPCI-SSH) (Thomson Reuters, 1900 to 29 January 2018).

We used the Cochrane sensitivity-maximising RCT filter for MEDLINE, and we applied to our Embase search terms recommended in the *Cochrane Handbook for Systematic Reviews of Interventions* (Lefebvre 2011). We applied adaptations of this filter to CINAHL, PsycINFO, and Web of Science. We imposed no restrictions on language of publication.

We also conducted a search of two trial registers.

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

For the original review and the first update (Davies 2010; Rees 2004), we searched CENTRAL, in the Cochrane Library (2001, Issue 1; 2007, Issue 1); MEDLINE; Embase; and CINAHL (1984 to January 2008) (see Appendix 2 and Appendix 3). The search strategy developed in 2008 for the second review update included broader terms, as this search was part of a review strategy that sought to identify evidence for cardiac rehabilitation that included an update of this review and exercise-based rehabilitation for coronary heart disease (Heran 2011), as well as home- versus centre-based cardiac rehabilitation (Taylor 2010). For the last update (Taylor 2014), we updated the search from the previous version (Davies 2010), and we included CENTRAL, in the Cochrane Library (2013, Issue 1); MEDLINE (Ovid, 30 January 2013 week 4); 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 the January 2013 search strategy to reflect more recent use of the terms 'HFPEF' and 'HFREF'.

Searching other resources

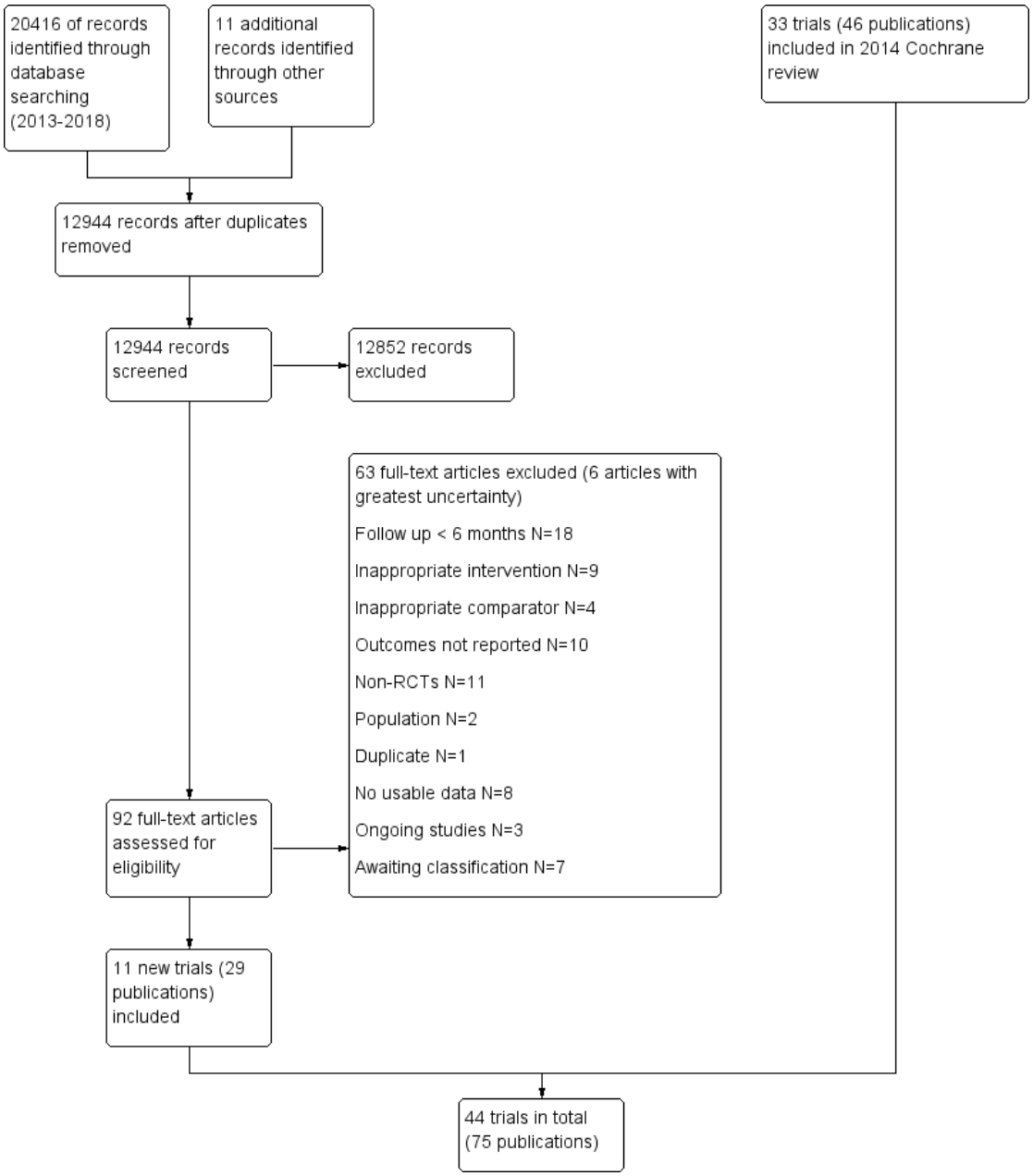
We handsearched the reference lists of all eligible trials and conducted forward citation searching of all primary studies and review articles for additional references not identified by electronic searches. We contacted experts in the field for unpublished and ongoing trials, and we contacted trial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

Data collection and analysis

Selection of studies

Two review authors (LL and IM) independently screened references identified by the search strategy by reviewing titles and abstracts and discarded clearly irrelevant studies. To be selected, abstracts had to clearly identify the study 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 (LL and IM) independently assessed them for eligibility based on the defined inclusion criteria. We resolved disagreements by discussion with a third review author (RST). RST undertook data study selection in previous review versions. We recorded the selection process in sufficient detail to complete a PRISMA flow diagram (Figure 1).

Figure 1. Study flow diagram.



Data extraction and management

We extracted relevant data regarding inclusion criteria (study 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 (LL and IM) independently extracted data using a standardised data extraction form that had been piloted on at least one of the studies included in the review. We resolved disagreements by discussion with a third review author (RST). We contacted study authors when necessary to seek clarification on issues of reporting or to obtain further outcome details. We have detailed excluded studies and reasons for their exclusion in the Characteristics of excluded studies table.

We extracted the following study characteristics.

- Methods: study design, total duration of study, number of study centres and locations, study setting, withdrawals, and study dates.
- Participants: N, 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 (RST) transferred data into Review Manager 5.3 (RevMan 2014), and another review author (LL) double-checked that data were entered correctly by checking study characteristics for accuracy against the study report.

Assessment of risk of bias in included studies

Factors considered included the quality of random sequence generation and allocation concealment, selective outcome reporting, incomplete outcome data, blinding of outcome assessors, and incomplete outcome data (Higgins 2011). Two review authors (LL and IM) assessed the risk of bias of eligible trials, and a third review author (RST) verified the decision. RST undertook risk of bias assessments in previous review versions. We conducted a sensitivity analysis and stratified results by risk of bias at the study level (presence of low risk of bias for either allocation concealment or sequence generation).

We assessed three additional quality criteria: whether study 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 quality in several of our previous Cochrane Reviews on CR (Taylor 2010; Taylor 2014). We assessed these additional quality criteria 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 receiving 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 study 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 investigators performed an intention-to-treat analysis
- *High risk of bias:* the trial does not include an intention-to-treat analysis, or researchers 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

We graded each potential source of bias as high, low, or unclear, and we provided a quote from the study report together with a justification for our judgement in the 'Risk of bias' table. We summarised the 'Risk of bias' judgements across different studies for each of the domains listed. When information on risk of bias was related to unpublished data or correspondence with a study author, we noted this in the 'Risk of bias' table.

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

Measures of treatment effect

We processed data in accordance with the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011). We expressed dichotomous outcomes as risk ratios (RRs) and 95% confidence intervals (CIs) for each study. 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 study. We calculated SMDs when all studies 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 CR. 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 Section 16.4 of the *Cochrane Handbook for Systematic Reviews of Intervention* (Higgins 2011), 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 investigators or study sponsors to verify key study characteristics and to obtain missing numerical outcome data when possible (e.g. when we identified a study 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 studies on the overall assessment of results by performing a sensitivity analysis.

Assessment of heterogeneity

We explored heterogeneity among included studies qualitatively (by comparing the characteristics of included studies) and quantitatively (using the Chi² test for heterogeneity and the I² statistic).

Assessment of reporting biases

We used funnels plots and Egger tests to assess potential small-study effects and publication bias for those outcomes with an adequate number of trials (more than 10) (i.e. all-cause mortality, hospital admissions, and HRQoL) (Egger 1997; Higgins 2011).

Data synthesis

We processed data in accordance with the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011), 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 study using a fixed-effect model, except when we identified substantial statistical heterogeneity (I² statistic > 50%), in which case we applied 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 5.3 software (RevMan 2014).

'Summary of findings' table

Two review authors (LL and IM) independently employed the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach to interpret study results (Schünemann 2011). We used the five GRADE considerations (study limitations, consistency of effect, imprecision, indirectness, and publication bias) to assess the quality of a body of evidence as it related to studies that contributed data to the meta-analyses and narrative summaries for pre-specified outcomes. We resolved any discrepancies in judgement through discussion. One review

author (LL) used GRADEproGDT software (GRADEpro GDT 2015) to import data from Review Manager to create a 'Summary of Findings' table that included the following pre-specified outcomes: all-cause mortality; all-cause hospital admissions; heart failure hospital admissions; and HRQoL.

Subgroup analysis and investigation of heterogeneity

We explored potential heterogeneity in exercise-based rehabilitation 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 study co-variates.

- Mean per cent left ventricular ejection fraction (LVEF).
- Dose of aerobic exercise (calculated as overall number of weeks of training × mean number of sessions per week × mean duration of sessions in minutes).
- Type of exercise (aerobic training alone or aerobic plus resistance training).
- Mean age.
- Sex (per cent male).
- Setting (hospital only, home only, both hospital and home).
- Type of rehabilitation (exercise only vs comprehensive).
- Overall risk of bias ('low', i.e. absence of bias in allocation concealment and/or sequence generation).
- Single centre versus multi-centre.
- Publication date.

We added year of publication as an additional study level factor (pre- vs 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 HF (Shekelle 2003). Given the relatively small ratio of trials to co-variates, we limited meta-regression to univariate analysis (Higgins 2011). We used the permute option in STATA to allow for multiple testing in meta-regression. Due to the risks of multiple testing, we used a conservative cut-off of $P < 0.01$.

Sensitivity analysis

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

RESULTS

Description of studies

We have presented the details of studies included in this review in the Characteristics of included studies table, and reasons for exclusion in the Characteristics of excluded studies table. We have detailed the status of ongoing trials in the Characteristics of ongoing studies table, and we have provided information on studies awaiting classification in the Characteristics of studies awaiting classification table.

Results of the search

The electronic search for this update yielded a total of 20,416 titles and abstracts. We identified 11 additional studies through additional searches. After de-duplication, we found that 12,944 studies were eligible for screening. Following screening, we formally evaluated 92 studies for inclusion or exclusion by retrieving the full-text publications. We newly included a total of 11 RCTs (29 publications) in the review, bringing the total of included studies to 44 (75 publications). Backwards and forwards searching of the reference lists of eligible publications did not reveal additional publications for inclusion. We identified three ongoing trial protocols (NCT01914315; NCT02196038; NCT03041376). We have summarised the study selection process in the PRISMA flow diagram (Figure 1).

Included studies

The 2004 and 2010 versions of this Cochrane review contributed eight (Rees 2004),11 (Davies 2010), and 14 trials to this latest update (Taylor 2014). We excluded from the 2010 review several trials included in the 2004 review, as their follow-up was less than six months, or investigators reported only exercise capacity outcomes. For this update, we identified 11 additional trials - 13 comparisons in patients with HF (Antonicelli 2016; Chen 2018; Cowie 2014; Dalal 2018; Dehkordi AH 2015; Du 2018; Giallauria 2008; Kaltsatou 2014; Lang 2018; Mehani 2013; Reeves 2017). We have summarised the study selection process in the PRISMA flow diagram shown in Figure 1.

The 44 included trials (75 publications) randomised 5783 participants predominantly with HFrEF and NYHA classes II and III heart failure. Six trials included an (undefined) proportion of people with HFpEF (Antonicelli 2016; Davidson 2010; Gary 2010; Nilsson 2008; Reeves 2017; Wall 2010). Most trials were small, single-centre studies, and one large trial contributed ~40% (2331 participants) of all included participants (HF ACTION 2009). The mean age of participants across the included studies ranged from 51 to 81 years. Studies recruited predominantly men (median 79%), although evidence shows that recent trials recruited more women. Only 10 trials reported on ethnicity. Seven trials reported follow-up in excess of 12 months (Austin 2005; Belardinelli 1999; Belardinelli 2012; Cowie 2014; HF ACTION 2009; Jónsdóttir 2006a; Mueller 2007). Four trials included more than one exer-

cise intervention arm, and each contributed two separate comparative arms for the purpose of the meta-analysis (Cowie 2014; Gary 2010; Kaltsatou 2014; Klocek 2005).

All trials evaluated an aerobic intervention, and 14 studies (15 comparisons) also included resistance training (Austin 2005; Chen 2018; DANREHAB 2008; Dracup 2007; Jolly 2009; Jónsdóttir 2006a; Kaltsatou 2014; Koukouvou 2004; McKelvie 2002; Norman 2012; Pozehl 2008; Reeves 2017; Witham 2005; Witham 2012). Researchers most commonly delivered exercise training in an exclusively centre-based setting or in a centre-based setting in combination with some home exercise sessions. Ten studies (13 comparisons) were conducted in a largely home-based setting (Cowie 2014; Dalal 2018; Dracup 2007; Du 2018; Gary 2010; Jolly 2009; Kaltsatou 2014; Lang 2018; Passino 2006; Wall 2010). The dose of exercise training ranged widely across studies, with session duration of 10 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, 14 trials included other ('comprehensive rehabilitation') elements that consisted of educational and psychological interventions (Chen 2018; Cowie 2014; Dalal 2018; DANREHAB 2008; Davidson 2010; Gary 2010; Jolly 2009; Jónsdóttir 2006a; Lang 2018; Mueller 2007; Myers 2000; Nilsson 2008; Pozehl 2008; Witham 2012).

All included studies included a no formal exercise training intervention comparator. However, a wide range of comparators were seen across studies that included active intervention (i.e. education, psychological intervention) or usual medical care alone.

All but 18 studies reported their funding sources (Belardinelli 1999; Bocalini 2008; Chen 2018; Davidson 2010; Giallauria 2008; Giannuzzi 2003; Gielen 2003; Gottlieb 1999; Hambrecht 1995; Jónsdóttir 2006a; Klocek 2005; Koukouvou 2004; McKelvie 2002; Mehani 2013; Nilsson 2008; Norman 2012; Passino 2006; Witham 2005). Two studies were funded by the pharmaceutical industry (HF ACTION 2009; Keteyian 1996).

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

Excluded studies

We excluded 63 studies identified in the search for this update for reasons listed in the Characteristics of excluded studies table. The most common reason for exclusion was follow-up less than six months.

In total, we excluded 124 studies (63 studies from this update and 61 studies from the previous review) for the following reasons: 18 (14.5%) studies were not RCTs; one (0.8%) study was a duplicate; three (2.4%) studies were not conducted in adults with heart failure; 35 (28.2%) studies did not report relevant outcomes; 12 (9.7%) studies provided an inappropriate intervention; four (3.2%) studies provided an inappropriate comparator; eight (6.45%) studies generated no usable data; and 43 (34.7%) studies reported follow-up less than six months. See Characteristics of excluded studies and Figure 1.

Ongoing studies and studies awaiting classification

Three clinical trials were still ongoing when we completed this update (NCT01914315; NCT02196038; NCT03041376).

Seven studies were completed and are awaiting classification (ACTR12608000263392; ISRCTN86879094; NCT01033591; NCT01785121; NCT02078947; NCT02696486; NCT02903225). Two studies included patients with HFrEF and HFpEF (NCT01785121; NCT03041376). See Characteristics of ongoing studies and Characteristics of studies awaiting classification.

Risk of bias in included studies

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

Figure 2. Methodological quality graph: review authors' judgements about each methodological quality item presented as percentages across all included studies.

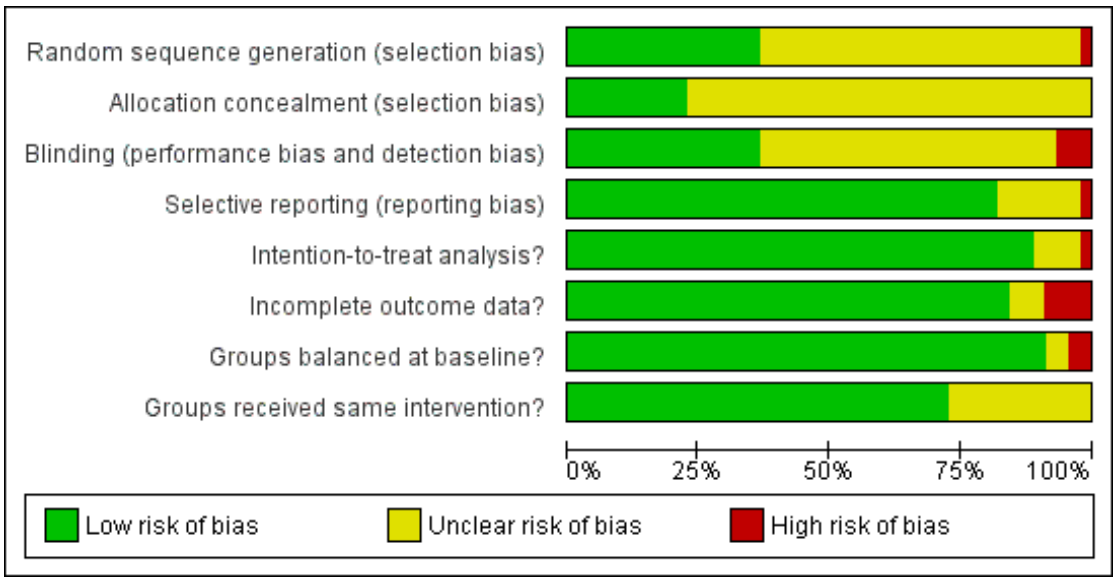


Figure 3. Methodological quality summary: review authors' judgements about each methodological quality item for each included study.

Allocation

We judged Austin 2005, Cowie 2014, Dalal 2018, DANREHAB 2008, Davidson 2010, Dehkordi AH 2015, Du 2018, Hambrecht 2000, HF ACTION 2009, Jolly 2009, Kaltsatou 2014, Lang 2018, McKelvie 2002, Reeves 2017, Witham 2005, Witham 2012, and Yeh 2011 to be at low risk of bias for allocation concealment and/or sequence generation.

All studies randomly allocated participants to study conditions. We deemed that 27 studies had unclear risk of bias and 16 studies had low risk of bias in the method used to generate randomisation sequence. Mehani 2013 had high risk of bias in the method used to generate randomisation sequence.

A total of 34 studies had unclear risk of bias and 10 studies had low risk of bias in the methods used to conceal participant allocation.

Blinding

Given the nature of an exercise intervention, it is not possible to blind participants and carers. However, we judged only three studies 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 studies. We judged 37 studies to be at low risk of bias, as they described the numbers of and reasons for dropouts, which were balanced across groups. We judged four studies to be at high risk of bias (Bocalini 2008; Cowie 2014; Du 2018; Willenheimer 2001). Bocalini provided data at follow-up for only 42 of 53 (79%) participants. Du 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. Cowie provided follow-up data for only 46 of 60 participants (77%). Willenheimer 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 study, 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 seven studies (Antonicelli 2016; Dehkordi AH 2015; Giallauria 2008; Kaltsatou 2014; McKelvie 2002; Mehani 2013; Passino 2006). We considered the risk of bias to be high in one additional study because researchers did not report the outcome 'number of hospitalisations' and we obtained the data from the study's lead investigator (Cowie 2014).

Other potential sources of bias

With the exception of three studies (Cowie 2014; Dalal 2018; Lang 2018), all included studies did not provide objective evidence of imbalance in baseline characteristics. Most studies performed an intention-to-treat analysis, comparing exercise and control group outcomes according to the initial random allocation. Because some studies did not report co-intervention details for both exercise and control groups, they may be prone to performance bias (Belardinelli 1999; Giannuzzi 2003; Gielen 2003; Hambrecht 1995; Hambrecht 2000; Keteyian 1996; Klecha 2007; Klocek 2005; McKelvie 2002; Nilsson 2008; Pozehl 2008).

Effects of interventions

See: **Summary of findings for the main comparison** Exercise-based cardiac rehabilitation compared to usual care for heart failure

All-cause mortality

A total of 27 studies (28 comparisons; 2596 participants) reported all-cause mortality at up to 12 months' follow-up. Several trials reported no deaths in either the exercise or the control arm (Dehkordi AH 2015; Gielen 2003; Kaltsatou 2014; Klecha 2007; Lang 2018; Reeves 2017). Results show no difference in pooled mortality at up to 12 months' follow-up between groups (intervention 67/1302 (5.1%) vs control 75/1294 (5.8%) events: risk ratio (RR) 0.89, 95% confidence interval (CI) 0.66 to 1.21; P = 0.47; I^2 = 0%; Chi^2 = 15.85; P = 0.96; fixed-effect analysis) (Analysis 1.1). We assessed the evidence to be of low quality via the GRADE method because of concerns about risk of bias (random sequence generation and allocation concealment) and concerns about imprecision (small number of events at < 300) (Ryan 2016).

Austin 2005, Belardinelli 1999, HF ACTION 2009, Jónsdóttir 2006a, and Mueller 2007 reported mortality at 60, 26, 30, 28, and 74 months, respectively. Although not reported in their original publication, we obtained mortality data at 10 years from Belardinelli 2012 by contacting the study authors. We found high-quality evidence towards a slight reduction in all-cause mortality when pooled across the longest follow-up point of the six trials (six comparisons; 2845 participants) with more than 12 months' follow-up (intervention 244/1418 (17.2%) vs control 280/1427 (19.6%) events): RR 0.88, 95% CI 0.75 to 1.02; P = 0.09; I^2 = 34%; Chi^2 = 7.54; P = 0.18; fixed-effect analysis) (Analysis 1.2). HF ACTION 2009 dominated this effect estimate. We assessed the evidence to be of high quality using GRADE.

HF mortality

Studies did not consistently report deaths due to HF.

All-cause hospital admissions

Exercise-based rehabilitation probably reduces the number of people experiencing all-cause hospital admissions at up to 12 months' follow-up (21 trials; 21 comparisons; 2182 participants) (intervention 180/1093 (16.5%) vs control 258/1089 (23.7%) events: RR 0.70, 95% CI 0.60 to 0.83; P = 0.0001; I^2 = 19%; Chi^2 = 24.56; P = 0.21; fixed-effect analysis) (Analysis 1.3). Using GRADE, we assessed the evidence to be of moderate quality because of concerns about risk of bias (random sequence generation, allocation concealment, and groups balanced at baseline).

We are uncertain whether exercise-based rehabilitation reduced all-cause hospital admissions in trials with more than 12 months' follow-up (six trials; seven comparisons; 2691 participants) (intervention 772/1348 (57.2%) vs control 825/1343 (61.4%) events: RR 0.70, 95% CI 0.47 to 1.05; P = 0.08; I^2 = 66%; Chi^2 = 17.81; P = 0.007) (Analysis 1.4). Using GRADE, we assessed the evidence to be of very low quality because of concerns about risk of bias (random sequence generation, allocation concealment, and groups balanced at baseline), as well as high levels of statistical heterogeneity and imprecision (confidence intervals including potential for important harm or benefit).

HF hospital admissions

Exercise-based rehabilitation may reduce HF-specific hospital admissions (14 trials; 15 comparisons; 1114 participants) (intervention 40/562 (7.1%) vs control 61/552 (11.1%) events: RR 0.59, 95% CI 0.42 to 0.84; P = 0.003; I^2 = 11%; Chi^2 = 15.81; P = 0.32) (Analysis 1.5). Using GRADE, we assessed the evidence to be of low quality because of concerns about risk of bias (random sequence generation, allocation concealment, and blinding of outcome assessment) and imprecision due to small numbers of events (< 300) (Ryan 2016). None of the studies reported HF hospital admissions at longer than 12 months' follow-up.

Health-related quality of life

Of the 44 included trials, 29 (31 comparisons) reported a validated HRQoL measure (Table 1). Most studies reported disease-specific quality of life using the MLWHF questionnaire; HF ACTION 2009 used the Kansas City Cardiomyopathy Questionnaire (KCCQ). Investigators also assessed generic HRQoL using the EuroQoL Group Quality of Life Questionnaire based on 5 dimensions (EQ-5D), the SF-36, the Psychological General Well-being 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 exercise group but not for the control group. Of the 31 comparisons, 18 (55%) reported statistical superiority in one or more HRQoL domains following exercise-based CR compared with control. No trials reported a lower HRQoL domain score with CR than with control.All included studies included HRQoL outcome at ≥ six months follow up except Belardinelli 1999 and Reeves 2017 that were reported at around three months follow up.

