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[Intervention Review]

Exercise-based rehabilitation for heart failure

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ABSTRACT

Background

Previous systematic reviews and meta-analyses consistently show the positive effect of exercise-based rehabilitation for heart failure (HF) on exercise capacity; however, the direction and magnitude of effects on health-related quality of life, mortality and hospital admissions in HF remain less certain. This is an update of a Cochrane systematic review previously published in 2010.

Objectives

To determine the effectiveness of exercise-based rehabilitation on the mortality, hospitalisation admissions, morbidity and health-related quality of life for people with HF. Review inclusion criteria were extended to consider not only HF due to reduced ejection fraction (HFREF or 'systolic HF') but also HF due to preserved ejection fraction (HFPEF or 'diastolic HF').

Search methods

We updated searches from the previous Cochrane review. We searched the Cochrane Central Register of Controlled Trials (CENTRAL) (Issue1, 2013) from January 2008 to January 2013. We also searched MEDLINE (Ovid), EMBASE (Ovid), CINAHL (EBSCO) and PsycINFO (Ovid) (January 2008 to January 2013). We handsearched Web of Science, bibliographies of systematic reviews and trial registers (Controlled-trials.com and Clinicaltrials.gov).

Selection criteria

Randomised controlled trials of exercise-based interventions with six months' follow-up or longer compared with a no exercise control that could include usual medical care. The study population comprised adults over 18 years and were broadened to include individuals with HFPEF in addition to HFREF.

Data collection and analysis

Two review authors independently screened all identified references and rejected those that were clearly ineligible. We obtained full-text papers of potentially relevant trials. One review author independently extracted data from the included trials and assessed their risk of bias; a second review author checked data.

Main results

We included 33 trials with 4740 people with HF predominantly with HFREF and New York Heart Association classes II and III. This latest update identified a further 14 trials. The overall risk of bias of included trials was moderate. There was no difference in pooled mortality between exercise-based rehabilitation versus no exercise control in trials with up to one-year follow-up (25 trials, 1871 participants: risk ratio (RR) 0.93; 95% confidence interval (CI) 0.69 to 1.27, fixed-effect analysis). However, there was trend towards a reduction in mortality with exercise in trials with more than one year of follow-up (6 trials, 2845 participants: RR 0.88; 95% CI 0.75 to 1.02, fixed-effect analysis). Compared with control, exercise training reduced the rate of overall (15 trials, 1328 participants: RR 0.75; 95% CI 0.62 to 0.92, fixed-effect analysis) and HF specific hospitalisation (12 trials, 1036 participants: RR 0.61; 95% CI 0.46 to 0.80, fixed-effect analysis). Exercise also resulted in a clinically important improvement superior in the Minnesota Living with Heart Failure questionnaire (13 trials, 1270 participants: mean difference: -5.8 points; 95% CI -9.2 to -2.4, random-effects analysis) - a disease specific health-related quality of life measure. However, levels of statistical heterogeneity across studies in this outcome were substantial. Univariate meta-regression analysis showed that these benefits were independent of the participant's age, gender, degree of left ventricular dysfunction, type of cardiac rehabilitation (exercise only vs. comprehensive rehabilitation), mean dose of exercise intervention, length of follow-up, overall risk of bias and trial publication date. Within these included studies, a small body of evidence supported exercise-based rehabilitation for HFPEF (three trials, undefined participant number) and when exclusively delivered in a home-based setting (5 trials, 521 participants). One study reported an additional mean healthcare cost in the training group compared with control of USD3227/person. Two studies indicated exercise-based rehabilitation to be a potentially cost-effective use of resources in terms of gain in quality-adjusted life years (QALYs) and life-years saved.

Authors' conclusions

This updated Cochrane review supports the conclusions of the previous version of this review that, compared with no exercise control, exercise-based rehabilitation does not increase or decrease the risk of all-cause mortality in the short term (up to 12-months' follow-up) but reduces the risk of hospital admissions and confers important improvements in health-related quality of life. This update provides further evidence that exercise training may reduce mortality in the longer term and that the benefits of exercise training on appear to be consistent across participant characteristics including age, gender and HF severity. Further randomised controlled trials are needed to confirm the small body of evidence seen in this review for the benefit of exercise in HFPEF and when exercise rehabilitation is exclusively delivered in a home-based setting.

PLAIN LANGUAGE SUMMARY

Exercise-based rehabilitation for heart failure

Background

People with heart failure experience marked reductions in their exercise capacity, which has detrimental effects on their activities of daily living, health-related quality of life and ultimately their hospital admission rate and mortality.

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 being randomly allocated to participants) looking at the effectiveness of exercise-based treatments compared with no exercise on heart failure in adults over 18 years of age. The inclusion criteria of this updated review were extended to consider not only HF due to reduced ejection fraction (HFREF or 'systolic HF') (ejection fraction is a measure of how well your heart is pumping), but also HF due to preserved