Lower MLWHF questionnaire scores indicate better patient HRQoL. We found evidence of high levels of statistical heterogeneity in the exercise-control difference in MLWHF scores at follow-up across studies. When pooled across the 17 trials (18 comparisons; 1995 participants) that reported the total MLWHF score up to 12 months' follow-up, results may show clinically important improvement with exercise (mean difference (MD) -7.11, 95% CI -10.49 to -3.73; P < 0.0001; I^2 = 82%; Chi^2 = 93.22; P < 0.00001; random-effects analysis) (Analysis 1.6). Using GRADE, we assessed the evidence to be of low quality because of concerns about risk of bias (random sequence generation, allocation concealment, and blinding of outcome assessment) and inconsistency with considerable heterogeneity.

Pooling across all studies, regardless of the HRQoL measure used, shows there may be clinically important improvement with exercise at up to 12 months' follow-up (26 trials; 29 comparisons; 3833 participants) (standardised mean difference (SMD) -0.60, 95% CI -0.82 to -0.39; P < 0.0001; I^2 = 87%; Chi^2 =215.03; P < 0.0001; random-effects analysis) (Analysis 1.7). As advised in the *Cochrane Handbook for Systematic Reviews of Interventions*, we excluded McKelvie 2002 from this SMD analysis, as it reported the difference in HRQoL between baseline and follow-up, while all other included studies were based on final HRQoL outcome scores.

Using GRADE, we assessed this evidence to be of low quality because of concerns about risk of bias (random sequence generation, allocation concealment, and blinding of outcome assessment) and inconsistency along with considerable heterogeneity. However, it is notable that when considering evidence from studies at low risk of bias for this outcome, we judged that exercise-based CR probably improved HRQoL. We are uncertain whether exercise-based CR improves HRQoL because of the very low quality of the evidence.

The three trials (three comparisons; 329 participants) that reported MLWHF score at follow-up greater than 12 months show improvement compared with control (MD -9.49, 95% CI -17.48 to -1.50; P = 0.02; I^2 = 73%; Chi^2 = 7.33; P = 0.03; random-effects analysis) (Analysis 1.8). Using GRADE, we assessed this evidence to be of very low quality because of concerns about risk of bias (random sequence generation, allocation concealment, blinding of outcome assessment, intention-to-treat analysis, and groups not receiving the same intervention), inconsistency with considerable heterogeneity, and imprecision due to small numbers of participants (< 400) (Ryan 2016).

Costs and cost-effectiveness

Six included trials reported economic data, with two undertaking a full cost-effectiveness analysis (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 and colleagues estimated an additional mean healthcare cost in the exercise training group compared with the control group of USD3227 per person (Georgiou 2001). Researchers calculated this cost by subtracting the averted hospitalisation cost - USD1336/person - from the cost of exercise training and wages lost due to exercise training - estimated at USD4563/person. Based on exponential survival modelling to 15.5 years, the estimated increment in life expectancy with exercise was 1.82 years/person compared with control, and the incremental cost-effectiveness ratio was USD1773/life-year saved. The HF ACTION group estimated a mean gain in quality-adjusted life-years (QALYs) of 0.03 at an additional mean cost of USD1161 per person at 2.5 years' follow-up (HF ACTION 2009). Although they did not report an incremental cost-effectiveness ratio, study authors stated that there was an 89.9% probability that exercise training was more cost-effective than usual care at a maximum willingness to pay threshold of USD50,000. Witham and colleagues reported that mean costs in the exercise group were lower (by £477.85 per person) than in the control group at six months' follow-up (Witham 2012). 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. None of the between-group differences in costs or outcomes across these three studies achieved statistical significance at P = 0.05 or less. Cowie 2014 reported that CR programmes incurred similar costs, whether delivered in the patient's home (£196.53 per patient) or in a supervised hospital setting (£221.58 per patient).

Meta-regression

We examined predictors of all-cause mortality, all-cause hospitalisation, and HRQoL intervention effects (follow-up of 12 months or less) using univariate meta-regression. The no evidence of significant association (at P<0.05) between outcomes and study level covariates with the expection of study risk of bias (Table 3). The effect size for HRQoL and hospiatlisation for studies at high risk of bias were larger than for studies at low risk of bias.

Within-trial subgroup analyses

Several study 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 (e.g. 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 studies reported subgroup analyses when the methods were unclear (Pozehl 2008; Yeh 2011). Only the large HF ACTION trial undertook pre-defined formal interaction tests of differences in intervention effects between subgroups. HF ACTION study authors reported no evidence of differences in intervention effects as assessed for either the primary outcome (all-cause mortality or hospitalisation) or HRQoL (Kansas City Cardiomyopathy Questionnaire (KCCQ) overall score) across several participant-defined subgroups (Table 4). The HF ACTION 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.

Small-study bias

We found no evidence of funnel plot asymmetry for all-cause mortality or hospitalisations, nor for all HRQoL scores (Egger test P > 0.05) (Figure 4 Figure 5 Figure 6 and Figure 7). However, we found evidence of asymmetry for MLWHF measures (Egger test P < 0.0001) (Figure 8).

Figure 4. Funnel plot of comparison: 1 All exercise interventions versus usual care, outcome: 1.1 All-cause mortality up to 12 months' follow-up.

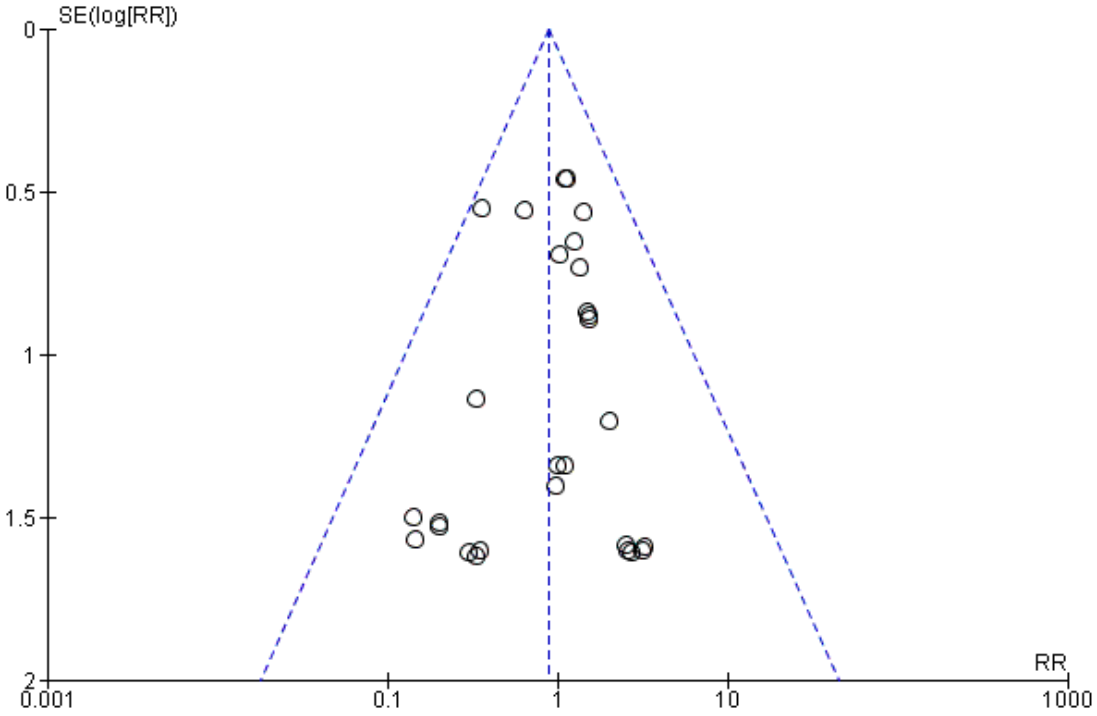


Figure 5. Funnel plot of comparison: 1 All exercise interventions versus usual care, outcome: 1.3 Hospital admission up to 12 months' follow-up.

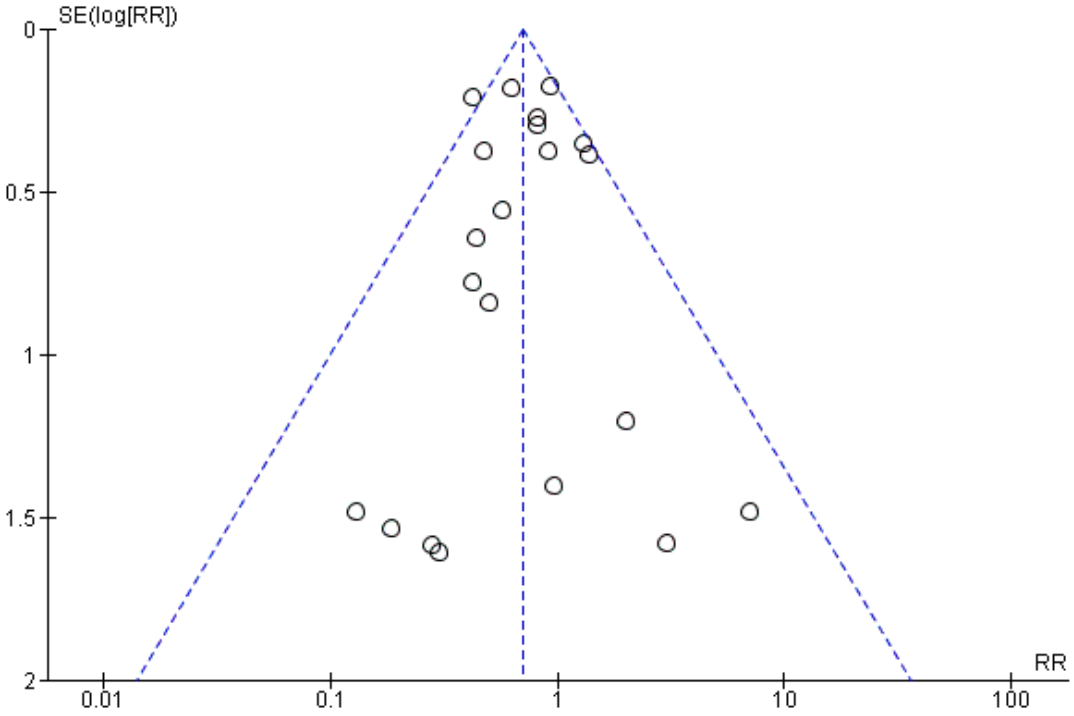


Figure 6. Funnel plot of comparison: 1 All exercise interventions versus usual care, outcome: 1.5 Hospital admission heart failure only.

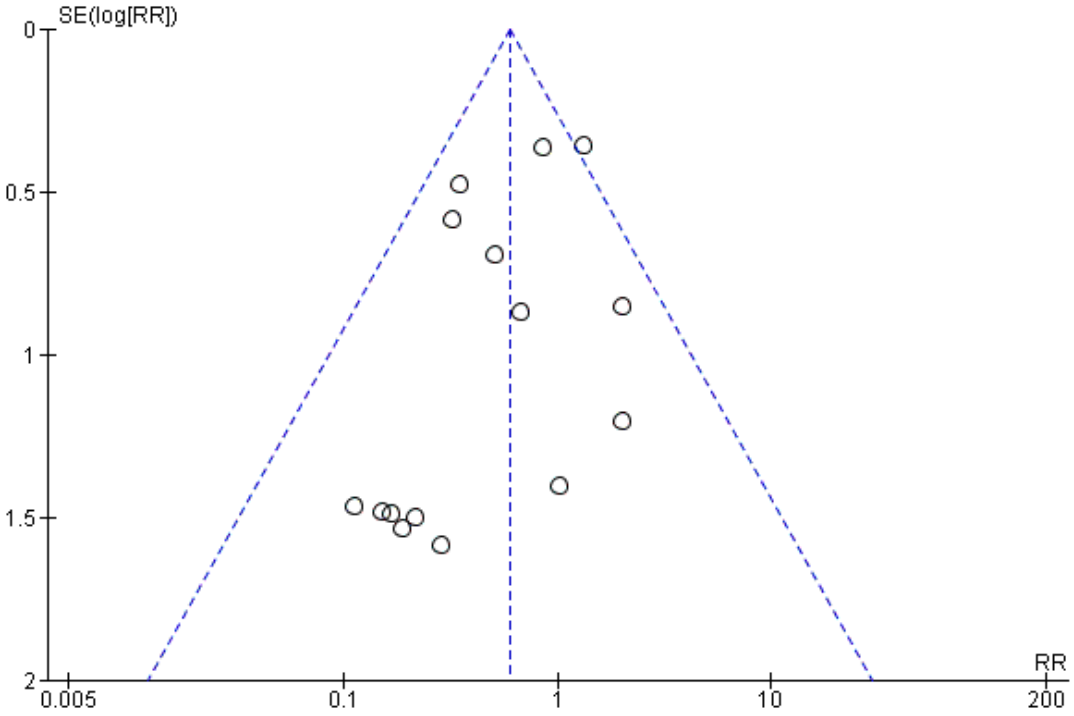


Figure 7. Funnel plot of comparison: 1 All exercise interventions versus usual care, outcome: 1.6 Health-related quality of life - MLWHF up to 12 months' follow-up.

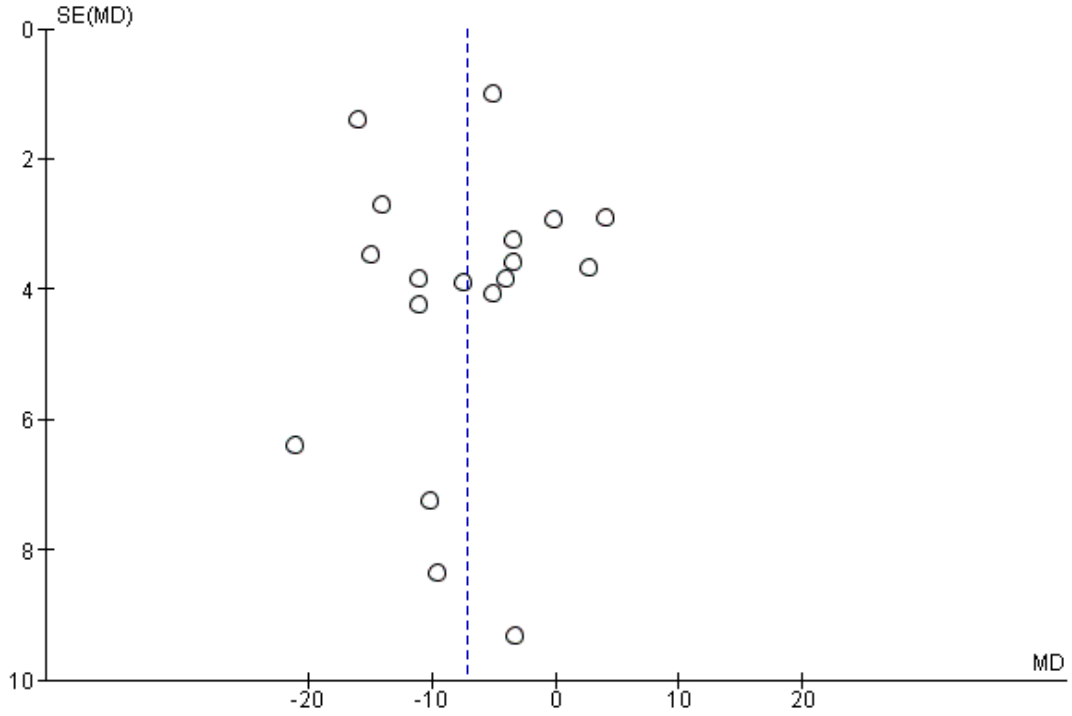
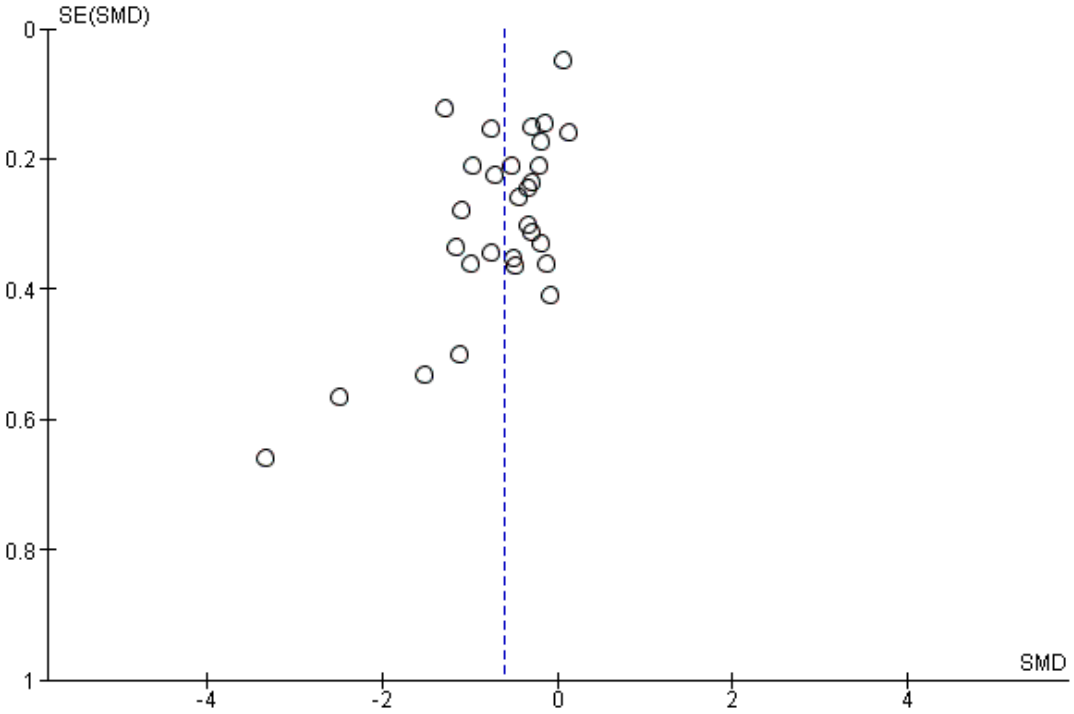


Figure 8. Funnel plot of comparison: 1 All exercise interventions versus usual care, outcome: 1.7 Health-related quality of life - MLWHF and other scales up to 12 months' follow-up.



DISCUSSION

Summary of main results

This review update shows that, based on low-quality evidence, when compared with no exercise control, exercise-based cardiac rehabilitation (CR) may have little or no effect on the risk of short-term (up to 12 months' follow-up) all-cause mortality. The included studies did not provide data on heart failure (HF)-related mortality. High-quality evidence shows a slight reduction in all-cause mortality in trials on exercise-based CR with follow-up in excess of 12 months. Low-quality evidence suggests a reduction in hospital admissions related to HF. Because evidence is of very low quality, we are uncertain about the effects of exercise-based CR on health-related quality of life (HRQoL). It is important to note that statistical heterogeneity was substantial among studies assessing HRQoL. Although studies support the cost-effectiveness of exercise-based CR compared to control, available evidence is sparse.

Overall completeness and applicability of evidence

The generalisability of the previous version of this review was limited as most included studies recruited only low- to moderate-risk younger men. However, with inclusion of more women, older patients, and people with HF with preserved ejection fraction (HFpEF) in recent trials, and with more trials of CR delivered in a home-based setting, the findings of this updated review have potentially greater external validity and applicability.

Quality of the evidence

The general lack of reporting of methods used in the included trials makes it difficult to assess their methodological quality; we therefore judged them to be at unclear risk of bias. Evidence of a large treatment effect for HRQoL outcomes in studies judged to be at overall high risk of bias compared with studies at low risk of bias suggests that risk of bias may be a major driver of the substantive statistical heterogeneity seen across trials for this outcome. Improvement in the quality of reporting is apparent in more recent trials.

Using the GRADE method, we assessed the quality of evidence

to range from high to very low across outcomes. We downgraded outcomes for hospital admissions (both all-cause over 12 months' follow-up and HF-related admissions) for risk of both bias and imprecision. In addition, we downgraded all-cause hospital admissions over 12 months' follow-up for inconsistency. We downgraded all-cause re-admissions at up to 12 months only for risk of bias. We downgraded all HRQoL outcomes for risk of bias and inconsistency, with HRQoL measured by the Minnesota Living With Heart Failure questionnaire (MLWHF) over 12 months' follow-up downgraded for imprecision, in addition to risk of bias and inconsistency. We downgraded all-cause mortality up to 12 months for risk of bias and imprecision; we considered evidence for all-cause mortality over 12 months to be of high quality and did not downgrade it based on any GRADE criteria.

Potential biases in the review process

We believe this is the most comprehensive systematic review to date of randomised controlled trial (RCT) evidence on the impact of exercise-based CR for people with HF. However, our review has some limitations. The overall risk of bias of included trials was generally low or unclear, although evidence shows improvement in the level of reporting in trials published over the last five to ten years. However, details of generation and concealment of random allocation sequence and blinding of outcome assessments were particularly poorly reported and therefore were subject to bias. Funnel plot asymmetry for HRQoL is indicative of small-study bias and possible publication bias. Although a specific goal of this updated review was to clarify the impact of exercise training programmes on clinical events, many included trials were relatively small and provided short-term follow-up (< 12 months), so that the numbers of deaths and hospitalisations reported by most trials were small. Indeed, for many studies, we located event data in the trial descriptions of losses to follow-up and exclusions rather than as reported outcomes per se. All included studies included a no formal exercise training intervention comparator. However, a wide range of comparators were seen across studies that included active intervention (i.e. education, psychological intervention) or usual medical care alone.

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 origjnally 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 HF with reduced ejection fraction (HFrEF). 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 (CIs) were wide (all-cause mortality: hazard ratio (HR) 0.83, 95% CI 0.67 to 1.04; HF-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 HF-specific hospitalisation: HR 0.98, 95% CI 0.72 to 1.35). Lack of statistically significant impact of CR on all-cause mortality is consistent with the findings of this updated Cochrane Review. However, the finding of no reduction in all-cause or HF hospitalisations with CR 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 HF 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 CR across patient characteristics (i.e. age, sex, ethnicity, New York Heart Association (NYHA) functional class, ischaemic aetiology, ejection fraction, exercise capacity) on mortality or hospitalisation outcomes.

Our findings are consistent with those of other systematic reviews/meta-analyses of RCTs for CR for HF published since the 2014 version of this review. Zhang and colleagues collated trial-level data from 2533 patients with HF enrolled in 28 published RCTs (Zhang 2018). Based on the MLWHF questionnaire, study 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, Chen and colleagues reported a pooled improvement in MLWHF score of -6.8 (95% CI -9.7 to -3.8; P < 0.0001) (Chen 2018). Finally, in accord with our updated Cochrane Review, Vromen 2018 found in a meta-regression analysis that CR exercise programme characteristics of frequency, intensity, and session duration were not predictive of CR outcomes. However, exercise programmes with higher overall energy expenditure did lead to better exercise capacity outcomes.

AUTHORS' CONCLUSIONS

Implications for practice

Results of this update review show that CR results in clinical improvement in HRQoL and reduces risk of hospitalisation, and that these benefits appear to be consistent across ExCR programme

characteristics (including centre and home CR settings) and support the recommendations provided in current international clinical guidelines that the offer of exercise-based CR should be made taking account of patient's preference for CR setting (ACCF/AHA 2013; ESC 2016; NICE 2018).

Implications for research

Despite clinical guidelines stating support of exercise-based CR for management of HF, internationally the provision and uptake of rehabilitation in HF remain poor (Bjarnason-Wehrens 2010; Golwala 2015). Further robust randomised trials are needed to assess the clinical effectiveness and economic value (costs and cost-effectiveness) of alternative models of exercise-based CR delivered as conventional centre-based programmes, as well as home- and technology-based programmes. Future trials must consider the generalisability of trial populations (women, older people, and people with HFpEF remain under-represented in trial populations); application of interventions to enhance long-term maintenance of exercise training and outcomes (Karmali 2014); and costs and cost-effectiveness of exercise-based CR programmes.

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REFERENCES

References to studies included in this review

Antonicelli 2016 *{published data only}*

Antonicelli R, Spazzafumo L, Scalvini S, Olivieri F, Matassini MV, Parati G, et al. Exercise: a "new drug" for elderly patients with chronic heart failure. *Aging* 2016;**8**(5): 860–72.

Austin 2005 *{published data only}*

Austin J, Williams R, Ross L, Moseley L, Hutchison S. Randomised controlled trial of cardiac rehabilitation in elderly patients with heart failure. *European Journal of Heart Failure* 2005;**7**(3):411–7.

Austin J, Williams WR, Hutchison S. Multidisciplinary management of elderly patients with chronic heart failure: five year outcome measures in death and survivor groups. *European Journal of Cardiovascular Nursing: Journal of the Working Group on Cardiovascular Nursing of the European Society of Cardiology* 2009;**8**(1):34–9. PUBMED: 18534911]

Austin J, Williams WR, Ross L, Hutchison S. Five-year follow-up findings from a randomized controlled trial of cardiac rehabilitation for heart failure. *European Journal of Cardiovascular Prevention and Rehabilitation* 2008;**15**(2): 162–7.

Belardinelli 1999 *{published data only}*

Belardinelli R, Georgiou D, Cianci G, Purcaro A. Randomized, controlled trial of long-term moderate exercise training in chronic heart failure: effects on functional capacity, quality of life, and clinical outcome. *Circulation* 1999;**99**(9):1173–82.

Georgiou D, Chen Y, Appadoo S, Belardinelli R, Greene R, Parides MK, et al. Cost-effectiveness analysis of long-term moderate exercise training in chronic heart failure. *American Journal of Cardiology* 2001;**87**:984–8.

Belardinelli 2012 *{published data only}*

Belardinelli R, Georgiou D, Cianci G, Purcaro A. 10-year exercise training in chronic heart failure: a randomized controlled trial. *Journal of the American College of Cardiology* 2012;**60**:1521–8.

Bocalini 2008 *{published data only}*

Bocalini DS, dos Santos L, Serra AJ. Physical exercise improves the functional capacity and quality of life in patients with heart failure. *Clinics (Sao Paulo, Brazil)* 2008; **63**:437–42.

Chen 2018 *{published data only}*

* Chen Y, Funk M, Wen J, Tang X, He G, Liu H. Effectiveness of a multidisciplinary disease management program on outcomes in patients with heart failure in China: a randomized controlled single center study. *Heart & Lung* 2018;**47**(1):24–31.

Chen YY, Liu H, Funk M, Wen J, Tang XH, He GX. Effectiveness of disease management program on clinical outcomes in patients with heart failure in China. *Journal of the American Geriatrics Society* 2016;**64**:S369.

Cowie 2014 *{published data only}*

Cowie A, Moseley O. Home- versus hospital-based exercise training in heart failure: an economic analysis. *British Journal of Cardiology* 2014;**21**(2):1–6.

Cowie A, Thow MK, Granat MH, Mitchell SL. A comparison of home- and hospital-based exercise training in heart failure: immediate and long-term effects upon physical activity level. *European Journal of Cardiovascular Prevention and Rehabilitation* 2011;**18**:158–66.

Cowie A, Thow MK, Granat MH, Mitchell SL. Effects of home- versus hospital-based exercise training in chronic heart failure. *International Journal of Cardiology* 2012;**158** (2):295–98.

Dalal 2018 *{published and unpublished data}*

* Dalal H, Taylor RS, Jolly K, Davis R, Doherty P, Miles J, et al. Facilitated self-care and rehabilitation for people with heart failure with reduced ejection fraction: the REACH-HF(Rehabilitation EnAblement in CHronic Heart Failure)

multicentre randomised controlled trial. Manuscript submitted for publication (obtained from authors).
Taylor RS, Hayward C, Eyre V, Austin J, Davies R, Doherty P, et al. The clinical effectiveness and cost-effectiveness of the Rehabilitation Enablement in Chronic Heart Failure (REACH-HF) facilitated self-care rehabilitation intervention in heart failure patients and caregivers: rationale and protocol for a multicentre randomised controlled trial. *BMJ Open* 2015;**5**(12):e009994.

DANREHAB 2008 ***{published data only}***
Zwisler AD, Schou L, Soja AM, Brønnum-Hansen H, Gluud C, Iversen L, et al. A randomized clinical trial of hospital-based, comprehensive cardiac rehabilitation versus usual care for patients with congestive heart failure, ischemic heart disease, or high risk of ischemic heart disease (the DANREHAB trial) - design, intervention, and population. *American Heart Journal* 2005;**899**:e16.
Zwisler AD, Soja AM, Rasmussen S, Frederiksen M, Abedini S, Appel J, et al. Hospital-based comprehensive cardiac rehabilitation versus usual care among patients with congestive heart failure, ischemic heart disease, or high risk of ischemic heart disease: 12-month results of a randomized clinical trial. *American Heart Journal* 2008;**155**:1106–13.

Davidson 2010 ***{published data only}***
Davidson PM, Cockburn J, Newton PJ, Webster JK, Betihavas V, Howes L, et al. Can a heart failure-specific cardiac rehabilitation program decrease hospitalizations and improve outcomes in high-risk patients?. *European Journal of Cardiovascular Prevention & Rehabilitation* 2010; **17**:393–402.

Dehkordi AH 2015 ***{published data only}***
Dehkordi AH, Far AK. Effect of exercise training on the quality of life and echocardiography parameter of systolic function in patients with chronic heart failure: a randomized trial. *Asian Journal of Sports Medicine* 2015;**6** (1):e22643.

Dracup 2007 ***{published data only}***
* Dracup K, Evangelista LS, Hamilton MA, Erickson V, Hage A, Moriguchi J, et al. Effects of a home-based exercise program on clinical outcomes in heart failure. *American Heart Journal* 2007;**154**(5):877–83.
Evangelista LS, Doering LV, Lennie T, Moser DK, Hamilton MA, Fonarow GC, et al. Usefulness of a home-based exercise program for overweight and obese patients with advanced heart failure. *American Journal of Cardiology* 2006;**97**(6):886–90. PUBMED: 16516595]
Evangelista LS, Hamilton MA, Fonarow GC, Dracup K. Is exercise adherence associated with clinical outcomes in patients with advanced heart failure?. *Physician & Sports Medicine* 2010;**38**:28–36.

Du 2018 ***{published data only}***
Du H, Newton PJ, Budhathoki C, Everett B, Salamonson Y, Macdonald PS, et al. The Home-Heart-Walk study: the effect of a self-administered walk test on perceived physical functioning and self-care behaviour in people with stable chronic heart failure: a randomized controlled trial. *European Journal of Cardiovascular Nursing* 2018;**17**: 235–45.

Gary 2010 ***{published data only}***
Gary RA, Dunbar SB, Higgins MK, Musselman DL, Smith AL. Combined exercise and cognitive behavioral therapy improves outcomes in patients with heart failure. *Journal of Psychosomatic Research* 2010;**69**(2):119–31. PUBMED: 20624510]

Giallauria 2008 ***{published data only}***
Giallauria F, Cirillo P, Lucci R, Pacileo M, De Lorenzo A, D'Agostino M, et al. Left ventricular remodelling in patients with moderate systolic dysfunction after myocardial infarction: favourable effects of exercise training and predictive role of N-terminal pro-brain natriuretic peptide. *European Journal of Cardiovascular Prevention and Rehabilitation* 2008;**15**(1):113–118.
Giallauria F, De Lorenzo A, Pilerci F, Manakos A, Lucci R, Psaroudaki M, et al. Reduction of N terminal-pro-brain (B-type) natriuretic peptide levels with exercise-based cardiac rehabilitation in patients with left ventricular dysfunction after myocardial infarction. *European Society of Cardiology* 2006;**13**(4):625–31.

Giannuzzi 2003 ***{published data only}***
Giannuzzi P, Temporelli PL, Corra U, Tavazzi L. Antiremodeling effect of long-term exercise training in patients with stable chronic heart failure: results of the Exercise in Left Ventricular Dysfunction and Chronic Heart Failure (ELVD-CHF) trial. *Circulation* 2003;**108**(5): 554–9.

Gielen 2003 ***{published data only}***
Gielen S, Adams V, Mobius-Winkler S, Linke A, Erbs S, Yu J, et al. Anti-inflammatory effects of exercise training in the skeletal muscle of patients with chronic heart failure. *Journal of the American College of Cardiology* 2003;**42**(5): 861–8.

Gottlieb 1999 ***{published data only}***
Gottlieb SS, Fisher ML, Freudenberger R, Robinson S, Zietowski G, Alves L, et al. Effects of exercise training on peak performance and quality of life in congestive heart failure patients. *Journal of Cardiac Failure* 1999;**5**(3): 188–94.

Hambrecht 1995 ***{published data only}***
Hambrecht R, Niebauer J, Fiehn E, Kalberer B, Offner B, Hauer K, et al. Physical training in patients with stable chronic heart failure: effects on cardiorespiratory fitness and ultrastructural abnormalities of leg muscles. *Journal of the American College of Cardiology* 1995;**25**(6):1239–49.

Hambrecht 1998 ***{published data only}***
Hambrecht R, Fiehn E, Weigl C, Gielen S, Hamann C, Kaiser R, et al. Regular physical exercise corrects endothelial dysfunction and improves exercise capacity in patients with chronic heart failure. *Circulation* 1998;**98**(24):2709–15.

Hambrecht 2000 ***{published data only}***
Hambrecht R, Gielen S, Linke A, Fiehn E, Yu J, Walther C, et al. Effects of exercise training on left ventricular function and peripheral resistance in patients with chronic

heart failure: a randomized trial. *JAMA* 2000;**283**(23): 3095–101.

HF ACTION 2009 ***{published data only}***

Banks AZMRJ, Stebbins A, Mikus CR, Schulte PJ, Fleg JL, Cooper LS, et al. Response to exercise training and outcomes in patients with heart failure and diabetes mellitus: insights from the HF-ACTION trial. *Journal of Cardiac Failure* 2016;**22**(7):485–91.

Flynn KE, Piña IL, Whellan DJ, Lin L, Blumenthal JA, Ellis SJ, et al. Effects of exercise training on health status in patients with chronic heart failure: HF-ACTION randomized controlled trial. *JAMA* 2009;**153**:1451–9.

Jones LW, Douglas PS, Khouri MG, Mackey JR, Wojdyla D, Kraus WE, et al. Safety and efficacy of aerobic training in patients with cancer who have heart failure: an analysis of the HF-ACTION randomized trial. *Journal of Clinical Oncology* 2014;**32**(23):2496–502.

Keteyian SJ, Leifer ES, Houston-Miller N, Kraus WE, Brawner CA, O'Connor CM, et al. Relation between volume of exercise and clinical outcomes in patients with heart failure. *Journal of the American College of Cardiology* 2012;**60**:1899–905.

Luo N, Merrill P, Whellan DJ, Pina IL, Fiuzat M, Kraus WE, et al. Exercise training in patients with chronic heart failure and atrial fibrillation: results from the HF-action trial. *Journal of Cardiac Failure* 2016;**22**:S71.

Luo NMP, Parikh KS, Whellan DJ, Pina IL, Fiuzat M, Kraus WE, et al. Exercise training in patients with chronic heart failure and atrial fibrillation. *Journal of the American College of Cardiology* 2017;**69**(13):1683–91.

Mentz RJ, Schulte PJ, Fleg JL, Fiuzat M, Kraus WE, Pina IL, et al. Clinical characteristics, response to exercise training, and outcomes in patients with heart failure and chronic obstructive pulmonary disease: findings from Heart Failure and A Controlled Trial Investigating Outcomes of Exercise TraiNing (HF-ACTION). *American Heart Journal* 2013;**165**(2):193–9.

Mentz RJBV, Schulte PJ, Fleg JL, Pina IL, Keteyian SJ, Moe G, et al. Race, exercise training, and outcomes in chronic heart failure: findings from Heart Failure - A Controlled Trial Investigating Outcomes in Exercise TraiNing (HF-ACTION). *American Heart Journal* 2013;**166**(3):488–95.

* O'Connor CM, Whellan DJ, Lee KL, Keteyian SJ, Cooper LS, Ellis SJ, et al. Efficacy and safety of exercise training in patients with chronic heart failure: HF-ACTION randomized controlled trial. *JAMA* 2009;**301**:1439–50.

Parikh KSCA, Schulte PJ, Kraus WE, Fleg JL, Keteyian SJ, Pina IL, et al. Relation of angina pectoris to outcomes, quality of life, and response to exercise training in patients with chronic heart failure (from HF-ACTION). *American Journal of Cardiology* 2016;**118**:1211–6.

Piccini JP, Hellkamp AS, Whellan DJ, Ellis SJ, Keteyian SJ, Kraus WE, et al. Exercise training and implantable cardioverter-defibrillator shocks in patients with heart failure: results from HF-ACTION (Heart Failure and A Controlled Trial Investigating Outcomes of Exercise TraiNing). *JACC Heart Failure* 2013;**1**(2):142–8.

Pina IL, Bittner V, Clare RM, Swank A, Kao A, Safford R, et al. Effects of exercise training on outcomes in women with heart failure: analysis of HF-ACTION (Heart Failure - A Controlled Trial Investigating Outcomes of Exercise TraiNing) by sex. *JACC Heart Failure* 2014;**2**(2):180–6.

Pina ILLL, Weinfurt KP, Isitt JJ, Whellan DJ, Schulman KA, Flynn KE, Investigators HF-ACTION. Hemoglobin, exercise training, and health status in patients with chronic heart failure (from the HF-ACTION randomized controlled trial). *American Journal of Cardiology* 2013;**112**:971–6.

Reed SD, Li Y, Dunlap ME, Kraus WE, Samsa GP, Schulman KA, et al. In-hospital resource use and medical costs in the last year of life by mode of death (from the HF-ACTION randomized controlled trial). *American Journal of Cardiology* 2012;**110**:1150–5.

Reed SD, Whellan DJ, Li Y, Friedman JY, Ellis SJ, Pina IL, et al. Economic evaluation of the HF-ACTION (heart failure: a controlled trial investigating outcomes of exercise training) randomized controlled trial: an exercise training study of patients with chronic heart failure. *Circulation: Cardiovascular Quality and Outcomes* 2010;**3**:374–81.

Verma AKS, Phillip J, Bittner V, Keteyian SJ, Fleg JL, Piña IL, et al. Socioeconomic and partner status in chronic heart failure: relationship to exercise capacity, quality of life, and clinical outcomes. *American Heart Journal* 2017;**183**: 54–61.

Whellan DJ, O'Connor CM, Lee KL, Keteyian SJ, Cooper LS, Ellis SJ, et al. Heart failure and a controlled trial investigating outcomes of exercise training (HF-ACTION): design and rationale. *American Heart Journal* 2007;**153**: 201–11.

Zeitler EPPJP, Hellkamp AS, Whellan DJ, Jackson KP, Ellis SJ, Kraus WE, et al. Exercise training and pacing status in patients with heart failure: results from HF-ACTION. *Journal of Cardiac Failure* 2015;**21**(1):60–7.

Jolly 2009 ***{published data only}***

Jolly K, Taylor RS, Lip GY, Davies M, Davis R, Mant J, et al. A randomized trial of the addition of home-based exercise to specialist heart failure nurse care: the Birmingham Rehabilitation Uptake Maximisation study for patients with Congestive Heart Failure (BRUM-CHF) study. *European Journal of Heart Failure* 2009;**11**:205–13.

Jolly K, Taylor RS, Lip GYH, Greenfield SM, Davies MK, Davis RC, et al. Home based exercise rehabilitation in addition to specialist heart failure nurse care: design, rationale and recruitment to the Birmingham Rehabilitation Uptake Maximisation study for patients with congestive heart failure (BRUM-CHF): a randomised controlled trial. *BMC Cardiovascular Disorders* 2007;**7**:7–9.

Jónsdóttir 2006a ***{published data only}***

Jónsdóttir S, Andersen KK, Sigurðsson AF, Sigurðsson SB. The effect of physical training in chronic heart failure. *European Journal of Heart Failure* 2006;**8**(1):97–101.

Kaltsatou 2014 ***{published data only}***

Kalsatou ACH, Kouidi EI, Anifanti MA, Douka SI, Deligiannis AP. Functional and psychosocial effects of either

a traditional dancing or a formal exercising training program in patients with chronic heart failure: a comparative randomized controlled study. *Clinical Rehabilitation* 2014; **28**(2):128–38.

Keteyian 1996 ***{published data only}***
Keteyian SJ, Levine AB, Brawner CA, Kataoka T, Rogers FJ, Schairer JR, et al. Exercise training in patients with heart failure. A randomized, controlled trial. *Annals of Internal Medicine* 1996;**124**(12):1051–7.

Klecha 2007 ***{published data only}***
Klecha A, Kawecka-Jaszcz K, Bacior B, Kubinyi A, Pasowicz M, Klimeczek P, et al. Physical training in patients with chronic heart failure of ischemic origin: effect on exercise capacity and left ventricular remodeling. *European Journal of Cardiovascular Prevention and Rehabilitation* 2007;**14**(1): 85–91.

Klocek 2005 ***{published data only}***
Klocek M, Kubinyi A, Bacior B, Kawecka-Jaszcz K. Effect of physical training on quality of life and oxygen consumption in patients with congestive heart failure. *International Journal of Cardiology* 2005;**103**(1):323–9.

Koukouvou 2004 ***{published data only}***
Koukouvou G, Kouidi E, Iacovides A, Konstantinidou E, Kaprinis G, Deligiannis A. Quality of life, psychological and physiological changes following exercise training in patients with chronic heart failure. *Journal of Rehabilitation Medicine* 2004;**36**:36–41.

Lang 2018 ***{published data only}***
Eyre V, Lang CC, Smith K, Jolly K, Davis R, Hayward C, et al. Rehabilitation Enablement in Chronic Heart Failure - a facilitated self-care rehabilitation intervention in patients with heart failure with preserved ejection fraction (REACH-HFpEF) and their caregivers: rationale and protocol for a single-centre pilot randomised controlled trial. *BMJ Open* 2016;**6**:e012853.
Lang CC, Smith K, Wingham J, Eyre V, Greaves C, Warren FC, et al. A randomised controlled trial of a facilitated home-based rehabilitation intervention in patients with heart failure with preserved ejection fraction and their caregivers: REACH-HFpEF pilot study. *BMJ Open* 2018;**8** (4):e019649.

McKelvie 2002 ***{published data only}***
McKelvie RS, Teo KK, Roberts R, McCartney N, Humen D, Montague T, et al. Effects of exercise training in patients with heart failure: the Exercise Rehabilitation Trial (EXERT). *American Heart Journal* 2002;**144**(1):23–30.

Mehani 2013 ***{published data only}***
Mehani SHM. Correlation between changes in diastolic dysfunction and health-related quality of life after cardiac rehabilitation program in dilated cardiomyopathy. *Journal of Advanced Research* 2013;**4**:189–200.

Mueller 2007 ***{published data only}***
Mueller L, Myers J, Kottman W, Oswald U, Boesch C, Arbrol N, et al. Exercise capacity, physical activity patterns and outcomes six years after cardiac rehabilitation in patients with heart failure. *Clinical Rehabilitation* 2007;**21** (10):923–31.

Myers 2000 ***{published data only}***
Myers J, Goebbels U, Dzeikan G, Froelicher V, Bremerich J, Mueller P, et al. Exercise training and myocardial remodeling in patients with reduced ventricular function: one-year follow-up with magnetic resonance imaging. *American Heart Journal* 2000;**139**(2 Pt 1):252–61. PUBMED: 10650298]

Nilsson 2008 ***{published data only}***
Nilsson BB, Westheim A, Risberg MA. Long-term effects of a group-based high-intensity aerobic interval-training program in patients with chronic heart failure. *American Journal of Cardiology* 2008;**102**:1220–4.

Norman 2012 ***{published data only}***
Norman JF, Pozehl BJ, Duncan KA, Hertzog MA, Krueger SK. Effects of exercise training versus attention on plasma B-type natriuretic peptide, 6-minute walk test and quality of life in individuals with heart failure. *Cardiopulmonary Physical Therapy Journal* 2012;**23**:19–25.
Pozehl B, Duncan K, Hertzog M, Norman JF. Heart failure exercise and training camp: effects of a multicomponent exercise training intervention in patients with heart failure. *Heart & Lung* 2010;**39**:S1–13.

Passino 2006 ***{published data only}***
Passino C, Severino S, Poletti R, Piepoli MF, Mammini C, Clerico A, et al. Aerobic training decreases B-type natriuretic peptide expression and adrenergic activation in patients with heart failure. *Journal of the American College of Cardiology* 2006;**47**:1835–9.

Pozehl 2008 ***{published data only}***
Pozehl B, Duncan K, Hertzog M. The effects of exercise training on fatigue and dyspnea in heart failure. *European Journal of Cardiovascular Nursing* 2008;**7**(2):127–32.

Reeves 2017 ***{published data only}***
Reeves GR, Whellan DJ, O'Conner CM, Duncan P, Eggebeen JD, Morgan TM, et al. A novel rehabilitation intervention for older patients with acute decompensated heart failure: the REHAB-HF pilot study. *JACC: Heart Failure* 2014;**5**(5):361.

Wall 2010 ***{published data only}***
Wall HK, Ballard J, Troped P, Njike VY, Katz DL. Impact of home-based, supervised exercise on congestive heart failure. *International Journal of Cardiology* 2010;**145**:267–70.

Willenheimer 2001 ***{published data only}***
Willenheimer R, Rydberg E, Cline C, Broms K, Hillberger B, Oberg L, et al. Effects on quality of life, symptoms and daily activity 6 months after termination of an exercise training programme in heart failure patients. *International Journal of Cardiology* 2001;**77**(1):25–31.

Witham 2005 ***{published data only}***
Witham MD, Gray JM, Argo IS, Johnston DW, Struthers AD, McMurdo ME. Effect of a seated exercise program to improve physical function and health status in frail patients

> or = 70 years of age with heart failure. *American Journal of Cardiology* 2005;**95**(9):1120–4. PUBMED: 15842989]

Witham 2012 *{published data only}*
Witham MD, Fulton RL, Greig CA, Johnston DW, Lang CC, van der Pol M, et al. Efficacy and cost of an exercise program for functionally impaired older patients with heart failure: a randomized controlled trial. *Circulation: Heart Failure* 2012;**5**:209–16.

Yeh 2011 *{published data only}*
Yeh GY, McCarthy EP, Wayne PM, Stevenson LW, Wood MJ, Davis RB, et al. Tai chi exercise in patients with chronic heart failure: a randomized clinical trial. *Archives of Internal Medicine* 2011;**171**:750–7.

References to studies excluded from this review

Abreu 2015 *{published data only}*
Abreu A, Santa CH, Santos V, Morais L, Oliveira L, Portugal G, et al. High intensity interval training effects in patients with heart failure submitted to cardiac resynchronization therapy. *European Heart Journal* 2015;**36**:461–2.

Adamopoulos 2001 *{published data only}*
Adamopoulos S, Parissis J, Kroupis C, Georgiadis M, Karatzas D, Karavolias G, et al. Physical training reduces peripheral markers of inflammation in patients with chronic heart failure. *European Heart Journal* 2001;**22**(9):791–7.

Agvall 2013 *{published data only}*
Agvall B, Alehagen U, Dahlstrom U. The benefits of using a heart failure management programme in Swedish primary healthcare. *European Journal of Heart Failure* 2013;**15**(2): 228–36.

Ahmad 2014 *{published data only}*
Ahmad T, Fiuzat M, Mark DB, Neely B, Neely M, Kraus WE, et al. The effects of exercise on cardiovascular biomarkers in patients with chronic heart failure. *American Heart Journal* 2014;**167**(2):193–202.

Alves 2012 *{published data only}*
Alves AJ, Ribeiro F, Goldhammer E, Rivlin Y, Rosenschein U, Viana JL, et al. Exercise training improves diastolic function in heart failure patients. *Medicine & Science in Sports & Exercise* 2012;**44**:776–85.

Ambrosy 2016 *{published data only}*
Ambrosy AP, Cerbin L, DeVore A, Greene S, Kraus WE, O'Connor C, et al. Aerobic exercise training and health status in ambulatory heart failure patients with a reduced ejection fraction: an analysis from the HF-ACTION trial. *Journal of the American College of Cardiology* 2016;**1**:1312.

Ambrosy 2017 *{published data only}*
Ambrosy AP, Cerbin L, DeVore A, Greene S, Kraus WE, O'Connor C, et al. Aerobic exercise training and health status in ambulatory heart failure patients with a reduced ejection fraction: An analysis from the HF-action trial. *Journal of the American College of Cardiology* 2016;**67**(13): 1312.
Ambrosy AP, Cerbin LP, DeVore AD, Greene SJ, Kraus WE, O'Conner CM, et al. Aerobic exercise training and general health status in ambulatory heart failure patients with a reduced ejection fraction - findings from the Heart Failure and A Controlled Trial Investigating Outcomes of Exercise Training (HF-ACTION) trial. *American Heart Journal* 2016;**186**:130–7.

Aronov 2015 *{published data only}*
Aronov DMB, Anzimirova NV, Novikova NK. Efficacy of the physical training in patients with heart failure after myocardial infarction. *European Journal of Heart Failure Abstracts Supplement* 2015;**17**(Suppl 1, 5-441):109. (P466).

Ascione 2013 *{published data only}*
Ascione A, Aversa M, Attena E, Sciarappa A, Borgia M, Parato V, Sangiuolo R. Benefits of exercise training in type2 diabetic patients with heart failure with preserved ejection fraction. *European Journal of Preventive Cardiology* 2013;**1**: S100.

Bachman 2015 *{published data only}*
Bachmann C. Effect of endurance training and hawthorn extract WS 1442 in patients with heart failure with preserved ejection fraction - a randomized controlled trial. *Schweizerische Zeitschrift fur Ganzheitsmedizin* 2015;**27**(5): 264–7.

Banks 2015 *{published data only}*
Banks AZ, Mentz R, Stebbins A, Mikus C, Schulte P, Fleg J, et al. Response to exercise training and outcomes in heart failure patients with diabetes mellitus: insights from HF-ACTION. *Journal of the American College of Cardiology* 2015;**1**:A1034.

Barrow 2008 *{published data only}*
Barrow DE, Bedford A, Ives G, O'Toole L, Channer KS. An evaluation of the effects of Tai Chi Chuan and Chi Kung training in patients with symptomatic heart failure: a randomised controlled pilot study. *Postgraduate Medical Journal* 2008;**83**(985):717–21.

Belardinelli 2005 *{published data only}*
Belardinelli R, Lacalaprice F, Faccenda E, Purcaro A, Perna G. Effects of short-term moderate exercise training on sexual function in male patients with chronic stable heart failure. *International Journal of Cardiology* 2005;**101**(1):83–90.

Belardinelli 2013 *{published data only}*
Belardinelli R, Georgiou D, Cianci G, Purcaro A. A 10-year exercise training in chronic heart failure: a randomized controlled trial. *Journal of the American College of Cardiology* 2012;**60**:1521–8.

Bernocchi 2016 *{published data only}*
Bernocchi P, Scalvini S, Galli T, Paneroni M, Baratti D, Turla O, et al. A multidisciplinary telehealth program in patients with combined chronic obstructive pulmonary disease and chronic heart failure: study protocol for a randomized controlled trial. *Trials* 2016;**17**(1):462.

Bittencourt 2015 *{published data only}*
Bittencourt L, Servante D, Javaheri S, Tufik S. Effects of exercise training and CPAP in patients with heart failure and obstructive sleep apnea. *Sleep* 2015;**38**:A177.

Borland 2014 *{published data only}*
Borland M, Rosenkvist A, Cider A. A group-based exercise program did not improve physical activity in patients with chronic heart failure and comorbidity: a randomized controlled trial. *Journal of Rehabilitation Medicine* 2014;**46** (5):461–7.

Boyd 2015 *{published data only}*
Boyd AM. Regular exercise improves weight stability in patients with advanced heart failure. *Therapeutic Advances in Cardiovascular Disease* 2015;**9**(5):297–304.

Brand 2014 *{published data only (unpublished sought but not used)}*
Brand AVADA, Giverts IYU, Gnedina AA, Dikur ON, Doletsky AA, Kuzmina ER, et al. Impact of short-term aerobic training program on long-term cardiovascular mortality in patients with systolic heart failure. *European Journal of Preventive Cardiology* 2014;**1**:575.

Briffa 2005 *{published data only}*
Briffa TG, Eckermann SD, Griffiths AD, Harris PJ, Heath MR, Freedman SB, et al. Cost-effectiveness of rehabilitation after an acute coronary event: a randomised controlled trial. *Medical Journal of Australia* 2005;**183**(9):450–5.

Brotons 2009 *{published data only}*
Brotons C, Falces C, Alegre J, Ballarín E, Casanovas J, Catà T, et al. Randomized clinical trial of the effectiveness of a home-based intervention in patients with heart failure: the IC-DOM study. *Revista Espanola de Cardiologia* 2009;**62**: 400–8.

Cameron 2015 *{published data only}*
Cameron J, Rendell PG, Ski CF, Kure CE, McLennan SM, Rose NS, et al. PROspective MEmory Training to improve HEart failUre Self-care (PROMETHEUS): study protocol for a randomised controlled trial. *Trials* 2015;**16**:196.

Chang 2005 *{published data only}*
Chang B, Zhang X, Peng W. Movement training for exercise tolerance and cardiac function in patients with chronic heart failure. *Chinese Journal of Clinical Rehabilitation* 2005;**9** (23):241–2.

Chrysohoou 2013 *{published data only}*
Chrysohoou C, Tsitsinakis G, Tsiachris D, Vogiatzis J, Tsantilas A, Dimopoulos D, et al. High intensity, interval exercise improves the quality of life and psychological status of patients with chronic heart failure: a phase III randomized clinical trial. *European Heart Journal* 2013;**34**: 670.

Chrysohoou 2014 *{published data only}*
Chrysohoou C, Tsitsinakis G, Vogiatzis I, Cherouveim E, Antoniou C, Tsiantilas A, et al. High intensity, interval exercise improves quality of life of patients with chronic heart failure: a randomized controlled trial. *QJM* 2014;**107** (1):25–32.

Chrysohoou 2016 *{published data only}*
Chrysohoou C, Tsitsinakis G, Aggelis A, Herouvim E, Tsiachris D, Vogiatzis I, et al. High-intensity interval training combined with strength exercise effect on aorto-ventricular coupling in patients with chronic heart failure. A randomized phase III clinical trial. *European Journal of Heart Failure* 2016;**18**:115.

Coats 1992 *{published data only}*
Coats A, Adamopoulos S, Radaelli A, McCance A, Meyer TE, Bernardi L, et al. Controlled trial of physical training in chronic heart failure. Exercise performance, haemodynamics, ventilation and autonomic function. *Circulation* 1992;**85**(6):2119–31.

Collins 2004 *{published data only}*
Collins E, Langbein WE, Dilan-Koetje J, Bammert C, Hanson K, Reda D, et al. Effects of exercise training on aerobic capacity and quality of life in individuals with heart failure. *Heart Lung* 2004;**33**(3):154–61.

Corvera-Tindel 2004 *{published data only}*
Corvera-Tindel T, Doering LV, Woo MA, Khan S, Dracup K. Effects of a home walking exercise program on functional status and symptoms in heart failure. *American Heart Journal* 2004;**147**(2):339–46.

Cowie 2011 *{published data only}*
Cowie A, Thow MK, Granat MH, Mitchell SL. A comparison of home- and hospital-based exercise training in heart failure: immediate and long-term effects upon physical activity level. *European Journal of Cardiovascular Prevention and Rehabilitation* 2011;**18**:158–66.

Cowie 2012 *{published data only}*
Cowie A, Thow MK, Granat MH, Mitchell SL. Effects of home- versus hospital-based exercise training in chronic heart failure. *International Journal of Cardiology* 2012;**158** (2):296–8.

Deng 2006 *{published data only}*
Deng Y, Zhang H, Wang F, lui S, Bi Y. Effects of six-minutes walking training on left ventricular ejection fractions and motor ability in chronic heart failure patients. *Chinese Journal of Clinical Rehabilitation* 2006;**7**(18):2542–3.

Dingli 2002 *{published data only}*
Xu D, Wang B, Hou Y, Hui H, Meng S, Liu Y. The effects of exercise training on plasma tumor necrosis factor-alpha, blood leucocyte and its components in congestive heart failure patients. *Chinese Journal of Internal Medicine* 2002; **41**(4):237–40.

Doukky 2016 *{published data only}*
Doukky R, Mangla A, Ibrahim Z, Poulin MF, Avery E, Collado FM, et al. Impact of physical inactivity on mortality in patients with heart failure. *American Journal of Cardiology* 2016;**117**(7):1135–43.

Duncan 2014 *{published data only}*
Duncan K, Pozehl B, Hertzog M, Norman JF. Psychological responses and adherence to exercise in heart failure. *Rehabilitation Nursing Journal* 2014;**39**(3):130–9.

Edelmann 2011 *{published data only}*
Edelmann F, Gelbrich G, Düngen HD, Fröhling S, Wachter R, Stahrenberg R, et al. Exercise training improves exercise capacity and diastolic function in patients with heart failure with preserved ejection fraction: results of the Ex-DHF (exercise training in diastolic heart failure) pilot study.

Journal of the American College of Cardiology 2011;**58**: 1780–91.

Erbs 2003 ***{published data only}***
Erbs S, Linke A, Gielen S, Fiehn E, Walther C, Yu J, et al. Exercise training in patients with severe chronic heart failure: impact on left ventricular performance and cardiac size. A retrospective analysis of the Leipzig Heart Failure Training Trial. *European Journal of Cardiovascular Prevention and Rehabilitation* 2003;**10**(5):223–44.

Erbs 2010 ***{published data only}***
Erbs S, Hollriegel R, Linke A, Beck EB, Adams V, Gielen S, et al. Exercise training in patients with advanced chronic heart failure (NYHA IIIb) promotes restoration of peripheral vasomotor function, induction of endogenous regeneration, and improvement of left ventricular function. *Circulation. Heart Failure* 2010;**3**(4):486–94. PUBMED: 20430934]

ExTraMATCH 2004 ***{published data only}***
Piepoli MF, Davos C, Francis DP, Coats AJ. Exercise training: meta-analysis of trials in patients with chronic heart failure (ExTraMATCH). *BMJ* 2004;**328**(7433):189.

Fernhall 2013 ***{published data only}***
Fernhall B. Long-term aerobic exercise maintains peak VO (2), improves quality of life, and reduces hospitalisations and mortality in patients with heart failure. *Journal of Physiotherapy* 2013;**59**(1):56.

Fischer 2015 ***{published data only}***
Fischer T, Alves M, Rolim N, Werner S, Schuett N, Bowen TS, et al. High intensity interval training attenuates endothelial dysfunction in heart failure with preserved ejection fraction (HFpEF). *European Journal of Preventive Cardiology* 2015;**1**:S160.

Franco 2006 ***{published data only}***
de Mello Franco FG, Santos AC, Rondon MU, Trombetta IC, Strunz C, Braga AM, et al. Effects of home-based exercise training on neurovascular control in patients with heart failure. *European Journal of Heart Failure* 2006;**8**(8): 851–5.

Fu 2013 ***{published data only}***
Fu TC, Wang CH, Lin PS, Hsu CC, Cherng WJ, Huang SC, et al. Aerobic interval training improves oxygen uptake efficiency by enhancing cerebral and muscular hemodynamics in patients with heart failure. *International Journal of Cardiology* 2013;**167**(1):41–50.

Galenko 2016 ***{published data only}***
Galenko VLLTA, Sitnikova MY. The analysis of efficiency of physical rehabilitation of patients with chronic heart failure. *European Journal of Heart Failure* 2016;**18**:54.

Gary 2004 ***{published data only}***
Gary RA, Sueta CA, Dougherty M, Rosenberg B, Cheek D, Preisser J, et al. Home-based exercise improves functional performance and quality of life in women with diastolic heart failure. *Heart Lung* 2004;**33**(4):210–8.

Gary 2007 ***{published data only}***
Gary R, Lee SY. Physical function and quality of life in older women with diastolic heart failure: effects of a progressive walking program on sleep patterns. *Progress in Cardiovascular Nursing* 2007;**22**(2):72–80. PUBMED: 17541316]

Gelbrich 2014 ***{published data only}***
Gelbrich G, Störk S, Kreißl-Kemmer S, Faller H, Prettin C, Heuschmann P, et al. Effects of structured heart failure disease management on mortality and morbidity depend on patients' mood: results from the Interdisciplinary Network for Heart Failure Study. *European Journal of Heart Failure* 2014;**16**(10):1133–41.

Haykowsky 2007 ***{published data only}***
Haykowsky MJ, Liang Y, Pechter D, Jones LW, McAlister FA, Clark AM. A meta-analysis of the effect of exercise training on left ventricular remodeling in heart failure patients: the benefit depends on the type of training performed. *Journal of the American College of Cardiology* 2007;**19**:2329–36.

Hollriegal 2016 ***{published data only}***
Hollriegel R, Winzer EB, Linke A, Adams V, Mangner N, Sandri M, et al. Long-term exercise training in patients with advanced chronic heart failure: sustained benefits on left ventricular performance and exercise capacity. *Journal of Cardiopulmonary Rehabilitation & Prevention* 2016;**36**(2): 117–24.

Huang 2014 ***{published data only (unpublished sought but not used)}***
Huang WLYL. Cardiac rehabilitation in elderly patients with chronic heart failure. *Journal of the American Geriatrics Society* 2014;**62**:S367. (P106).

Hwang 2015 ***{published data only}***
Hwang R, Morris N, Mandrusiak A, Mudge A, Suna J, Adsett J, et al. Timed up and go test: a reliable test in patients with chronic heart failure?. *Heart Lung and Circulation* 2015;**24**:S458.

Hwang 2016 ***{published data only}***
Hwang R, Bruning J, Mandrusiak A, Morris N, Russell T. Providing heart failure rehabilitation in the home via telerehabilitation. *Heart Lung and Circulation* 2016;**25**:54.

Inglis 2006 ***{published data only}***
Inglis SC, Pearson S, Treen S, Gallasch T, Horowitz JD, Stewart S. Extending the horizon in chronic heart failure: effects of multidisciplinary, home-based intervention relative to usual care. *Circulation* 2006;**114**(23):2466–73.

Jónsdóttir 2006b ***{published data only}***
Jónsdóttir S, Andersen KK, Sigurosson AF, Sigurosson SB. The effect of physical training in chronic heart failure. *European Journal of Heart Failure* 2006;**1**(97):97–101.

Kaltsatou 2013 ***{published data only}***
Kaltsatou A, Kouidi E, Anifanti M, Douka S, Deligiannis A. Functional and psychosocial effects of exercise training with traditional dancing in patients with chronic heart failure EBTR. *European Journal of Preventive Cardiology* 2013;**1**: S31.

Kelly 2016 ***{published data only}***
Kelly JP, Dunning A, Schulte PJ, Fiuzat M, Leifer ES, Fleg JL, et al. Statins and exercise training response in heart

failure patients: insights from HF-ACTION. *JACC Heart Failure* 2016;**4**(8):617–24.

Keteyian 2016 ***{published data only}***

Keteyian SJ, Patel M, Kraus WE, Brawner CA, McConnell TR, Piña IL, et al. Variables measured during cardiopulmonary exercise testing as predictors of mortality in chronic systolic heart failure. *Journal of the American College of Cardiology (JACC)* 2016;**67**(7):780–9.

Kiilavuori 1999 ***{published data only}***

Kiilavuori K, Näveri H, Salmi T, Härkönen M. The effect of physical training on hormonal status and exertional hormonal response in patients with chronic congestive heart failure. *European Heart Journal* 1999;**20**:456–64.

Kitzman 2010 ***{published data only}***

Kitzman DW, Brubaker PH, Morgan TM, Stewart KP, Little WC. Exercise training in older patients with heart failure and preserved ejection fraction: a randomized, controlled, single-blind trial. *Circulation: Heart Failure* 2010;**3**:659–67.

Kitzman 2013 ***{published data only}***

Kitzman DW, Brubaker PH, Herrington DM, Morgan TM, Stewart KP, Hundley WG, et al. Effect of endurance exercise training on endothelial function and arterial stiffness in older patients with heart failure and preserved ejection fraction: a randomized, controlled, single-blind trial. *Journal of the American College of Cardiology* 2013;**62**(7):584–92.

Kitzman 2016 ***{published data only}***

Kitzman DW, Brubaker PH, Morgan TM, Haykowsky MJ, Hundley WG, Kraus W, et al. Effect of caloric restriction of aerobic exercise training on peak oxygen consumption and quality of life in obese older patients with heart failure and preserved ejection fraction: a randomized clinical trial. *JAMA* 2016;**315**(1):36–46.

Kobayashi 2003 ***{published data only}***

Kobayashi N, Tsuruya Y, Iwasawa T, Ikeda N, Hashimoto S, Yasu T, et al. Exercise training in patients with chronic heart failure improves endothelial function predominantly in the trained extremities . *Circulation* 2003;**67**(6):505–10.

Kolesnikova 2015 ***{published data only (unpublished sought but not used)}***

Kolesnikova EAG, Rylova A, Lobzeva V. Physical rehabilitation in patients with severe heart failure. *Circulation* 2015;**131**:AP 385.

Korzeniowska-Kubacka 2010 ***{published data only}***

Korzeniowska-Kubacka I, Bilińska M, Michalak E, Kuśmierczyk-Droszcz B, Dobraszkiewicz-Wasilewska B, Piotrowicz R. Influence of exercise training on left ventricular diastolic function and its relationship to exercise capacity in patients after myocardial infarction. *Cardiology* 2010;**23**:136–42.

Koufaki 2014 ***{published data only}***

Koufaki P, Mercer TH, George KP, Nolan J. Low-volume high-intensity interval training vs continuous aerobic cycling in patients with chronic heart failure: a pragmatic randomised clinical trial of feasibility and effectiveness. *Journal of Rehabilitation Medicine* 2014;**46**(4):348–56.

Koukoui 2015 ***{published data only}***

Koukoui F, Desmoulin F, Lairy G, Bleinc D, Boursiquot L, Galinier M, et al. Benefits of cardiac rehabilitation in heart failure patients according to etiology: INCARD French study. *Medicine* 2015;**94**(7):e544.

Larsen 2016 ***{published data only}***

Larsen P, Pedersen PU. The effectiveness of individual rehabilitation on health status in patients with heart failure: a quasi-experimental study. *International Journal of Nursing Practice* 2016;**22**(1):15–21.

Lewinter 2014 ***{published data only (unpublished sought but not used)}***

Lewinter CTL, Doherty P, Kober L, Zwisler AD. Effectiveness of cardiac rehabilitation in HF patients: a long-term follow-up of the DANREHAB-trial. *European Journal of Heart Failure Abstarcts Supplement* 2014;**16**(Suppl 2):60.

Lloyd-Williams 2002 ***{published data only}***

Lloyd-Williams F, Mair FS, Leitner M. Exercise training and heart failure: a systematic review of current evidence. *British Journal of General Practice* 2002;**52**(474):47–55.

Masterson 2014 ***{published data only}***

Masterson CRM, Lee CS, Margulies K, Ellis S, Riegel B. Exercise in heart failure and patterns of inflammation and myocardial stress over time. *Circulation* 2014;**130**(Suppl 2): A11902.

McCarthy 2013 ***{published data only}***

McCarthy M. Exercise Counseling in Low-Income Ethnic Minority Individuals With Heart Failure: A Pilot Study [PhD Thesis]. New York (USA): New York University 2013.

Mediano 2016 ***{published data only}***

Mediano MFF, Mendes F, Pinto VLM, da Silva GMS, da Silva PS, Carneiro FM, et al. Cardiac rehabilitation program in patients with Chagas heart failure: a single-arm pilot study. *Revista Da Sociedade Brasileira De Medicina Tropical* 2016;**49**(3):319–28.

Mehralian 2014 ***{published data only}***

Mehralian H, Salehi S, Moghaddasi J, Amiri M, Rafiei H. The comparison of the effects of education provided by nurses on the quality of life in patients with congestive heart failure (CHF) in usual and home-visit cares in Iran. *Global Journal of Health Science* 2014;**6**(3):256–60.

Mendes 2014 ***{published data only}***

Mendes RG, Simoes RP, Costa Fde S, Pantoni CB, Di Thommazo-Luporini L, Luzzi S, et al. Is applying the same exercise-based inpatient program to normal and reduced left ventricular function patients the best strategy after coronary surgery? A focus on autonomic cardiac response. *Disability & Rehabilitation* 2014;**36**(2):155–62.

Meyer 2005 ***{published data only}***

Meyer T, Görge G, Schwaab B, Hildebrandt K, Walldorf J, Schäfer C, et al. An alternative approach for exercise

prescription and efficacy testing in patients with chronic heart failure: a randomized controlled training study. *American Heart Journal* 2005;**149**(5):e1–7.

Molloy 2006 ***{published data only}***
Molloy GJ, Johnston DW, Gao C, Witham MD, Gray JM, Argo IS, et al. Effects of an exercise intervention for older heart failure patients on caregiver burden and emotional distress. *European Journal of Cardiovascular Prevention and Rehabilitation* 2006;**13**(3):381–7.

Myers 2001 ***{published data only}***
Myers J, Gianrossi R, Schwitter J, Wagner D, Dubach P. Reduced ventricular function oxygen uptake kinetics in patients with effect of exercise training on postexercise. *Chest* 2001;**120**(4):1206–11.

Myers 2002 ***{published data only}***
Myers J, Wagner D, Schertler T, Beer M, Luchinger R, Klein M, et al. Effects of exercise training on left ventricular volumes and function in patients with nonischemic cardiomyopathy: application of magnetic resonance myocardial tagging. *American Heart Journal* 2002;**144**(4): 719–25.

Myers 2007 ***{published data only}***
Myers J, Hadley D, Oswald U, Bruner K, Kottman W, Hsu L, et al. Effects of exercise training on heart rate recovery in patients with chronic heart failure. *American Heart Journal* 2007;**152**(6):1056–63.

Newton 2013 ***{published data only (unpublished sought but not used)}***
Newton P, Du H, Everett B, Salamonson Y, Davidson P. Home heart walk to improve self-care in chronic heart failure: a randomised controlled trial. *Heart Lung and Circulation* 2013;**22**(Suppl 1):S242.

Niebauer 2005a ***{published data only}***
Niebauer J, Clark AL, Webb-Peploe KM, Coats AJ. Exercise training in chronic heart failure: effects on pro-inflammatory markers. *European Journal of Heart Failure* 2005;**7**(2):189–93.

Niebauer 2005b ***{published data only}***
Niebauer J, Clark AL, Webb-Peploe KM, Böger R, Coats AJ. Home-based exercise training modulates pro-oxidant substrates in patients with chronic heart failure. *European Journal of Heart Failure* 2005;**7**(2):183–8.

Oka 2000 ***{published data only}***
Oka RK, De Marco T, Haskell WL, Botvinick E, Dae MW, Bolen K, et al. Impact of a home-based walking and resistance training program on quality of life in patients with heart failure. *American Journal of Cardiology* 2000;**85** (3):365–9.

Oliveira 2015 ***{published data only}***
Oliveira MF, Santos RL, Mendez VM, Sperandio PA, Umeda II, Correa EB, et al. Safety and efficacy of non-invasive ventilation during exercise training in patients with acute heart failure. A randomized prospective controlled study. *Circulation* 2015;**132**(Suppl 3):A15821.

Owen 2000 ***{published data only}***
Owen A, Croucher L. Effect of an exercise programme for elderly patients with heart failure. *European Journal of Heart Failure* 2000;**2**(1):65–70.

Parnell 2002 ***{published data only}***
Parnell MM, Holst DP, Kaye DM. Exercise training increases arterial compliance in patients with congestive heart failure. *Clinical Science (London)* 2002;**102**(1):1–7.

Passino 2008 ***{published data only}***
Passino C, Del Ry S, Severino S, Gabutti A, Prontera C, Clerico A, et al. C-type natriuretic peptide expression in patients with chronic heart failure: effects of aerobic training. *European Journal of Cardiovascular Prevention & Rehabilitation* 2008;**15**:168–72.

Pinto 2015 ***{published data only}***
Pinto R, Abreu A, Santos V, Melo X, Cunha P, Oliveira M, et al. Optimizing patient benefit from CRT response with the addition of high intensity interval training - a randomized controlled trial. *European Heart Journal* 2015; **36**:516.

Piotrowicz 2015 ***{published data only}***
Piotrowicz E, Zielinski T, Bodalski R, Rywik T, Dobraszkiewicz-Wasilewska B, Sobieszczanska-Malek M, et al. Home-based telemonitored Nordic walking training is well accepted, safe, effective and has high adherence among heart failure patients, including those with cardiovascular implantable electronic devices: a randomised controlled study. *European Journal of Preventive Cardiology* 2015;**22** (11):1368–77.

Ponikowski 1997 ***{published data only}***
Ponikowski P, Szelemej R, Kowalska-Superlak M, Kratochwil D, Sobkowicz B, Sebzda T, et al. Exercise rehabilitation in patients with moderate-severe chronic heart failure. *Kardiologia Polska* 1997;**47**(10):291–300.

Pozehl 2003 ***{published data only}***
Pozehl B, Duncan K, Krueger S, VerMaas P. Adjunctive effects of exercise training in heart failure patients receiving maximum pharmacologic therapy. *Progress in Cardiovascular Nursing* 2003;**18**(4):177–83.

Pu 2001 ***{published data only}***
Pu CT, Johnson MT, Forman DE, Hausdorff JM, Roubenoff R, Foldvari M, et al. Randomized trial of progressive resistance training to counteract the myopathy of chronic heart failure. *Journal of Applied Physiology* 2001; **90**(6):2341–50.

Roscani 2016 ***{published data only}***
Roscani MG, Valadao TFC, Ribeiro FHO, Araujo Junior JA, Rossi DAA, Borra RC, et al. What is the role of diastolic function in the quality of life and functional capacity of patients with heart failure undergoing a combined exercise program. *Journal of the American Society of Echocardiography* 2016;**29**(6):B126.

Sabelis 2004 ***{published data only}***
Sabelis LW, Senden PJ, Te Boekhorst BC, Hulzebos HJ, Van De Wiel A, Van Haeften TW, et al. Does physical training

increase insulin sensitivity in chronic heart failure patients?. *Clinical Science (London)* 2004;**106**(5):459–66.

Santos 2015 *{published data only}*

Santos VT, Abreu A, Pinto R, Melo X, Cunha P, Oliveira M, et al. Effectiveness of high intensity interval training on cardiac remodelling in cardiac resynchronization therapy responders and non-responders: a randomized control trial. *European Journal of Preventive Cardiology* 2015;**1**:S95.

Sarullo 2006 *{published data only}*

Sarullo MF, Gristina T, Brusca I, Milia S, Raimondi R, Sajeva M, et al. Effect of physical training on exercise capacity, gas exchange and N-terminal pro-brain natriuretic peptide levels in patients with chronic heart failure. *European Journal of Cardiovascular Prevention and Rehabilitation* 2006;**13**(5):812–7.

Scalvini 2016 *{published data only}*

Scalvini SBP, Baratti D, Gatti T, Paneroni M, La Rovere MT, Volterrani M, Vitacca M. Multidisciplinary telehealth program for patients affected by chronic heart failure and chronic obstructive pulmonary disease. *European Journal of Heart Failure (Abstracts for European Society of Cardiology)* 2016;**94**:P391.

Schuang 2014 *{published data only}*

Shuang G, Yue L, Bin Y. Observation of effects of individualized rehabilitation guidance on patients with heart failure after myocardial infarction. *Journal of the American College of Cardiology* 2014;**1**:C187.

Selig 2004 *{published data only}*

Selig SE, Carey MF, Menzies DG, Patterson J, Geerling RH, Williams AD, et al. Moderate-intensity resistance exercise training in patients with chronic heart failure improves strength, endurance, heart rate variability, and forearm blood flow. *Journal of Cardiac Failure* 2004;**10**(1):21–30.

Senden 2005 *{published data only}*

Senden PJ, Sabelis LW, Zonderland ML, Hulzebos EH, Bol E, Mosterd WL. The effect of physical training on workload, upper leg muscle function and muscle areas in patients with chronic heart failure. *International Journal of Cardiology* 2005;**100**(2):293–300.

Smart 2004 *{published data only}*

Smart N, Marwick TH. Exercise training for patients with heart failure: a systematic review of factors that improve mortality and morbidity. *American Journal of Medicine* 2004;**116**:693–706.

Smart 2007 *{published data only}*

Smart N, Haluska B, Jeffriess L, Marwick TH. Exercise training in systolic and diastolic dysfunction: effects on cardiac function, functional capacity, and quality of life. *American Heart Journal* 2007;**119**:1097.

Smolis-Bak 2015 *{published data only}*

Smolis-Bak E, Dabrowski R, Piotrowicz E, Chwyczko T, Dobraszkiewicz-Wasilewska B, Kowalik I, et al. Hospital-based and telemonitoring guided home-based training programs: effects on exercise tolerance and quality of life in patients with heart failure (NYHA class III) and cardiac resynchronization therapy. A randomized, prospective observation. *International Journal of Cardiology* 2015;**199**: 442–7.

Smolis-Bak 2017 *{published data only}*

Smolis-Bąk E, Rymuza H, Kazimierska B, Kowalik I, Chwyczko T, Borowiec A, et al. Improvement of exercise tolerance in cardiopulmonary testing with sustained safety after regular training in outpatients with systolic heart failure (NYHA III) and an implantable cardioverter-defibrillator. Prospective 18-month randomized study. *Archives of Medical Science* 2017;**13**(5):1094–101.

Soska 2014 *{published data only}*

Soska V, Dobsak P, Pohanka M, Spinarova L, Vitovec J, Krejci J, et al. Exercise training combined with electromyostimulation in the rehabilitation of patients with chronic heart failure: a randomized trial. *Biomedical Papers of the Medical Faculty of Palacky University in Olomouc, Czech Republic* 2014;**158**(1):98–106.

Stewart 1998 *{published data only}*

Stewart S, Pearson S, Horowitz JD. Effects of a home-based intervention among patients with congestive heart failure discharged from acute hospital care. *Archives of Internal Medicine* 1998;**158**(10):1067–72.

Suna 2015 *{published data only}*

Suna JM, Mudge A, Stewart I, Marquart L, O'Rourke P, Scott A. The effect of a supervised exercise training programme on sleep quality in recently discharged heart failure patients. *European Journal of Cardiovascular Nursing* 2015;**14**(3):198–205.

Sviridenko 2013 *{published data only}*

Sviridenko VP, Poltavskaya MG, Brand AV, Giverts, IYU, Dikur ON, Andreev DA, et al. Comparison of functional electric stimulation and conventional bicycle exercise training in patients hospitalized for decompensation of chronic heart failure. *European Heart Journal* 2013;**34**:671.

Takase 2015 *{published data only}*

Takase K, Matsuo Y, Yanagisawa Y, Higashine K, Oda M, Manabe M, et al. Efficacy of a home-based exercise program for recently hospitalized chronic heart failure patients. *Physiotherapy* 2015;**101**:eS1477.

Taylor-Piliae 2004 *{published data only}*

Taylor-Piliae RE, Froelicher ES. The effectiveness of Tai Chi exercise in improving aerobic capacity: a meta-analysis. *Holistic Nursing Practice* 2004;**18**(5):254–63.

Tyni-Lenne 2001 *{published data only}*

Tyni-Lenné R, Dencker K, Gordon A, Jansson E, Sylvén C. Comprehensive local muscle training increases aerobic working capacity and quality of life and decreases neurohormonal activation in patients with chronic heart failure. *European Journal of Heart Failure* 2001;**3**(1):47–52.

van den Berg-Emons 2004 *{published data only}*

van den Berg-Emons R, Balk A, Bussmann H, Stam H. Does aerobic training lead to a more active lifestyle and improved quality of life in patients with chronic heart

failure?. *European Journal of Heart Failure* 2004;**6**(1): 95–100.

van Tol 2006 ***{published data only}***
van Tol BA, Huijsmans RJ, Kroon DW, Schothorst M, Kwakkel G. Effects of exercise training on cardiac performance, exercise capacity and quality of life in patients with heart failure: a meta-analysis. *European Journal of Heart Failure* 2006;**8**:841–50.

Vasiliauskas 2007 ***{published data only}***
Vasiliauskas D, Benetis R, Jasiukeviciene L, Grizas V, Marcinkeviciene J, Navickas R, et al. Exercise training after coronary angioplasty improves cardiorespiratory function. *Scandinavian Cardiovascular Journal* 2007;**41**(3):142–8. PUBMED: 17487762]

Von Oehsen 2013 ***{published data only}***
Von Oehsen K, Wachter R, Durstewitz K, Duvinage A, Stahrenberg R, Holzendorf V, et al. Exercise training benefits according to age and sex in diastolic heart failure. *Internist* 2013;**54**:103.

Wagenaar 2014 ***{published data only}***
Wagenaar KP, Broekhuizen BDL, Jaarsma T, Mosterd A, Willems FF, Dickstein K, et al. Effectiveness of an interactive platform with disease management facilities, and of the ESC/HFA heartfailurematters.org website: a 3-arm multicenter randomised trial, the e-Vita heart failure study. *European Journal of Heart Failure* 2014;**16**:256.

Wielenga 1998 ***{published data only}***
Wielenga RP, Erdman RA, Huisveld IA, Bol E, Dunselman PH, Baselier MR, et al. Effect of exercise training on quality of life in patients with chronic heart failure. *Journal of Psychosomatic Research* 1998;**45**(5):459–64.

Williams 2007 ***{published data only}***
Williams AD, Carey MF, Selig S, Hayes A, Krum H, Patterson J, et al. Circuit resistance training in chronic heart failure improves skeletal muscle mitochondrial ATP production: a randomized controlled trial. *Journal of Cardiac Failure* 2007;**13**(2):79–85.

Wisløff 2007 ***{published data only}***
Wisløff U, Støylen A, Loennechen JP, Bruvold M, Rognmo Ø, Haram PM, et al. Superior cardiovascular effect of aerobic interval training versus moderate continuous training in heart failure patients. *Circulation* 2007;**115**(24): 3042–94.

Yasushi 2015 ***{published data only}***
Yasushi TY. The impact of aerobic exercise training with vascular occlusion in patients with chronic heart failure. *European Journal of Preventive Cardiology* 2015;**1**:S93.

Yeh 2004 ***{published data only}***
Yeh GY, Wood MJ, Lorell BH, Stevenson LW, Eisenberg DM, Wayne PM, et al. Effects of tai chi mind-body movement therapy on functional status and exercise capacity in patients with chronic heart failure: a randomized controlled trial. *American Journal of Medicine* 2004;**117**(8): 541–8.

Zhang 2003 ***{published data only}***
Zhang F, Lui J, Zhang S, Yuan M. Effect of walking movement on plasma TNF and receptor in chronic heart failure patients. *Chinese Journal of Clinical Rehabilitation* 2003;**7**(24):2248–9.

Zhao 2005 ***{published data only}***
Zhao X. Effects of exercise training on the improvement of cardiac function and exercise endurance in patients with chronic heart failure. *Chinese Journal of Clinical Rehabilitation* 2005;**9**(16):170–1.

References to studies awaiting assessment

ACTR12608000263392 ***{published data only}***
Mudge AM, Denaro CP, Scott AC, Atherton JJ, Meyers DE, Marwick TH, et al. Addition of supervised exercise training to a post-hospital disease management program for patients recently hospitalized with acute heart failure: the EJECTION-HF randomized phase 4 trial. *JACC: Heart Failure* 2018;**6**(2):143–52.
Mudge AM, Denaro CP, Scott AC, Atherton JJ, Meyers DE, Marwick TH, et al. Exercise training in recently hospitalized heart failure patients enrolled in a disease management programme: design of the EJECTION-HF randomized controlled trial. *European Journal of Heart Failure* 2011;**13**:1370–5.

ISRCTN86879094 ***{published data only}***
Edelmann F, Bobenko A, Gelbrich G. Hasenfuss G, Herrmann-Lingen C, Duvinage A, et al. Exercise training in diastolic heart failure (Ex-DHF): rationale and design of a multicentre, prospective, randomized, controlled, parallel group trial. *European Journal of Heart Failure* 2017;**19**(8): 1067–74.
ISRCTN86879094. Exercise training in diastolic heart failure: a prospective, randomized, controlled study to determine the effects of exercise training in patients with heart failure and preserved ejection fraction (Ex-DHF). www.controlled-trials.com/ISRCTN86879094/ (accessed 11 April 2014).

NCT01033591 ***{published data only}***
NCT01033591. Exercise for patients with heart failure in primary care: the EFICAR. ClinicalTrials.gov/show/NCT01033591 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2835681/ (accessed 18 April 2018).

NCT01785121 ***{published data only}***
Jaarsma T, Klompstra L, Ben Gal T, Boyne J, Vellone E, Back M, et al. Increasing exercise capacity and quality of life of patients with heart failure through Wii gaming: the rationale, design and methodology of the HF-Wii study; a multicentre randomized controlled trial. *European Journal of Heart Failure* 2015;**17**:743–8.

NCT02078947 ***{published data only}***
Suchy C, Massen L, Rognmo O, Van Craenenbroeck EM, Beckers P, Kraigher-Krainer E, et al. Optimising exercise training in prevention and treatment of diastolic heart failure (OptimEx-CLIN): rationale and design of a

prospective, randomised, controlled trial. *European Journal of Preventive Cardiology* 2014;**21**:18–25.

NCT02696486 ***{published data only}***

NCT02903225 ***{published data only}***

References to ongoing studies

NCT01914315 ***{published data only}***

Koifman E, Grossman E, Elis A, Dicker D, Koifman B, Mosseri M, et al. Multidisciplinary rehabilitation program in recently hospitalized patients with heart failure and preserved ejection fraction: rationale and design of a randomized controlled trial. *American Heart Journal* 2014; **168**(6):830–7.

NCT02196038 ***{published data only}***

Reeves GR, Whellan DJ, Duncan P, O'Connor CM, Pastva AM, Eggebeen JD, et al. Rehabilitation Therapy in Older Acute Heart Failure Patients (REHAB-HF) trial: design and rationale. *American Heart Journal* 2017;**185**:130–9.

NCT03041376 ***{published data only}***

Vetrovsky T, Siranec M, Parenica J, Griva M, Stastny J, Precek J, et al. Effect of a 6-month pedometer-based walking intervention on functional capacity in patients with chronic heart failure with reduced (HFrEF) and with preserved (HFpEF) ejection fraction: study protocol for two multicenter randomized controlled trials. *Journal of Translational Medicine* 2017;**15**:153.

Additional references

ACCF/AHA 2013

Yancy CW, Jessup M, Bozkurt B, Butler J, Casey DE Jr, Drazner MH, et al. 2013 ACCF/AHA guideline for the management of heart failure: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *Journal of the American College of Cardiology* 2013;**15**:e147–239.

BACPR 2017

British Association for Cardiovascular Prevention and Rehabilitation (BACPR). The BACPR standards and core components for cardiovascular disease prevention and rehabilitation, 3rd edition, 2017. http://www.bacpr.com/resources/6A7_BACR_Standards_and_Core_Components_2017.pdf (accessed 2 May 2018).

Belardinelli 1998

Belardinelli R, Georgiou D, Ginzton L, Cianci G, Purcaro A. Effects of moderate exercise training on thallium uptake and contractile response to low-dose dobutamine of dysfunctional myocardium in patients with ischemic cardiomyopathy. *Circulation* 1998;**97**:553–61.

Bjarnason-Wehrens 2010

Bjarnason-Wehrens B, McGee H, Zwisler AD. Cardiac rehabilitation in Europe: results from the European Cardiac Rehabilitation Inventory Survey. *European Journal of Cardiovascular Prevention and Rehabilitation* 2010;**17**: 410–8.

Braunwald 2015

Braunwald E. The war against heart failure: the Lancet lecture. *Lancet* 2015;**385**:812–24.

Calvert 2007

Calvert MJ, Freemantle N, Cleland JGF. The impact of chronic heart failure on health-related quality of life data acquired in the baseline phase of the CARE-HF study. *European Journal of Heart Failure* 2007;**7**:243–51.

Cook 2014

Cook C, Cole G, Asaria P, Jabbour R, Francis DP. The annual global economic burden of heart failure. *International Journal of Cardiology* 2014;**171**:368–76.

Corra 2005

Corra U, Giannuzzia, P, Adamopoulos S, Bjornstad Bjarnason-Wehernsd HB, Cohen-Solale A, Dugmore D, et al. Executive summary of the position paper of the Working Group on Cardiac Rehabilitation and Exercise Physiology of the European Society of Cardiology (ESC): core components of cardiac rehabilitation in chronic heart failure. *European Journal of Cardiovascular Prevention and Rehabilitation* 2005;**12**:32–105.

Dalal 2015

Dalal HM, Doherty P, Taylor RS. Cardiac rehabilitation. *BMJ* 2015;**351**:h5000.

Dunley 2017

Dunley SM, Roger VL, Redfield MM. Epidemiology of heart failure with preserved ejection fraction. *Nature Reviews Cardiology* 2017;**14**:591–602.

Egger 1997

Egger M, Davey Smith G, Schneiger M, Minder C. Bias in meta-analysis detected by a simple, graphical test. *BMJ* 1997;**315**(7109):629–34.

ESC 2016

Ponikowski P, Voors AA, Anker SD, Bueno H, Cleland JG, Coats AJ, et al. ESC guidelines for the diagnosis and treatment of acute and chronic heart failure: the task force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC). Developed with the special contribution of the Heart Failure Association (HFA) of the ESC. *European Journal of Heart Failure* 2016;**16**:891–975.

Evangelista 2010

Evangelista LS, Hamilton MA, Fonarow GC, Dracup K. Is exercise adherence associated with clinical outcomes in patients with advanced heart failure?. *Physician and Sportsmedicine* 2010;**38**:28–36.

ExTraMatch 2004

Piepoli MF, Davos C, Francis DP, Coats AJ. Exercise training meta-analysis of trials in patients with chronic heart failure (ExTraMATCH). *BMJ* 2004;**328**:189.

ExTraMATCH II

Taylor RS, Walker S, Smart NA, Piepoli MF, Warren FC, Ciani O, et al. Impact of exercise-based cardiac rehabilitation in patients with heart failure (ExTraMATCHII) on mortality and hospitalisation: an individual patient data

meta-analysis of randomised trials. *European Journal of Heart Failure* 2018;**1311**:[Epub ahead of print].

Georgiou 2001
Georgiou D, Chen Y, Appadoo S, Belardinelli R, Greene R, Parides MK, et al. Cost-effectiveness analysis of long-term moderate exercise training in chronic heart failure. *American Journal of Cardiology* 2001;**87**:984–8.

Golwala 2015
Golwala H, Pandey A, Ju C, et al. Temporal trends and factors associated with cardiac rehabilitation referral among patients hospitalized with heart failure: findings from Get With the Guidelines - Heart Failure Registry. *Journal of the American College of Cardiology* 2015;**66**:917–26.

GRADEpro GDT 2015 [Computer program]
McMaster University (developed by Evidence Prime). GRADEpro GDT. Version accessed 10 December 2018. Hamilton (ON): McMaster University (developed by Evidence Prime), 2015.

Heran 2011
Heran BS, Chen JMH, Ebrahim S, Moxham T, Oldridge N, Rees K, et al. Exercise-based cardiac rehabilitation for coronary heart disease. *Cochrane Database of Systematic Reviews* 2011, Issue 7. DOI: 10.1002/14651858.CD001800.pub2

Higgins 2011
Higgins JPT, Green S (editors). Cochrane Handbook for Systematic Reviews of Interventions 5.1.0 (updated March 2011). The Cochrane Collaboration, 2011. Available from www.cochrane-handbook.org.

Holland 2011
Holland DJ, Kumbhani DJ, Ahmed SH, Marwick TH. Effects of treatment on exercise tolerance, cardiac function, and mortality in heart failure with preserved ejection fraction. A meta-analysis. *Journal of the American College of Cardiology* 2011;**19**:1676–86.

Karmali 2014
Karmali KN, Davies P, Taylor F, Beswick A, Martin N, Ebrahim S. Promoting patient uptake and adherence in cardiac rehabilitation. *Cochrane Database of Systematic Reviews* 2014, Issue 6. DOI: 10.1002/14651858.CD007131.pub3

Keteyian 2012
Keteyian SJ, Leifer ES, Houston-Miller N, Kraus WE, Brawner CA, O'Connor CM, et al. Relation between volume of exercise and clinical outcomes in patients with heart failure. *Journal of the American College of Cardiology* 2012;**60**:1899–905.

Komajda 2017
Komajda M, Isnard R, Cohen-Solal A, et al. Effect of ivabradine in patients with heart failure with preserved ejection fraction: the EDIFY randomized placebo-controlled trial. *European Journal of Heart Failure* 2017;**19**:1495–503.

Lam 2011
Lam CSP, Donal E, Kraigher-Krainer E, Vasan RS. Epidemiology and clinical course of heart failure with preserved ejection fraction. *European Journal of Heart Failure* 2011;**13**:18–28.

Lefebvre 2011
Lefebvre C, Manheimer E, Glanville J. Chapter 6. Searching for studies. In: Higgins JPT, Green S editor(s). *Cochrane Handbook for Systematic Reviews of Interventions Version 5.1*. The Cochrane Collaboration. Available from www.cochrane-handbook.org, 2011.

NICE 2018
National Institute for Health and Care Excellence (NICE). Chronic heart failure: management of chronic heart failure in adults in primary and secondary care. Clinical guideline. https://www.nice.org.uk/guidance/ng106 2018; Vol. NG106, September 2018.

Packer 2001
Packer M. Proposal for a new clinical end point to evaluate the efficacy of drugs and devices in the treatment of chronic heart failure. *Journal of Cardiac Failure* 2001;**7**:176–82.

Paulus 2007
Paulus WJ, Tschöpe C, Sanderson JE, Rusconi C, Flachskampf FA, Rademakers FE, et al. How to diagnose diastolic heart failure: a consensus statement on the diagnosis of heart failure with normal left ventricular ejection fraction by the Heart Failure and Echocardiography Associations of the European Society of Cardiology. *European Heart Journal* 2007;**28**:2539–50.

Piepoli 1998
Piepoli M, Maugeri FS, Campana M, Ferrari R, Giordano A, Scalvini S, et al. Experience from controlled trials of physical training in chronic heart failure. Protocol and patient factors in effectiveness in the improvement in exercise tolerance. *European Heart Journal* 1998;**19**:466–75.

Piepoli 2015
Piepoli MF, Binno S, Corrà U, Seferovic P, Conraads V, Jaarsma T, et al. ExtraHF survey: the first European survey on implementation of exercise training in heart failure patients. *European Journal of Heart Failure* 2015;**17**(6):631–6.

Rector 1992
Rector TS, Cohn JN. Assessment of patient outcome with the Minnesota Living with Heart Failure questionnaire: reliability and validity during a randomized, double-blind, placebo-controlled trial of pimobendan. Pimobendan Multicenter Research Group. *American Heart Journal* 1992;**124**:1017–25.

RevMan 2014 [Computer program]
The Cochrane Collaboration. Review Manager (RevMan) Version 5.3.. Copenhagen: The Nordic Cochrane Centre: The Cochrane Collaboration, 2014.

Ryan 2016
Ryan R, Hill S. How to GRADE the quality of the evidence, version 3. Cochrane Consumers and Communication

Group, 2016 (available at http://cccrg.cochrane.org/author-resources).

Schünemann 2011

Sch nemann HJ, Oxman AD, Vist GE, Higgins JPT, Deeks JJ, Glasziou P, et al. Chapter 12. Interpreting results and drawing conclusions. In: In: Higgins JPT, Green S editor(s). *Cochrane Handbook for Systematic Reviews of interventions (available from www.cochrane-handbook.org)*. Wiley, 2011.

Shekelle 2003

Shekelle P, Morton S, Atkinson S, Suttorp M, Tu W, Heidenreich P, et al. Pharmacologic management of heart failure and left ventricular systolic dysfunction: effect in female, black, and diabetic patients, and cost-effectiveness. *Evidence Report/Technology Assessment (Summary)* 2003;**82**: 1–6.

Taylor 2010

Taylor RS, Dalal H, Jolly K, Moxham T, Zawada A. Home-based versus centre-based cardiac rehabilitation. *Cochrane Database of Systematic Reviews* 2010, Issue 1. DOI: 10.1002/14651858.CD007130.pub2

Vromen 2018

Vromen T, Kraal JJ, Kuiper J, Spee RF, Peek N, Kemps HM. The influence of training characteristics on the effect of aerobic exercise training in patients with chronic heart failure: a meta-regression analysis. *International Journal of Cardiology* 2016;**208**:120–7.

Zannad 2013

Zannad F, Garcia AA, Anker SD, Armstrong PW, Calvo G, Cleland JG, et al. Clinical outcome endpoints in heart failure trials: a European Society of Cardiology Heart Failure Association consensus document. *European Journal of Heart Failure* 2013;**15**:1082–94.

Zhang 2018

Zhang Y, Xu L, Yao Y, Guo X, Sun Y, Zhang J, et al. Effect of short-term exercise intervention on cardiovascular functions and quality of life of chronic heart failure patients: a meta-analysis. *Journal of Exercise Science & Fitness* 2016; **14**:67–75.

Ziaeian 2016

Ziaeian B, Fonarow GC. Epidemiology and aetiology of heart failure. *Nature Reviews Cardiology* 2016;**13**:368–78.

References to other published versions of this review

Davies 2010

Davies EJ, Moxham T, Rees K, Singh S, Coats AJ, Ebrahim S, et al. Exercise based rehabilitation for heart failure. *Cochrane Database of Systematic Reviews* 2010, Issue 4. DOI: 10.1002/14651858.CD003331.pub3

Rees 2001

Rees K, Taylor RRS, Ebrahim SBJ. Exercise based rehabilitation for heart failure. *Cochrane Database of Systematic Reviews* 2001, Issue 4. DOI: 10.1002/14651858.CD003331

Rees 2004

Rees K, Taylor RS, Singh S, Coats AJS, Ebrahim S. Exercise based rehabilitation for heart failure. *Cochrane Database of Systematic Reviews* 2004, Issue 3. DOI: 10.1002/14651858.CD003331.pub2

Taylor 2014

Taylor RS, Sagar VA, Davies EJ, Briscoe S, Coats AJS, Dalal H, et al. Exercise-based rehabilitation for heart failure. *Cochrane Database of Systematic Reviews* 2014;**4**:CD003331.

* *Indicates the major publication for the study*

CHARACTERISTICS OF STUDIES

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

Antonicelli 2016

Methods	Parallel-group RCT
Participants	**N randomised:** 343 (exercise 170, control 173) **Diagnosis (% of pts):** *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 **Case mix:** not reported **Age (mean ± SD), years:** total 76.9 ± 5.67, exercise 76.21 ± 5.21, control 77.6 ± 6.02 **Percentage male:** total 56.9%, exercise 60.6%, control 53.2% **Percentage white:** not reported I**nclusion/exclusion criteria:** *Inclusion:* inpatients or outpatients > 70 years of age, CHF from any cause with reduced or preserved ejection fraction (EF), NYHA functional class ≥ II, Mini Mental State Examination score > 24 *Exclusion:* survival prognosis < 6 months, severe uncontrolled diabetes, acute heart decompensation in previous 2 months, severe chronic obstructive pulmonary disease, severe liver failure with survival prognosis < 12 months; severe chronic kidney disease with glomerular filtration rate < 15 mL/min/1.73 m², severe disabling systemic disease, severe cognitive impairment, inability to perform ET
Interventions	**Exercise:** *Total duration:* 24 weeks *Aerobic/resistance/mix:* aerobic (cycling) *Frequency*: 3 sessions/week (for 24 weeks) *Duration:* 50 minutes (30 minutes on cycle ergometer) *Intensity:* 20 minutes intense exercise on cycle ergometer per exercise session (60 rpm, achieving 60% to 70% maximum predicted heart rate) *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 and 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 heart failure 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
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding (performance bias and detection bias) All outcomes	Unclear risk	Not reported
Selective reporting (reporting bias)	Unclear risk	No protocol identified
Intention-to-treat analysis?	Low risk	Although the term ITT was not stated, it appears from the CONSORT diagram that ITT analysis was undertaken
Incomplete outcome data?	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
Groups balanced at baseline?	Low risk	"There were no differences between the two groups at baseline"
Groups received same intervention?	Low risk	All participants continued with usual medication and received education/advice before discharge from the hospital

Austin 2005

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 *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-hour class (for 8 weeks) and 1-hour 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"

Austin 2005 (*Continued*)

Blinding (performance bias and detection bias) All outcomes	High risk	Not for HRQoL; data on deaths, admissions from hospital records department
Selective reporting (reporting bias)	Low risk	All outcomes described in the methods were reported in the results
Intention-to-treat analysis?	Low risk	Although the term ITT was not stated, it appears from the CONSORT diagram that ITT analysis was undertaken
Incomplete outcome data?	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
Groups balanced at baseline?	Low risk	"There are no significant differences in the baseline parameters of the standard care and experimental groups"
Groups received same intervention?	Low risk	Yes, both groups received usual medical care; the only difference between groups was the exercise intervention provided

Belardinelli 1999

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 minutes/session *Intensity:* 60% max VO_2

Belardinelli 1999 (*Continued*)

	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**
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
Selective reporting (reporting bias)	Low risk	All outcomes described in the methods were reported in the results
Intention-to-treat analysis?	Unclear risk	Not reported
Incomplete outcome data?	Low risk	Losses to follow-up were reported
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, and left ventricular ejection fraction. There were no differences in type and doses of medications, blood chemistry, and previous cardiac events"
Groups received same intervention?	Unclear risk	Not reported

Belardinelli 2012

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:** *Total duration:* 10 years; 8 weeks' supervised, then 12 months' maintenance *Aerobic/resistance/mix:* aerobic *Frequency:* 2 to 3 sessions/week *Duration:* 40 minutes/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 minutes. 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

Belardinelli 2012 (*Continued*)

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
Selective reporting (reporting bias)	Low risk	All outcomes described in the methods were reported in the results
Intention-to-treat analysis?	Low risk	"All analyses were performed with an intention-to-treat principle"
Incomplete outcome data?	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
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 same intervention?	Low risk	Both groups appeared to receive the same interventions apart from the CR intervention

Bocalini 2008

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:* aerobic *Frequency:* 3 sessions/week *Duration:* 90 minutes *Intensity:* target HR (50% of work at maximum HR) *Modality:* walking on a treadmill *Setting*: not reported *Other*: relaxation and stretching exercises before and after every session **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

Bocalini 2008 (*Continued*)

Blinding (performance bias and detection bias) All outcomes	Unclear risk	Not reported
Selective reporting (reporting bias)	Low risk	All outcomes described in the methods were reported in the results
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"
Incomplete outcome data?	High risk	Only 42/53 (79%) provided data at follow-up
Groups balanced at baseline?	Low risk	Table 1 of the publication shows that groups were well balanced
Groups received same intervention?	Low risk	"All patients continued with pharmacological therapy and individual dietary guidance"

Chen 2018

Methods	Parallel-group RCT
Participants	**N randomised:** 62 (exercise 31, control 31) **Diagnosis (% of participants):** *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 minutes/session *Intensity:* as tolerated by participant *Modality:* walking *Setting*: hospital *Other*: education, depression therapy, home visits **Control group / Comparison:** Standard of care (telephone call at 2 weeks, 2 clinic reviews at 90 and 180 days), mortality,

Chen 2018 (*Continued*)

	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
Selective reporting (reporting bias)	Low risk	All outcomes were reported (no protocol publication is available)
Intention-to-treat analysis?	Low risk	Although the term ITT was not stated, it appears that groups were analysed according to initial random allocation
Incomplete outcome data?	Low risk	Only 2 deaths were reported; no other losses to follow-up were described
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 same intervention?	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"

Cowie 2014

Methods	Parallel-group RCT - 2 arms
Participants	**N randomised:** 46; 15 hospital, 15 home, 16 control **Diagnosis (% of pts):** *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 **Percentage male:** 91.3%(total), exercise (home 86.7%, hospital 86.7%), control 100% **Percentage white:** not reported **Inclusion/exclusion criteria:** *Inclusion:* left ventricular systolic dysfunction 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, myocardial infarction within past 3 weeks, new-onset atrial fibrillation, 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 minutes *Intensity*: not specified *Modality*: circuit training *Setting*: hospital-based (intervention 1) and home-based (intervention 2) *Other:* hospital group with a senior cardiac rehabilitation physiotherapist, a physiotherapy technical instructor, and a senior cardiac nurse present at each class; home group monitored by a senior cardiac rehabilitation physiotherapist by telephone, twice during their 8-week intervention (estimated as two 20-minute calls, plus 10-minute documentation, i.e. 1 hour per participant) **Control group / Comparison:** Usual care, which included specialist HF nursing input
Outcomes	Hospitalisations; costs
Country and setting	United Kingdom
Follow-up	5.2 years
Notes	**Source of funding:** NHS Ayrshire and Aaran's Coronary Heart Disease Managed Clinical Network
Risk of bias	

Cowie 2014 (*Continued*)

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
Selective reporting (reporting bias)	High risk	Number of hospitalisations was not reported (obtained from study lead investigator)
Intention-to-treat analysis?	Low risk	Although the term ITT was not stated, it appears that groups were analysed according to initial random allocation
Incomplete outcome data?	High risk	46/60 (77%) provided follow-up data
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 same intervention?	Low risk	Usual care was standard in all 3 groups

Dalal 2018

Methods	Parallel-group RCT
Participants	**N randomised:** 216; 107 exercise, 109 control **Diagnosis (% of pts):** *Aetiology:* ischaemic intervention 45%, control intervention 46% *Female:* intervention 24%, control 19% *NYHA:* Class II: intervention 59%, control 58%; Class III: intervention 19%, control 24% *LVEF:* mean 34% **Case mix:** 100%, as above **Age:** intervention mean 69.7 (SD 10.9), control mean 69.9 (SD 11.0) **Percentage male:** 78% (total); intervention 76, control 81% **Percentage white:** 100% **Inclusion/exclusion criteria** *Inclusion:* men and women aged ≥ 18 years with a confirmed diagnosis of HFrEF on echocardiography or angiography (left ventricular ejection fraction < 45% within the preceding 5 years), no deterioration of HF symptoms in prior 2weeks resulting in hospitalisation or alteration of HF medication

	Exclusion: cardiac rehabilitation (CR) within the past 12months; received an intracardiac defibrillator (ICD); cardiac re-synchronisation therapy (CRT) or combined CRT/ICD device in prior 6months; 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 to 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	United Kingdom Multi-centre (4 sites)
Follow-up	4, 6, and 12 months
Notes	**Funding source:** National Institute for Health Research (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-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"

Dalal 2018 (*Continued*)

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
Selective reporting (reporting bias)	Low risk	All pre-specified outcomes were reported as in the published protocol
Intention-to-treat analysis?	Low risk	"Primary analyses were based on ITT complete case analyses"
Incomplete outcome data?	Low risk	All participants were accounted for in a CONSORT flow diagram
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 same intervention?	Low risk	Both groups received usual care

DANREHAB 2008

Methods	Parallel-group RCT
Participants	**N randomised:** 91 (exercise 45, control 46) **Age, years:** exercise median 66 (range 33 to 91), control median 65 (range 29 to 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/wk *Duration:* 90 minutes/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 general practitioner. 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 re-admission 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"

DANREHAB 2008 (*Continued*)

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"
Selective reporting (reporting bias)	Low risk	All outcomes listed in the methods were reported in the results
Intention-to-treat analysis?	Low risk	ITT analysis was stated
Incomplete outcome data?	Low risk	81% overall follow-up at 12 months
Groups balanced at baseline?	Low risk	"Patients were well matched at entry"
Groups received same intervention?	Low risk	Both groups received control care

Davidson 2010

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 to 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:* aerobic *Frequency:* 1 session/week *Duration:* 30 to 50 minutes *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 **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"
Selective reporting (reporting bias)	Low risk	All outcomes were described and all methods were reported
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
Incomplete outcome data?	Low risk	"No participants were lost to follow-up"
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"

Davidson 2010 (*Continued*)

Groups received same intervention?	Low risk	Both groups appeared to receive the same interventions apart from the CR intervention

Dehkordi AH 2015

Methods	Parallel-group RCT
Participants	**N randomised:** 61 (exercise 30, control 31) **Diagnosis (% of pts):** *Aetiology:* ischaemic cardiomyopathy 67.2%, hypertension 26.2%, dilated cardiomyopathy 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 **Percentage male:** 67.2% (exercise 60%, control 74%) **Percentage white:** not reported **Inclusion/exclusion criteria:** *Inclusion:* patients admitted to hospital with diagnosis of heart failure, with LVEF ≤ 40%, and in sinus rhythm *Exclusion:* difficulty with movement; no heart transplant 3 months after exercise programme; no advanced heart failure; 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 minutes *Intensity*: in short term (up to 6 weeks), < 3 MET (simple walking until heart rate reaches 60% of heart rate reserve); in longer term (≥ 6 weeks), heart rate 70% of heart rate 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
Selective reporting (reporting bias)	Unclear risk	No protocol was identified
Intention-to-treat analysis?	Low risk	Although the term ITT was not stated, it appears from the CONSORT diagram that ITT analysis was undertaken
Incomplete outcome data?	Low risk	No loss to follow-up was reported in either arm
Groups balanced at baseline?	Low risk	No differences were noted between groups
Groups received same intervention?	Low risk	Medications were unchanged in both groups

Dracup 2007

Methods	Parallel-group RCT
Participants	**N randomised:** 173 (exercise 86, control 87) **Diagnosis (% of participants):** *Aetiology:* ischaemic; idiopathic; valvular; DCM; other *NYHA*: Class II to 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 to 80 years, NYHA II to 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 forced expiratory volume < 1 L in 1 second

Dracup 2007 (*Continued*)

	as measured by spirometry, stenotic valvular disease as measured by echocardiogram, history of uncontrolled ventricular tachyarrhythmias (documented by electrophysiology study or 24-hour 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 to 45 minutes *Intensity:* 40% to 60% max HR *Modality:* walking *Setting:* home-based **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
Selective reporting (reporting bias)	Low risk	All outcomes described in the methods were reported in the results

Dracup 2007 (*Continued*)

Intention-to-treat analysis?	Low risk	Although not reported as ITT analysis, groups did appear to be analysed according to original randomised allocation
Incomplete outcome data?	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"
Groups balanced at baseline?	Low risk	**Current version:** "There were no differences between the control and exercise groups at baseline with respect to sociodemographic variables (Table I) and most clinical characteristics. However, patients in the exercise group had a significantly higher likelihood of having a history of coronary heart disease and taking antiplatelet medication than in the control group" **Our version:** "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 same intervention?	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"

Du 2018

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 to III *Exclusion:* unstable angina pectoris, unexplained syncope in previous 3 months, resting heart rate > 120 beats/min, participating in any structured exercise programme, inability to give informed consent, significant cognitive impairment

Du 2018 (*Continued*)

Interventions	**Exercise:** *Total duration:* 24 weeks *Aerobic/resistance/mix:* aerobic *Frequency:* 1 session/week *Duration:* 6 minutes/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 Multi-centre
Follow-up	3 months and 6 months
Notes	Australain New Zealand Clinical Trial Registry 12609000437268. Participants in this study were younger than the average age of the heart failure 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**
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)
Selective reporting (reporting bias)	Low risk	No differences were noted between the protocol and the study
Intention-to-treat analysis?	Low risk	"Data were analysed according to the intention-to-treat principle"
Incomplete outcome data?	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

Du 2018 (*Continued*)

Groups balanced at baseline?	Low risk	Tables 1 and 2
Groups received same intervention?	Low risk	Both groups received usual care

Gary 2010

Methods	Parallel-group RCT - 2 arms
Participants	**N randomised:** total 65; intervention 1 (comp): 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 (angiotensin-converting enzyme inhibitors, diuretics, beta blockers, angiotensin receptor blockers, hydralazine and nitrate combination, etc.); Hamilton Rating Scale for Depression (HAM-D) score ≥ 11; positive results on the Mini International Neuropsychiatric Interview (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 minutes; 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 to 45 minutes/session, maximum 1 hour *Intensity:* Borg < 15 ('moderate')

	Modality: walking *Setting*: home-based **Other:** exercise + CBT group also received 12 weeks of weekly 1-hour sessions of CBT for 12 weeks. 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
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"
Selective reporting (reporting bias)	Low risk	Outcome were described in the Methods and were reported in the Results
Intention-to-treat analysis?	Low risk	Although not stated, CONSORT diagram suggests that groups were analysed according to initial randomised allocation

Gary 2010 (*Continued*)

Incomplete outcome data?	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
Groups balanced at baseline?	Low risk	"There were no BL differences between groups on any demographic or outcome variables"
Groups received same intervention?	Low risk	Groups appeared to receive the same care other than exercise and CBT interventions

Giallauria 2008

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 minutes (30 minutes plus 5 minutes of warm-up and 5 minutes of cool-down) *Intensity:* tailored to individual (target 60% to 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)

Giallauria 2008 (*Continued*)

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

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
Selective reporting (reporting bias)	Unclear risk	No protocol available
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
Incomplete outcome data?	Low risk	All participants were accounted for
Groups balanced at baseline?	Low risk	No differences between groups were noted (Table 1)
Groups received same intervention?	Low risk	Medications were uptitrated to maximal in both groups

Giannuzzi 2003

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 to 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 ejection fraction < 35%; clinical stability for at least 3 months under optimised therapy; NYHA functional Class II to 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 variability (> 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 to 5 sessions/week *Duration:* 30 minutes *Intensity:* 60% peak VO_2 *Modality:* exercise cycle, daily brisk walk, calisthenic. In addition, requested to take brisk daily walk for > 30 minutes *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 Multi-centre (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
Selective reporting (reporting bias)	Low risk	All outcomes described in the methods were reported in the results

Giannuzzi 2003 (*Continued*)

Intention-to-treat analysis?	Low risk	Although not stated, it is clear from the CONSORT diagram that 2 groups were analysed according to ITT
Incomplete outcome data?	Low risk	45/45 (100%) in exercise training group, 44/45 (98%) available at 6 months' follow-up
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 same intervention?	Unclear risk	Not clearly stated whether co-treatments (i.e. cardiovascular medication) in the 2 groups were the same

Gielen 2003

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 to 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 minutes/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

Gielen 2003 (*Continued*)

	for 20 minutes/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**
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
Selective reporting (reporting bias)	Low risk	All outcomes described in the methods were reported in the results
Intention-to-treat analysis?	Low risk	Although ITT analysis not reported, groups do appear to be analysed according to original randomised allocation
Incomplete outcome data?	Low risk	No loss to follow-up
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 same intervention?	Unclear risk	Details of co-interventions not reported

Gottlieb 1999

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 to III for at least 3 months and on stable medications for the past 1 month. All participants were on maximal medical therapy with angiotensin-converting enzyme inhibitors, 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 *Exclusion:* not reported
Interventions	**Exercise:** *Total duration:* 3 months *Aerobic/resistance/mix:* aerobic *Frequency:* 3 sessions/week *Duration:* 30 minutes *Intensity:* Borg 12 to 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

Gottlieb 1999 (*Continued*)

Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding (performance bias and detection bias) All outcomes	Unclear risk	Not reported
Selective reporting (reporting bias)	Low risk	All outcomes described in the methods were reported in the results
Intention-to-treat analysis?	Unclear risk	Not reported
Incomplete outcome data?	Low risk	Yes, QUORUM flow diagram reported Unclear how loss to follow-up, dropout, and cross-over were dealt with
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 same intervention?	Low risk	"Medical follow-up of both the control and intervention patient groups was provided by specialized heart failure physicians"

Hambrecht 1995

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 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, peripheral vascular disease, COPD, orthopaedic or other conditions precluding regular participation in exercise sessions

Hambrecht 1995 (*Continued*)

Interventions	**Exercise:** *Total duration:* 6 months *Aerobic/resistance/mix:* aerobic *Frequency:* 4 to 6 sessions/week *Duration:* 10 to 60 minutes/session, 1 hour 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
Selective reporting (reporting bias)	Low risk	All outcomes described in the methods were reported in the results
Intention-to-treat analysis?	Unclear risk	Not reported
Incomplete outcome data?	Low risk	Dropouts and clinical events were fully reported for both groups. No imputation was undertaken
Groups balanced at baseline?	Low risk	"There were no significant differences in baseline variables between the training and control groups"

Hambrecht 1995 (*Continued*)

Groups received same intervention?	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 1998

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 to 6 sessions/d *Duration:* 10 to 20 minutes/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
Selective reporting (reporting bias)	Low risk	All outcomes described in the methods were reported in the results
Intention-to-treat analysis?	Low risk	It appears that groups were analysed according to original randomised allocation
Incomplete outcome data?	Low risk	Detailed description of losses to follow-up and dropouts was provided
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 same intervention?	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"

Hambrecht 2000

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 left ventricular function (LVEF < 40%) as a result of DCM or IHD; physical work

Hambrecht 2000 (*Continued*)

	capacity at baseline > 25 watts; clinical stability ≥ 3 months before study start *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 to 20 minutes/session *Intensity:* 70% of peak VO_2 *Modality:* cycle ergometer *Setting:* first 2 weeks in hospital, remainder home based **Other:** plus group sessions 1 hour 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
Selective reporting (reporting bias)	Low risk	All outcomes described in the methods were reported in the results
Intention-to-treat analysis?	Low risk	Not reported
Incomplete outcome data?	Low risk	QUORUM diagram and details of losses to follow-up were reported

Hambrecht 2000 (*Continued*)

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 same intervention?	Unclear risk	Co-interventions in the control group were not reported

HF ACTION 2009

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 *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 to 5 sessions/week *Duration:* 15 to 35 minutes/session *Intensity:* 60% to 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

HF ACTION 2009 (*Continued*)

Country and setting	USA Multi-centre
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 National Institutes of Health 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
Selective reporting (reporting bias)	Low risk	All outcomes described in the methods were reported in the results
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"
Incomplete outcome data?	Low risk	QUORUM diagram and details of losses to follow-up were reported
Groups balanced at baseline?	Low risk	Table 1 of the publication shows that the 2 groups were well balanced
Groups received same intervention?	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"

Jolly 2009

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 obstructive 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 to 30 minutes - *Intensity:* 70% peak VO_2 or Borg 12 to 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	UK West Midlands, 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	

Jolly 2009 (*Continued*)

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"
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
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"
Incomplete outcome data?	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
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 same intervention?	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"

Jónsdóttir 2006a

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:* chronic obstructive lung disease, 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 minutes *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)
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

Jónsdóttir 2006a (*Continued*)

Blinding (performance bias and detection bias) All outcomes	Unclear risk	Not reported
Selective reporting (reporting bias)	Low risk	All outcomes described in the methods were reported in the results
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
Incomplete outcome data?	Low risk	No losses to follow-up
Groups balanced at baseline?	Low risk	Table 2 of the publication suggests that the 2 groups were well balanced
Groups received same intervention?	Low risk	Yes, both groups appeared to receive the same interventions apart from the CR intervention

Kaltsatou 2014

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) **Male:** 100% **White:** not reported **Inclusion/exclusion criteria:** *Inclusion:* NYHA II/III, heart failure with at least 3 months' clinical stability, no participation in any form of regular exercise *Exclusion:* unstable angina, myocardial infarction within last 5 months, uncontrolled hypertension, chronic obstructive pulmonary disease, insulin-dependent diabetes mellitus, 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 minutes *Intensity:* moderate: exercise perceived exertion 13 to 14 (somewhat hard) on the Borg 6 to 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"
Selective reporting (reporting bias)	Unclear risk	No protocol available
Intention-to-treat analysis?	Low risk	Although the term ITT was not stated, it appears from the CONSORT diagram that ITT analysis was undertaken
Incomplete outcome data?	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 In the control group, 2/19 were lost to follow-up
Groups balanced at baseline?	Low risk	No differences between groups

Kaltsatou 2014 (*Continued*)

Groups received same intervention?	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"

Keteyian 1996

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 to 14) *Duration:* 33 minutes *Intensity:* 60% to 80% peak HR *Modality:* treadmills, stationary cycles, rowing machines, arm ergometers **Setting:** outpatient clinic **Other:** none reported **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	North America Single centre
Follow-up	6 months (after randomisation)

Keteyian 1996 (*Continued*)

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
Selective reporting (reporting bias)	Low risk	All outcomes described in the methods were reported in the results
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"
Incomplete outcome data?	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"
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 same intervention?	Unclear risk	Co-interventions in the control group were not reported

Klecha 2007

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% *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* minutes/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

Klecha 2007 (*Continued*)

Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding (performance bias and detection bias) All outcomes	Unclear risk	Not reported
Selective reporting (reporting bias)	Low risk	All outcomes described in the methods were reported in the results
Intention-to-treat analysis?	Low risk	Not implicit, but numbers used suggest that groups were analysed according to randomised allocation
Incomplete outcome data?	Low risk	No participants were lost to follow-up
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 same intervention?	Unclear risk	Not reported

Klocek 2005

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: e*xercise 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 group 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 minutes/session (4 minutes constant workload with 1 minute rest repeated 5 times) *Intensity:* group A: 60% max HR *Duration:* group B: 25 minutes/session (exercise workload gradually increased after each 5-minute training period to a total of 25 minutes) *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"
Selective reporting (reporting bias)	Low risk	All outcomes described in the methods were reported in the results
Intention-to-treat analysis?	Low risk	It appears that groups were analysed according to initial random allocation
Incomplete outcome data?	Unclear risk	No information was presented on loss to follow-up nor dropouts

Klocek 2005 (*Continued*)

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 same intervention?	Unclear risk	Details of co-interventions were not reported, although the degree of follow-up was stated to be equivalent

Koukouvou 2004

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 minutes/session *Intensity:* 50% to 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)

Koukouvou 2004 (*Continued*)

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
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"
Selective reporting (reporting bias)	Low risk	All outcomes outlined in the methods were reported
Intention-to-treat analysis?	Low risk	Not stated explicitly, but analysis appears to be done according to initial group allocation
Incomplete outcome data?	Unclear risk	Losses to follow-up, dropouts not 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 same intervention?	Unclear risk	Not reported

Lang 2018

Methods	Parallel-group RCT
Participants	**N randomised:** 50 (exercise 25, control 25) **Diagnosis (% of participants):** *Aetiology:* ischaemic Intervention 32%, control 64% *NYHA*: Class II: intervention 60%, control 64%; Class III: intervention 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

Lang 2018 (*Continued*)

	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 to 3 times/week *Duration*: not reported *Intensity*: not reported *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	United Kingdom Single centre
Follow-up	4 months and 6 months
Notes	**Funding source:** National Institute for Health Research (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

Lang 2018 (*Continued*)

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"
Selective reporting (reporting bias)	Low risk	All pre-specified outcomes were reported as in the published protocol
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"
Incomplete outcome data?	Low risk	All participants were accounted for in a CONSORT flow diagram
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"
Groups received same intervention?	Low risk	Both groups received usual care

McKelvie 2002

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 to III *LVEF:* < 40% **Case mix:** 100%, as above **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 to III; 6-minute walk test distance < 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 (forced expired volume in 1 second, or vital capacity < 60% of predicted, or both); poorly controlled cardiac arrhythmias; any non-cardiac 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 minutes/session *Intensity:* aerobic: 60% to 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 Multi-centre
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"
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"

McKelvie 2002 (*Continued*)

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"
Selective reporting (reporting bias)	Unclear risk	All outcomes described in the methods were reported in the results
Intention-to-treat analysis?	Low risk	Although ITT analysis was not reported, groups appear to have been analysed according to the original randomised allocation
Incomplete outcome data?	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
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 same intervention?	Unclear risk	"All patients were reviewed monthly throughout the study"

Mehani 2013

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 to 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

	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; atrial fibrillation (AF); severe functional mitral regurgitation (MR); clinical evidence of pulmonary disease (chronic obstructive lung disease, moderate to severe pulmonary hypertension)
Interventions	**Exercise:** *Total duration:* 28 weeks *Aerobic/resistance/mix:* aerobic *Frequency:* 3 sessions/week *Duration:* aerobic; 45 minutes/session *Intensity:* aerobic: maximal 80% of heart rate 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
Selective reporting (reporting bias)	Unclear risk	No protocol was available
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

Mehani 2013 (*Continued*)

Incomplete outcome data?	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
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"
Groups received same intervention?	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

Mueller 2007

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 minutes/session cycling, 90 minutes walking each day *Intensity:* Borg 12 to 14 (60% to 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

Mueller 2007 (*Continued*)

Country and setting	Switzerland Single centre
Follow-up	6.2 years (after randomisation)
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
Selective reporting (reporting bias)	Low risk	Outcomes described in the methods were reported in the results
Intention-to-treat analysis?	Low risk	ITT was not stated explicitly; however, groups appear to have been analysed according to the original allocation
Incomplete outcome data?	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
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 same intervention?	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"

Myers 2000

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) **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 hour; cycling: 45 minutes *Intensity:* walking: not reported; cycling: 60% to 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

Myers 2000 (*Continued*)

Blinding (performance bias and detection bias) All outcomes	Unclear risk	Not reported
Selective reporting (reporting bias)	Low risk	All outcomes described in the methods were reported in the results
Intention-to-treat analysis?	Low risk	Although not explicit, participants appeared to be analysed according to the initial random allocation
Incomplete outcome data?	Low risk	Losses to follow-up were reported
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"
Groups received same intervention?	Low risk	Yes, both groups appeared to receive the same interventions, apart from the CR intervention

Nilsson 2008

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 forced expiratory vital capacity < 50% of expected measured by spirometry; 6-minute walking distance > 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 minutes

	Intensity: 15 to 18 on Borg scale *Modality:* fast walking, side-stepping, and leg lifts in combination with overhead arm reaches *Setting:* hospital outpatient department **Other:** 15 to 30 minutes 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
Follow-up	12 months (after randomisation)
Notes	All training sessions were supervised by a physiotherapist - a specialist in heart rehabilitation **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"
Selective reporting (reporting bias)	Low risk	All outcomes described in the methods were reported in the results
Intention-to-treat analysis?	Low risk	"Intention-to-treat analyses were performed"
Incomplete outcome data?	Low risk	35/40 (88%) in the exercise training group and 37/40 (93%) in the control group were available at 12 months
Groups balanced at baseline?	Low risk	Table 1 of the publication suggests no differences between the 2 groups
Groups received same intervention?	Low risk	Yes

Norman 2012

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:** *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 minutes/session (30 minutes' warm-up); resistance: 8 to 10 exercises (upper and lower extremities) performed for 1 set of 10 to 15 repetitions *Intensity:* aerobic: 40% to 70% HR reserve, or Borg 11 to 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 to 3, then separate biweekly meetings during weeks 4 to 12 Phase 2: following the groups for an additional 12 weeks without group sessions Other trial report:

	Pozehl B, Duncan K, Hertzog M, Norman JF. Heart failure exercise and training camp: effects of a multicomponent exercise training intervention in patients with heart failure. Heart Lung 2010;39(6 Suppl):S1-13 **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"
Selective reporting (reporting bias)	Low risk	All outcomes described in the methods were reported in the results
Intention-to-treat analysis?	Low risk	Not stated, but groups were analysed according to randomised allocation
Incomplete outcome data?	Low risk	Due to mortality and dropout, KCCQ scores were available for 37 participants (88%) at 24 weeks
Groups balanced at baseline?	Low risk	"…no significant difference noted between groups"
Groups received same intervention?	Low risk	Both groups received group sessions (attention control), so the only difference between groups was the exercise-based intervention

Passino 2006

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 minutes/session *Intensity:* 65% max VO_2 *Modality:* cycle *Setting:* home-based **Other:** not reported **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
Selective reporting (reporting bias)	Unclear risk	Not reported
Intention-to-treat analysis?	Low risk	Although ITT was not stated, groups appear to have been analysed according to the original randomisation
Incomplete outcome data?	Low risk	Outcomes described in the methods were reported in the results

Passino 2006 (*Continued*)

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 same intervention?	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"

Pozehl 2008

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) *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 minutes aerobic, 20 minutes resistance *Intensity:* 60% to 85% max VO_2 , 12 to 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 1 to 10 lb 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:**

Pozehl 2008 (*Continued*)

	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
Selective reporting (reporting bias)	Low risk	Outcomes described in the methods were reported in the results
Intention-to-treat analysis?	Low risk	Although not stated, groups appear to have been analysed according to the initial randomised allocation
Incomplete outcome data?	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
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)"
Groups received same intervention?	Unclear risk	Not reported

Reeves 2017

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 chronic kidney disease defined as estimated glomerular filtration rate 20 mL/min/1.73 m², 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 minutes *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) **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 Multi-centre
Follow-up	6 months

Reeves 2017 (*Continued*)

Notes	Exercise was individually tailored and was delivered by trained internationalists in hospital over 12 weeks along with a home exercise prescription (unsupervised low-intensity walking at usual pace for up to 30 minutes 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"
Selective reporting (reporting bias)	Low risk	
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%)"
Incomplete outcome data?	Unclear risk	Three dropouts from total (N = 24) but no further details or reasons given
Groups balanced at baseline?	Low risk	"Baseline characteristics were balanced between the study arms"
Groups received same intervention?	Low risk	Control group received "attention" consisting of at least monthly contact with study personnel via scheduled phone calls and follow-up assessments

Wall 2010

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 to III congestive HF; EF ≤ 60%; systolic dysfunction; physician approval; ability to complete a minimum of 3 minutes 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 minutes *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 to 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

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

Wall 2010 (*Continued*)

Blinding (performance bias and detection bias) All outcomes	Unclear risk	Not reported
Selective reporting (reporting bias)	Low risk	All outcomes described in the methods were reported
Intention-to-treat analysis?	Low risk	Although not stated, it is clear from the CONSORT diagram that 2 groups were analysed according to ITT
Incomplete outcome data?	Low risk	QUORUM flow diagram report suggests that 19 were included in the analysis 15 participants (79%) completed final follow-up measures at month 12
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 same intervention?	Low risk	Both groups received comprehensive disease management

Willenheimer 2001

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 echocardiographic 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 (>.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

Willenheimer 2001 (*Continued*)

Interventions	**Exercise:** *Total duration:* 4 months *Aerobic/resistance/mix:* aerobic/interval *Frequency:* 2 to 3 sessions/week *Duration:* 15 minutes/session, increasing to 45 minutes/session *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
Selective reporting (reporting bias)	Low risk	All outcomes described in the methods were reported in the results
Intention-to-treat analysis?	Low risk	Although ITT is not implicit, it appears that groups were analysed according to the original randomised allocation
Incomplete outcome data?	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

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 same intervention?	Low risk	"No change in medication allowed during study"

Witham 2005

Methods	Parallel-group RCT
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 European Society of Cardiology guidelines; NYHA Class II or III symptoms and evidence of LVSD on echocardiography, 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 to 3 sessions/week *Duration:* 20 minutes *Intensity:* Borg 11 to 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 health-related quality-of-life (Guyatt Chronic Heart Failure Questionnaire); mortality; hospitalisation
Country and setting	UK Single centre

Witham 2005 (*Continued*)

Follow-up	6 months (after randomisation)
Notes	**Source of funding:** Grant 2006/918 from The Health Foundation (formerly PPP Health Foundation), London, United Kingdom

Risk of bias

Bias	Authors' judgement	Support for judgement
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"
Selective reporting (reporting bias)	Low risk	All outcomes described in the methods were reported in the results
Intention-to-treat analysis?	Low risk	It appears from the QUORUM diagram that groups were analysed according to the initial random allocation
Incomplete outcome data?	Low risk	75/82 (91%) and 68/82 (83%) were available at 3 months' and 6 months' follow-up, respectively
Groups balanced at baseline?	Low risk	Table 1 of the publication shows that groups were well balanced
Groups received same intervention?	Low risk	Yes, both groups appear to have received usual medical care; the only difference between groups was the exercise intervention

Witham 2012

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
Interventions	**Exercise:** *Total duration:* 24 weeks *Aerobic/resistance/mix:* mix *Frequency:* 2 sessions/week *Duration:* ≤ 60 minutes *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 week) **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"

Witham 2012 (*Continued*)

Blinding (performance bias and detection bias) All outcomes	Unclear risk	Not reported
Selective reporting (reporting bias)	Low risk	All outcomes described in the methods were reported in the results
Intention-to-treat analysis?	Low risk	Analyses were by ITT
Incomplete outcome data?	Low risk	89/104 (86%) and 87/104 (83%) were available for follow-up at 8 and 24 weeks, respectively
Groups balanced at baseline?	Low risk	Table 1 of the publication suggests no differences between the 2 groups
Groups received same intervention?	Low risk	It appeared that both groups received the same care, except for the exercise intervention

Yeh 2011

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 $\leq$ 40% in past 2 years, stable medical regimen, NYHA Class I to 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 (Mini-Mental State Examination score $\leq$ 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-hour class (30 minutes' warm-up)

	Intensity: not reported *Modality:* Tai Chi movements - Weeks 2 to 5: warm-up + raising the power; withdraw and push - Weeks 6 to 9: 1 + grasp sparrow's tail, brush knee twist step - Weeks 10 to 12: 2 + wave hands like clouds Participants were given 45-minute 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 minutes) explanation towards the end of 1 Tai Chi session weekly *Setting:* centre-based and home-based **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 Multi-site
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"
Selective reporting (reporting bias)	Low risk	All outcomes described in the methods were reported in the results
Intention-to-treat analysis?	Low risk	All participants were included in the analysis regardless of their attendance

Yeh 2011 (*Continued*)

Incomplete outcome data?	Low risk	Figure 1 of the publication shows 91% to 96% complete data across HRQoL and exercise outcomes
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 same intervention?	Low risk	Yes, both groups received comprehensive disease management

ACE: angiotensin-converting enzyme; AF: atrial fibrillation; BL: baseline; bpm: beats/min; CBT: cognitive-behavioural therapy; CHF: chronic heart failure; CONSORT: CONsolidated Standards of Reporting Trials; COPD: chronic obstructive pulmonary disease; CR: cardiac rehabilitation; CRT: cardiac re-synchronisation therapy; DCM: dilated cardiomyopathy; DM: diabetes mellitus; DSM-IV: *Diagnostic and Statistical Manual of Mental Disorders*, 4th Edition; 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; 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; 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; LVEDD: left ventricular end-diastolic diameter; LVEF: left ventricular ejection fraction; LVSD: left ventricular systolic dysfunction; max: maximum; MDMP: XXX; MET: metabolic equivalent; MI: myocardial infarction; MOS: Medical Outcomes Survey; MLWHF: Minnesota Living With Heart Failure questionnaire; MR: mitral regurgitation; MRI: magnetic resonance imaging; NIH: National Institutes of Health; NIHR: National Institute for Health Research; NYHA: New York Heart Association; PVD: peripheral vascular disease; 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; UC: usual care; VO_2 : oxygen consumption.

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

Study	Reason for exclusion
Abreu 2015	Relevant outcomes not reported. Emailed Abreu on 18 October 2018 to clarify outcomes but received no response
Adamopoulos 2001	Relevant outcomes not reported. Attempt to contact Adamopolous on 4 October 2018 to clarify outcomes was unsuccessful
Agvall 2013	Not exercise-based cardiac rehabilitation intervention
Ahmad 2014	Relevant outcomes not reported. Emailed Ahmad on 18 October 2018 to clarify outcomes but received no response
Alves 2012	Relevant outcomes not reported. Attempt to contact Alves on 4 October 2018 to clarify outcomes was unsuccessful
Ambrosy 2016	< 6 months' follow-up

(*Continued*)

Ambrosy 2017	No usable data
Aronov 2015	Abstract - study authors contacted; no usable data provided
Ascione 2013	< 6 months' follow-up
Bachman 2015	Inappropriate intervention - hawthorn extract
Banks 2015	< 6 months' follow-up
Barrow 2008	< 6 months' follow-up
Belardinelli 2005	< 6 months' follow-up
Belardinelli 2013	Not a randomised controlled trial
Bernocchi 2016	Combined population with chronic obstructive pulmonary disease and heart failure
Bittencourt 2015	< 6 months' follow-up
Borland 2014	< 6 months' follow-up
Boyd 2015	Relevant outcomes not reported. Emailed Boyd on 18 October 2018 to clarify outcomes but received no response
Brand 2014	Abstract - study authors contacted; no usable data provided
Briffa 2005	No heart failure
Brotons 2009	No exercise-based cardiac rehabilitation intervention
Cameron 2015	No exercise-based cardiac rehabilitation intervention - memory training
Chang 2005	Relevant outcomes not reported. Attempt to contact Chang on 4 October 2018 to clarify outcomes was unsuccessful
Chrysohoou 2013	< 6 months' follow-up
Chrysohoou 2014	< 6 months' follow-up
Chrysohoou 2016	< 6 months' follow-up
Coats 1992	< 6 months' follow-up
Collins 2004	< 6 months' follow-up
Corvera-Tindel 2004	< 6 months' follow-up

(*Continued*)

Cowie 2011	< 6 months' follow-up
Cowie 2012	< 6 months' follow-up
Deng 2006	Relevant outcomes not reported. Attempt to contact Deng on 4 October 2018 to clarify outcomes was unsuccessful
Dingli 2002	Relevant outcomes not reported. Attempt to contact Xu on 4 October 2018 to clarify outcomes was unsuccessful
Doukky 2016	No exercise-based cardiac rehabilitation intervention
Duncan 2014	Relevant outcomes not reported. Emailed Duncan on 18 October 2018 to clarify outcomes but received no response
Edelmann 2011	< 6 months' follow-up
Erbs 2003	Relevant outcomes not reported. Emailed Erbs on 4 October 2018 to clarify outcomes but received no response
Erbs 2010	Relevant outcomes not reported. Emailed Erbs on 4 October 2018 to clarify outcomes but received no response
ExTraMATCH 2004	Meta-analysis
Fernhall 2013	Not a randomised controlled trial
Fischer 2015	Wrong population - animal model
Franco 2006	< 6 months' follow-up
Fu 2013	< 6 months' follow-up
Galenko 2016	No usable data - assessment tool used to measure HRQoL not stated
Gary 2004	Relevant outcomes not reported. Attempt to contact Gary on 4 October 2018 to clarify outcomes was unsuccessful
Gary 2007	< 6 months' follow-up
Gelbrich 2014	No exercise-based cardiac rehabilitation intervention
Haykowsky 2007	Meta-analysis
Hollriegal 2016	Relevant outcomes not reported. Emailed Hollriegal on 18 October 2018 to clarify outcomes but received no response
Huang 2014	Abstract - study authors contacted; no usable data

(*Continued*)

Hwang 2015	No exercise-based cardiac rehabilitation intervention
Hwang 2016	Relevant outcomes not reported. Emailed Hwang on 18 October 2018 to clarify outcomes but received no response
Inglis 2006	Inappropriate intervention - exercise advice only
Jónsdóttir 2006b	< 6 months' follow-up
Kaltsatou 2013	Duplicate
Kelly 2016	Not a randomised controlled trial
Keteyian 2016	Not a randomised controlled trial
Kiilavuori 1999	Relevant outcomes not reported. Attempt to contact Kiilavuori on 4 October 2018 to clarify outcomes was unsuccessful
Kitzman 2010	< 6 months' follow-up
Kitzman 2013	< 6 months' follow-up
Kitzman 2016	Not a randomised controlled trial
Kobayashi 2003	Relevant outcomes not reported. Emailed Kobayashi on 4 October 2018 to clarify outcomes but received no response
Kolesnikova 2015	Abstract - study authors contacted; no usable data
Korzeniowska-Kubacka 2010	Not a randomised controlled trial
Koufaki 2014	Comparator contained exercise training
Koukoui 2015	Not a randomised controlled trial
Larsen 2016	Not a randomised controlled trial
Lewinter 2014	Abstract - study authors contacted; no usable data
Lloyd-Williams 2002	Meta-analysis
Masterson 2014	Relevant outcomes not reported. Attempt to contact Masterson on 18 October 2018 to clarify outcomes was unsuccessful
McCarthy 2013	Not a randomised controlled trial
Mediano 2016	Not a randomised controlled trial

(*Continued*)

Mehralian 2014	Inappropriate intervention - education only
Mendes 2014	Not a randomised controlled trial
Meyer 2005	Relevant outcomes not reported. Emailed Meyer on 4 October 2018 to clarify outcomes but received no response
Molloy 2006	Relevant outcomes not reported. Emailed Molloy on 4 October 2018 to clarify outcomes but received no response
Myers 2001	Relevant outcomes not reported. Myers contacted on 4 October 2018 and confirmed no relevant outcomes were measured
Myers 2002	Relevant outcomes not reported. Myers contacted on 4 October 2018 and confirmed no relevant outcomes were measured
Myers 2007	Relevant outcomes not reported. Myers contacted on 4 October 2018 and confirmed no relevant outcomes were measured
Newton 2013	Abstract - study authors contacted; no usable data
Niebauer 2005a	Relevant outcomes not reported. Emailed Niebauer on 4 October 2018 to clarify outcomes but received no response
Niebauer 2005b	Relevant outcomes not reported. Emailed Niebauer on 4 October 2018 to clarify outcomes but received no response
Oka 2000	Relevant outcomes not reported. Emailed Oka on 4 October 2018 to clarify outcomes but received no response
Oliveira 2015	< 6 months' follow-up
Owen 2000	< 6 months' follow-up
Parnell 2002	< 6 months' follow-up
Passino 2008	Relevant outcomes not reported. Emailed Passino on 4 October 2018 to clarify outcomes but received no response
Pinto 2015	Relevant outcomes not reported. Attempt to contact Pinto on 18 October 2018 to clarify outcomes was unsuccessful
Piotrowicz 2015	< 6 months' follow-up
Ponikowski 1997	< 6 months' follow-up
Pozehl 2003	< 6 months' follow-up

(*Continued*)

Pu 2001	Relevant outcomes not reported. Emailed Pu on 4 October 18 to clarify outcomes but received no response
Roscani 2016	< 6 months' follow-up
Sabelis 2004	Relevant outcomes not reported. Emailed Sabelis on 4 October 2018 to clarify outcomes but received no response
Santos 2015	Relevant outcomes not reported. Attempt to contact Santos on 18 October 2018 to clarify outcomes was unsuccessful
Sarullo 2006	< 6 months' follow-up
Scalvini 2016	Inappropriate comparator - control group received inpatient rehabilitation
Schuang 2014	Inappropriate intervention - education advice only
Selig 2004	< 6 months' follow-up
Senden 2005	Relevant outcomes not reported. Emailed Senden on 4 October 2018 to clarify outcomes but received no response
Smart 2004	Meta-analysis
Smart 2007	< 6 months' follow-up
Smolis-Bak 2015	Inappropriate comparator - control group received inpatient rehabilitation
Smolis-Bak 2017	Inappropriate comparator - control group received inpatient rehabilitation
Soska 2014	< 6 months' follow-up
Stewart 1998	Inappropriate intervention - exercise advice only
Suna 2015	< 6 months' follow-up
Sviridenko 2013	< 6 months' follow-up
Takase 2015	< 6 months' follow-up
Taylor-Piliae 2004	Meta-analysis
Tyni-Lenne 2001	< 6 months' follow-up
van den Berg-Emons 2004	< 6 months' follow-up
van Tol 2006	Meta-analysis

(*Continued*)

Vasiliauskas 2007	Relevant outcomes not reported. Emailed Vasiliauskas on 4 October 2018 to clarify outcomes but received no response
Von Oehsen 2013	< 6 months' follow-up
Wagenaar 2014	No exercise-based cardiac rehabilitation intervention
Wielenga 1998	< 6 months' follow-up
Williams 2007	Relevant outcomes not reported. Emailed Williams on 4 October 2018 to clarify outcomes but received no response
Wisløff 2007	< 6 months' follow-up
Yasushi 2015	Relevant outcomes not reported. Attempt to contact Yasushi on 18 October 2018 to clarify outcomes was unsuccessful
Yeh 2004	< 6 months' follow-up
Zhang 2003	< 6 months' follow-up
Zhao 2005	Relevant outcomes not reported. Attempt to contact Zhao on 2018 to clarify outcomes was unsuccessful

Characteristics of studies awaiting assessment *[ordered by study ID]*

ACTR12608000263392

Methods	RCT
Participants	360 adults less than or equal to 6 weeks post acute admission to hospital with symptomatic congestive heart failure as dominant clinical diagnosis
Interventions	A supervised exercise programme consisting of 36 one-hour sessions of gym-based aerobic and resistance exercise over 6 months with active encouragement of home-based exercise, administered in addition to an established disease management programme including education, early review, telephone and outreach support, and optimal drug titration. Comparator is an established disease management programme including education, early review, telephone and outreach support, and optimal drug titration, as well as standard exercise advice
Outcomes	**Primary outcomes:** all-cause 12-month death or re-admission **Secondary outcomes:** depressive symptoms based on the Geriatric Depression Scale and the Cardiac Depression Scale; time to first re-admission; time to first heart failure-related re-admission; number of hospitalisations; hospital bed days occupied; days alive out of hospital; rates of adherence to exercise classes and educational sessions; exercise adherence; walking capacity; functional decline; quality of life based on the Australian Quality of Life questionnaire; programme costs; quality of sleep assessed by the Pittsburgh Sleep Quality Index

ACTR12608000263392 (*Continued*)

Notes	**Note:** the protocol is published and the trial has concluded. Results from an associated full RCT were published in February 2018. This falls outside our search criteria; hence we have not included these data in this review update

ISRCTN86879094

Methods	RCT
Participants	Stable symptomatic HF with preserved ejection fraction (diagnosis according to criteria of the European Society of Cardiology; Paulus 2007)
Interventions	**Experimental intervention:** individually prescribed, supervised, combined endurance/strength training for 12 months (≥ 3 times/week) **Control intervention:** usual care
Outcomes	**Primary:** • Combined outcome score (modified 'Packer score'; Packer 2001). This combined score classifies participants as 1 (worsened), 0 (unchanged), or +1 (improved) **Secondary:** • Components of the primary endpoint (all-cause mortality, cardiovascular hospitalisations, change in NYHA class, change in global self-assessment, change in peak VO_2, change in E/e') • Change in echocardiographic parameters of diastolic function (left atrial volume index, grade of diastolic function, E/e', e', ratio between early (E) and late (atrial - A) ventricular filling velocity (E/A), deceleration time, isovolumic relaxation time), systolic function (LVEF), left ventricular dimensions (left ventricular end-diastolic diameter), and structure (left ventricular mass index) after 6 months and 12 months • Change in quality of life (SF-36, Minnesota Living With Heart Failure questionnaire, Hospital Anxiety and Depression Scale) after 6 months and 12 months • Change in ventilatory efficacy (VE/VCO_2) and submaximal exercise capacity (anaerobic threshold, 6-minute walk distance) after 6 months and 12 months • Change in neurohumoral activation (N-terminal pro brain natriuretic peptide) after 6 months and 12 months • Safety and tolerability of training intervention • Gender aspects of all primary and secondary endpoints
Notes	**Recruitment status:** no longer recruiting. Trial shown as completed on 31.08.2015, on ISRCTN registry, but no results posted. Study author contacted for further details

NCT01033591

Methods	RCT
Participants	Participants with HF with LVEF < 45%
Interventions	**Experimental:** supervised exercise + optimised treatment according to European Society of Cardiology guidelines **No intervention:** control optimised treatment according to European Society of Cardiology guidelines
Outcomes	**Primary outcomes:** • Change in HRQoL (SF-36 and Minnesota Living with Heart Failure Questionnaire)

NCT01033591 (*Continued*)

	Secondary outcomes: • Change in functional capacity (6-minute walking test) • Cardiac structural changes (B-type natriuretic peptide) • Muscle strength (dynamometer) • Body composition (fat and muscular weight) All at 12 months
Notes	Zuazagoitia A, Grandes G, Torcal J, Lekuona I, Echevarria P, Gómez MA, Domingo M, de la Torre MM, Ramírez JI, Montoya I, Oyanguren J, Pinilla RO; EFICAR Group (Ejercicio Físico en la Insuficiencia Cardiaca). Rationale and design of a randomised controlled trial evaluating the effectiveness of an exercise program to improve the quality of life of patients with HF in primary care: the EFICAR study protocol. BMC Public Health 2010;10:33 Protocol published **Recruitment status:** unknown **Estimated study completion date:** January 2015, on clinicaltrials.gov, but no results posted. Study author contacted for further details

NCT01785121

Methods	RCT
Participants	605 participants with HF (both patients with a preserved ejection fraction (HFpEF) and those with reduced ejection fraction (HFrEF) can be included)
Interventions	Patients randomised to the active intervention (Wii group) will be introduced to the Nintendo Wii game computer in an introduction lesson of approximately 2 hours, and the Wii will be installed at home. During the first 3 months after inclusion, participants will be phoned after 2, 4, 8, and 12 weeks to discuss their experiences with the Wii, or to solve possible problems. Patients randomised to the control group (motivational support only) will receive protocolised exercise advice from a member of the HF team (nurse, cardiologist, or physiotherapist). During the first 3 months after inclusion, participants will be phoned after 2, 4, 8, and 12 weeks to discuss their current activity
Outcomes	HRQoL (Minnesota Living With Heart Failure Questionnaire (MLWHFQ))
Notes	Protocol published. Trial completed April 2018, as reported on clinicaltrials.gov, but no results posted. Study authors contacted for additional details

NCT02078947

Methods	RCT
Participants	180 participants, 40 years of age and older, with heart failure with preserved ejection fraction
Interventions	High-intensity exercise, moderate continuous exercise, or usual care
Outcomes	**Primary outcome measures:** Change in peak VO_2 after 3 months **Secondary outcome measures:** Change in E/e' (representing diastolic filling pressure) at baseline and at 3 months

NCT02078947 (*Continued*)

	Change in E/e' at baseline and at 12 months Change in Peak VO_2 at baseline and at 12 months Change in NTproBNP at baseline and at 3 months Change in NTproBNP at baseline and at 12 months Change in health-related quality of life at baseline and at 3 months Change in health-related quality of life at baseline and at 12 months Change in left atrial volume index (LAVI) at baseline and at 3 months Change in left atrial volume index (LAVI) at baseline and at 12 months Change in e' medial at baseline and at 3 months Change in e' at baseline and at 12 months Change in submaximal exercise capacity at baseline and at 3 months Change in submaximal exercise capacity at baseline and at 12 months Change in VE/VCO_2 slope at baseline and at 3 months Change in VE/VCO_2 slope at baseline and at 12 months Change in flow-mediated dilation (FMD) at baseline and at 3 months Change in flow-mediated dilation (FMD) at baseline and at 12 months
Notes	Other study ID numbers: EU 602405-2; estimated study completion date: June 2018; reported on clinicaltrials.gov, but no results posted. Study authors contacted

NCT02696486

Methods	RCT
Participants	16 participants (55 years and older) with a diagnosis of HF with preserved ejection fraction (HFpEF)
Interventions	Study participants will receive medically supervised aerobic and resistance exercise training for 1 hour per session, 3 times per week, for 6 weeks, at the Cardiac Rehab Centre, then will transition to home-based or YMCA partnership-based exercise with staff follow-up contact for an additional 3 weeks
Outcomes	**Primary outcome measures:** Change in quality of life (QoL) score before and after exercise training (ET) [Time Frame: 9 weeks] **Secondary outcome measures:** Change in exercise capacity/tolerance before and after ET using cardiopulmonary exercise testing [Time Frame: 9 weeks]: symptom-limited treadmill testing with expired gas measurement and analysis; exercise capacity measured as peak VO_2 (peak exercise oxygen uptake) in mL/min/kg; continuous monitoring of 12-lead electrocardiogram and blood pressure measured every 2 minutes; peak VO_2 defined as highest VO_2 value of the last 30 seconds before termination of exercise; exercise time and peak workload measured for exercise tolerance; demonstrated ability to co-ordinate patient transition from clinic to home-based or YMCA partnership-based exercise programme with weekly staff follow-up within the study timeline [Time Frame: 9 weeks]: captured 90-day hospital re-admission data starting on study enrollment date and within participants' study timeline [Time Frame: 90 days]
Notes	Recruitment completed. Actual primary completion date reported in clinicaltrials.gov as January 2017. No results posted. Study authors contacted

NCT02903225

Methods	RCT
Participants	40 participants 18 to 80 years of age, males and females, with HF LVEF≤ 40%
Interventions	Exercise training L on a 3 days/week basis over 24 weeks (68 to 74 sessions). Each session started with a 10-minute warm-up walking period followed by 20 minutes of breathing exercises and free non-resistance movements of limbs. This stage was followed by pedaling during 20 minutes at a circuit resistance training protocol with a stationary cycle ergometer. Each session ended with a cool-down period (5 minutes) including diverse stretching manoeuvres of engaged muscle groups. The initial bicycle-ergometer workload (WL) was defined as 50% of maximum achieved in previous stress testing
Outcomes	**Primary outcome measures:** • Clinical events [Time Frame: 6 months]: change in New York Heart Association Functional Class; numbers of hospitalisations 6 months before and after the date of enrolment; temporary or permanent withdrawal from the study protocol (due to persistent atrial or ventricular arrhythmias; worsening of congestive heart failure symptoms; myocardial infarction; unstable angina; need for cardiac interventions: pacemaker, implantable cardioverter-defibrillator, coronary re-vascularisation, or cardiac transplantation; stroke or transient ischaemic attack; severe peripheral intermittent claudication or death observed during training or follow-up sessions) • Mean heart rate [Time Frame: 6 months]: mean value of 12-minute electrocardiogram recordings was considered the resting heart rate (beats per minute) • 6-Minute walk test [Time Frame: 6 months]: walking along a 20-metre-long corridor at their own pace, with the aim of covering as much ground as possible in 6 minutes. The distance walked was expressed in metres • Left ventricular ejection fraction [Time Frame: 1 year]: area-length method was measured to obtain biplane left ventricle volumes. Left ventricle ejection fraction was derived from the standard equation (%) • Quality of life [Time Frame: 6 months]: all participants completed the Short Form-36 Health Survey (SF-36), available in its Spanish version, for measuring physical and mental quality of life • Stress test [Time Frame: 6 months]: symptom-limited exercise testing, measured in metabolic units (MET) • Square root of mean squared successive differences of R-R intervals (rMSSD) [Time Frame: 6 months]: short-term continuous electrocardiographic recordings were performed for heart rate variability analysis. In the time domain, the square root of the mean squared successive differences of R-R intervals (rMSSD) was calculated. Units: ms • Heart rate power high-frequency (HF) [Time Frame: 6 months]: high frequency (HF), from 0.15 to 0.40 Hz of the power spectral analysis, was calculated. Units: ms^2/Hz
Notes	Recruitment completed. Study reported at ClinicalTrials.gov to be completed November 2014. No results posted. Study authors contacted

ET: exercise training; FMD: flow-mediated dilation; HF: heart failure; HFpEF: heart failure with preserved ejection fraction; HFrEF: heart failure with reduced ejection fraction; HRQoL: health-related quality of life; LAVI: left atrial volume index; LVEF: left ventricular ejection fraction; MET: metabolic equivalent; MLWHFQ: Minnesota Living With Heart Failure Questionnaire; NTproBNP: N-terminal prohormone of brain natriuretic peptide; NYHA: New York Heart Association; QoL: quality of life; RCT: randomised controlled trial; rMSSD: mean squared successive differences of R-R intervals; SF-36: Short Form-36; VE: ventilatory efficacy; VCO_2 : carbon dioxide production; VO_2 : oxygen uptake; WL: workload.

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

NCT01914315

Trial name or title	Rehabilitation Program in Heart Failure With Preserved Ejection Fraction
Methods	RCT
Participants	1100 participants
Interventions	Participants will participate in a 6-month cardiac rehabilitation programme, consisting of structured, 60-minute, bi-weekly exercise training sessions, according to a pre-defined protocol. Institutional activity will be complemented by 120 minutes of weekly home exercise prescribed by a specialist in cardiac rehabilitation. Following discharge, participants in the comparator arm will return to the IM outpatient clinics at 2 to 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 and 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, 6-minute walk test, and quality of life 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	Dr. Robert Klempfner Heart Rehabilitation Institute, Sheba Medical Center
Notes	WHO International Clinical Rrials Registry Platform states that trial is still recruiting

NCT02196038

Trial name or title	A Trial of Rehabilitation Therapy in Older Acute Heart Failure Patients (REHAB-HF)
Methods	RCT
Participants	360 participants ≥ 60 years old hospitalised with ADHF
Interventions	12-Week novel, progressive, multi-domain rehabilitation and exercise training intervention or attention control. The multi-domain rehabilitation intervention will include endurance, mobility, strength, and balance training and will be tailored according to participant performance in each of these domains. It will begin upon randomisation during hospitalisation and will continue 3 times per week in an outpatient setting
Outcomes	All participants will undergo measures of physical function and quality of life at baseline, 1 month, and 3 months. Clinical events will be monitored for 6 months following the index hospitalisation
Starting date	September 2014

NCT02196038 (*Continued*)

Contact information	Principal investigator: Dalane W Kitzman, MD; Wake Forest University Health Sciences, Winston-Salem, North Carolina, USA
Notes	Estimated study completion date: November 2020

NCT03041376

Trial name or title	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 chronic heart failure with preserved or mid-range ejection fraction
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 6-minute walk distance at 6 months **Secondary outcomes:** changes in serum biomarkers levels, pulmonary congestion assessed by ultrasound, average daily step count measured by accelerometry, anthropometric measures, symptoms of depression, health-related quality of life, self-efficacy, MAGGIC Risk Score
Starting date	April 2017
Contact information	Jan Belohlavek, Charles University, Czech Republic
Notes	Estimated study completion date: 31 January 2020

ADHF: acute decompensated heart failure; EQ-5D: EuroQoL Group Quality of Life Questionnaire based on 5 dimensions; HbA1C: glycosylated haemoglobin; HF: heart failure; NYHA: New York Heart Association; RCT: randomised controlled trial; WHO: World Health Organization.

DATA AND ANALYSES

Comparison 1. All exercise interventions versus usual care

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 All-cause mortality up to 12 months' follow-up	27	2596	Risk Ratio (M-H, Fixed, 95% CI)	0.89 [0.66, 1.21]
2 All-cause mortality more than 12 months' follow-up	6	2845	Risk Ratio (M-H, Fixed, 95% CI)	0.88 [0.75, 1.02]
3 Hospital admission up to 12 months' follow-up	21	2182	Risk Ratio (M-H, Fixed, 95% CI)	0.70 [0.60, 0.83]
4 Hospital admission more than 12 months' follow-up	6	2691	Risk Ratio (M-H, Random, 95% CI)	0.70 [0.47, 1.05]
5 Hospital admission heart failure only	14	1114	Risk Ratio (M-H, Fixed, 95% CI)	0.59 [0.42, 0.84]
6 Health-related quality of life - MLWHF up to 12 months' follow-up	17	1995	Mean Difference (IV, Random, 95% CI)	-7.11 [-10.49, -3.73]
7 Health-related quality of life - MLWHF and other scales up to 12 months' follow-up	26	3833	Std. Mean Difference (IV, Random, 95% CI)	-0.60 [-0.82, -0.39]
8 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]

ADDITIONAL TABLES

Table 1. Health-related quality of life results

Trial first author (year)	Follow-up	Measure	Outcome values (or change from baseline) at follow-up Mean (standard deviation) Control vs exercise, between-group P value	Between-group difference
Antonicelli (2016)	6 months	MLWHF total	44.5 (12.3) vs 28.6 (12.3); P < 0.001	Exercise > Control
Austin (2005/8)	6 months 5 years	MLWHF Physical MLWHF Emotional MLWHF Total EQ-5D MLWHF Physical	20.4 (12.2) vs 12.6 (9.7) ; P < 0.0001* 8.0 (7.1) vs 4.4 (10.4); P < 0.01* 36.9 (24.0) vs 22.9 (17.	Exercise > Control Exercise > Control Exercise > Control Exercise > Control Exercise = Control

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

		MLWHF Emotional MLWHF Total EQ-5D	8); P < 0.001* 0.58 (0.19) vs 0.70 (0.16); P < 0.0001* 19.3 (23.5) vs 18.3 (11.2); P = 0.66* 7.6 (7.1) vs 7.4 (6.5); P = 0.88* 37.1 (24.9) vs 35.5 (21.7); P = 0.72* 0.58 (0.22) vs 0.64 (0.19); P = 0.12*	Exercise = Control Exercise = Control Exercise = Control
Belardinelli (1999)	2 months 15 months 29 months	MLWHF total	52 (29) vs 40 (19); P < 0.001 52 (20) vs 39 (20); P < 0.001 54 (22) vs 44 (21); P < 0.001	Exercise > Control Exercise > Control Exercise > Control
Belardinelli (2012)	10 years	MWLHF total	58 (14) vs 43 (12); P < 0.001	Exercise > Control
Bocalini (2008)	6 months	WHOQoL Physical Psychological Social Environmental	2 (1) vs 23 (4); P < 0.0001* 1 (1) vs 20 (2); P < 0.0001* 3 (2) vs 16 (1); P < 0.0001* 2 (1) vs 15 (2); P < 0.0001*	Exercise > Control Exercise > Control Exercise > Control Exercise > Control
Chen (2018)	6 months	Physical (SPPB) MLWHF total	8.9 (2.3) vs 10.0 (2.1); P = 0.059 34.3 (14.4) vs 19.4 (12.2); P < 0.001	Exercise = Control Exercise > Control
Dalal (2018)	12 months	MLWHF total Physical Emotional Heart QoL Global Heart QoL Physical Heart QoL Emotional EQ-5D-3L	27.5 (23.2) vs 24.1 (20.9); P = 0.025 14.5 (11.8) vs 12.2 (10.8); P = 0.016 5.5 (6.4) vs 5.1 (5.8); P = 0.273 1.9 (0.9) vs 1.9 (0.9); P = 0.823 1.7 (0.9) vs 1.8 (0.9); P = 0.869 2.3 (0.8) vs 2.3 (0.8); P = 0.683 0.739 (0.263) vs 0.752 (0.240); P = 0.487	Exercise > Control Exercise > Control Exercise = Control Exercise = Control Exercise = Control Exercise = Control Exercise = Control

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

DANREHAB (2008)	12 months	SF-36 PCS SF-36MCS	37.4 (11.4) vs 42.7 (9.1) *; P = 0.14 50.5 (10.0) vs 49.7 (8.8) *; P = 0.81	Exercise = Control Exercise = Control
Davidson (2010)	12 months	MLWHF total	56.4 (18.3) vs 52.9 (15.7); P = 0.33	Exercise = Control
Dracup (2007)	6 months	MLWHF Physical MLWHF Emotional MLWHF Total	19.4 (11.5) vs 16.1 (10.0); P = 0.04* 10.5 (7.4) vs 7.8 (6.6); P = 0.01* 43.2 (26.5) vs 35.7 (23.7); P = 0.05	Exercise > Control Exercise > Control Exercise > Control
Du (2017)	6 months	MLWHF total SF-36	41 (22.4) vs 36.9 (21.59); P = 0.535 54.5 (25.31) vs 53.9 (22.78); P = 0.697	Exercise = Control Exercise = Control
Gary (2010) Comp	6 months	MLWHF total	34.3 (23.6) vs 24.2 (16.3); P = 0.18*	Exercise = Control
Gary (2010) Exer	6 months	MLWHF total	28.9 (29.9) vs 25.6 (19.7); P = 0.71*	Exercise = Control
Hassenpour-Dehkrodi (2015)	6 months	MacNew	58.43 (8.67) vs 63.34 (12.69); P < 0.05	Exercise > Control
Gottlieb (1999)	6 months	MLWHF total MOS PF MOS RL MOS GH	NR (NR) vs 22 (20); NR NR (NR) vs 68 (28); NR NR (NR) vs 50 (42); NR NR (NR) vs 361 (224); NR	NR NR NR NR
HF-ACTION (2009)	12 months	KCCQ+	71.4 (21.3) vs 72.8 (20.4)	Exercise > Control**
Jolly (2009)	6 months 12 months	MLWHF total EQ-5D MLWHF total EQ-5D	34.5 (24.0) vs 36.3 (24.1); P = 0.30 0.62 (0.32) vs 0.66 (0.24); P = 0.004 34.9 (24.8) vs 37.6 (21.0); P = 0.80 0.69 (0.28) vs 0.68 (0.21); P = 0.07	Exercise = Control Exercise > Control Exercise = Control Exercise = Control
Jónsdóttir (2006)	6 months	Icelandic quality of life questionnaire	4.10 (14.04) vs 47.55 (8.7); P = 0.34	Exercise = Control

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

Kaltsatou 2014 (dance)	8 months	SF-36 (physical)+ SF-36 (mental)+ SF-36 (total)+	-0.6 (0.9) vs 3.3 (1.6); P < 0.05 -0.2 (0.5) vs 3.1 (1.3); P < 0.05 -0.8 (1.2) vs 6.5 (2.4); P < 0.05	Exercise > Control Exercise > Control Exercise > Control
Kaltsatou 2014 (exercise)	8 months	SF-36 (physical)+ SF-36 (mental)+ SF-36 (total)+	-0.6 (0.9) vs 2.9 (1.5); P < 0.05 -0.2 (0.5) vs 2.7 (2.2); P < 0.05 -0.8 (1.2) vs 5.7 (3.0); P < 0.05	Exercise > Control Exercise > Control Exercise > 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	Exercise > Control
Koukouvou (2004)	6 months	MLWHF total Spritzer QLI total	34.1 (13.0) vs 45.1 (9.9) ; P = 0.05* 7.1 (1.1) vs 9.1 (1.1); P < 0.0001*	Exercise > Control Exercise > Control
Lang (2018)	6 months	MLWHF total Heart-QoL EQ-5D-5L	29.2 (25.8) vs 38.7 (30. 1); P > 0.05 2.0 (1.0) vs 1.9 (1.0); P > 0.05 0.65 (0.31) vs 0.55 (0. 29); P > 0.05	Exercise = Control Exercise = Control Exercise = Control
McKelvie (2002)	12 months	MLWHF total+	-3.3 (13.9) vs -3.4 (18.1) ; P = 0.98	Exercise = Control
Nilsson (2008)	12 months	MLWHF total	28 (20) vs 22 (12); P = 0. 003	Exercise > Control
Norman (2012)	6 months	KCCQ	77.9 (11.6) vs 81.0 (18. 2); P = 0.78	Exercise = Control
Passino (2006)	9.75 months	MLWHF total	53 (32) vs 32 (26.5); P < 0.0001*	Exercise > Control
Reeves (2017)	3 months	KCCQ	63 (22) vs 65 (19); P > 0. 05*	Exercise = Control
Willenheimer (2001)	10 months	PGAQoL	0 (1) vs 0.7 (0.9); P = 0. 023	Exercise > Control

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

Witham (2005)	6 months	GCHFQ	69 (13) vs 65 (10); P = 0. 48	Exercise = Control
Witham (2012)***	6 months	MLWHF total	15.4 (14.8) vs 11.3 (12. 1); P > 0.05	Exercise = Control
Yeh (2011)	12 months	MLWHF total	18 (6) vs 13 (4); P < 0. 0001	Exercise > Control

*P values: calculated by authors of this Cochrane review ; +: change in outcome from baseline; **We have calculated the between P value for this trial based on individual participant data; ***Data obtained from study authors.
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; 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.
Exercise = Control: no statistically significant difference (P > 0.05) in HRQoL between exercise and control groups at follow-up.
Exercise > Control: statistically significant (P ≤ 0.05) higher HRQoL in exercise group compared to control group at follow-up.
Exercise < Control: statistically significant (P ≤ 0.05) lower HRQoL in exercise group versus control group at follow-up.

Table 2. Costs and cost-effectiveness

Author (year)	**Georgiou (2001)**	**HF-ACTION Reed (2010)**	**Witham (2012)**	**Cowie (2014) Centre and home**	**Dalal (2018)**	**Lang (2018)**
Year of costs	1998	2008	2010	2013/2014	2016	2016
Country	US	US	UK	UK	UK	UK
Currency	USD	USD	GBP	GBP	GBP	GBP
Intervention cost						
Mean costs/patient	4,563	6,483 (SD 4, 884)	474.75	Not reported	418.39	362.61
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

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

Total mean healthcare cost/patient (exercise)	5,282*	57,338 (SD 81,343)+	1888.24 (SD 3111)	221. 58 (hospital) and 196.53 (home)	NR	NR
Total mean healthcare costs per patient (control)	2,055*	56,177 (SD 92,749)+	1943.93 (SD 4551)	Not calculated	NR	NR
Incremental healthcare costs	3227*	1,161 (95% CI -6,205 to 8,404)	- 447.85 (95% CI -1696.00 to 931.00)	NR	NR	NR
Additional healthcare costs considered	Hospitalisations	Medication, procedures, outpatient visits, emergency visits, hospitalisations, tests	Inpatient and outpatient admissions, primary care contacts, medication	NR	NR	NR
Mean healthcare benefit (exercise)	10.24 life-years	2.02 QALYs (SD 1.00)	NR	NR	0.74 QALYs (SD 0.22)	NR
Mean health care benefit (control)	7.96 life-years	1.99 QALYs (SD 1.01)	NR	NR	0.76 QALYs (SD 0.21)	NR
Incremental mean healthcare benefit	1.82 life-years	0.03 (95% CI -0.06 to 0.11)	NR	NR	NR	NR
Incremental cost-effectiveness ratio	1,773 per life-year saved	NR	NR	NR	NR	NR

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 analysis

	All-cause mortality P value	All hospitalisations P value	MLWHF P value	All HRQoL outcomes P value
Type of rehabilitation (exercise only vs comprehensive)	0.72	0.55	0.22	0.49

Table 3. Univariate meta-regression analysis (*Continued*)

Type of exercise (aerobic training alone vs aerobic plus resistance training)	0.93	0.06	0.15	0.66
Exercise dose (number of weeks ×number of sessions/week ×average duration of session in hours)	0.10	0.44	0.89	0.71
Exercise setting (hospital only, home only, both hospital and home)	0.09	0.60	0.62	0.08
Single vs multi-centre	0.46	0.60	0.09	0.06
Publication date	0.20	0.78	0.67	0.74
Risk of bias	0.28	0.05	0.01	0.01

CI: confidence interval; HRQoL: health-related quality of life; MLWHF: Minnesota Living With Heart Failure questionnaire.

Table 4. Trial level subgroup analysis

Author (year)	Outcome(s)	Subgroup(s)	Results (P value)	Data analysis methods	Predefined
HF ACTION (O'Connor 2009)	Composite primary endpoint of all-cause mortality or hospitalisation, median follow-up 30 months	Age (≤ 70 years vs > 70 years), gender (males vs females), race (white vs non-white), heart failure 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 blocker at baseline	"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*)

HF ACTION (Flynn 2009)	Kansas City Cardiomyopathy Questionnaire (KCCQ), overall score up to 36 months	Age, LVEF (≤ 25% or > 25%), previous re-vascularisation (coronary artery bypass graft surgery or percutaneous coronary intervention, or no previous re-vascularisation), history of myocardial infarction, and KCCQ overall summary score at baseline (0 to 50, 50 to 75, or 75 to 100)	No significant subgroup interactions (P > 0.05)	Interaction test	Yes
HF ACTION (Keteyian 2012)	All-cause mortality or hospitalisation and cardiovascular mortality or HF hospitalisation, median follow-up 28.2 months	Exercise volume defined as metabolic equivalent (MET)-hour per week (i.e. product of exercise intensity (where 1 MET is 3.5 mL VO_2 /kg/min) and hours of exercise per 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 to 5 metabolic equivalent (MET)-hours and 5 to 7 MET-hours per week were associated with reductions in subsequent risk that exceeded 30%	Regression-based methods (based only on exercise group data)	Post hoc
HF ACTION (Pina 2013)	Kansas City Cardiomyopathy Questionnaire (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	Interaction test	Post hoc

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

			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		
HF ACTION (Mentz 2013)	Mortality/hospitalisation, mortality, and CV mortality/HF hospitalisation	Chronic obstructive pulmonary disease (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 (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, here was evidence for an interaction between black race and exercise training for change in 6-minute walk distance. No other exercise or health status variable demonstrated a statistically significant interaction with race and exercise training	Interaction test	Post hoc
HF-ACTION (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	Interaction test	Post hoc

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

			significance		
HF-ACTION (Banks 2016)	6-Minute walk distance (6MWD) and peak VO_2	Diabetes mellitus	No evidence of an interaction between DM and exercise training on any clinical outcomes	Interaction test	Post hoc
HF-ACTION (Parikh 2016)	Kansas City Cardiomyopathy Questionnaire (KCCQ) and exercise capacity	Angina pectoris	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 (Luo 2017)	Mortality/hospitalisation, mortality, and CV mortality/HF hospitalisation/exercise capacity/HRQoL	Atrial fibrillation	No significant interactions between baseline AF status and randomisation group for change in quality of life 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

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

HF-ACTION (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

6MWD: 6-minute walking distance; ACE: angiotensin-converting enzyme; AF: atrial fibrillation; CI: confidence interval; COPD: chronic obstructive pulmonary disease; CV: cardiovascular; DM: diabetes mellitus; HF: heart failure; 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; SES: socioeconomic status; VO_2 : oxygen uptake.

WHAT'S NEW

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

(*Continued*)

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

HISTORY

Protocol first published: Issue 4, 2001

Review first published: Issue 3, 2004

Date	Event	Description
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

Linda Long and Ify Mordi undertook study selection, data extraction, assessment of risk of bias, and data analysis, including GRADE assessment and meta-analysis.

Rod Taylor led the update of the review and contributed to drafting of review update text and response to peer review. He undertook meta-regression analysis.

Linda Long wrote the first draft of the review update and response to peer review. All co-authors commented on a draft of the report.

DECLARATIONS OF INTEREST

Rod Taylor and Hayes Dalal 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). Rod Taylor declares that he is an author on three included studies - Jolly et al (2009); Lang et al (2018); and Dalal et al (2018). He was not involved in the latest round of risk of bias assessments for this updated review.

Linda Long has no conflicts of interest.

Ify Mordi has no conflicts of interest.

Charlene Bridges has no conflicts of interest.

Viral Segar has no conflicts of interest.

Edward Davies has no conflicts of interest.

Andrew Coats has no conflicts of interest.

Karen Rees has no conflicts of interest.

Sally Singh has no conflicts of interest.

SOURCES OF SUPPORT

Internal sources

- None, Other.

External sources

- None, Other.

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

NOTES

None.

INDEX TERMS

Medical Subject Headings (MeSH)

*Exercise Therapy [mortality]; Chronic Disease; Exercise Tolerance; Health Status; Heart Failure [mortality; *rehabilitation]; Hospitalization [statistics & numerical data]; Quality of Life; Randomized Controlled Trials as Topic

MeSH check words

Adult; Aged; Humans; Middle Aged; Young Adult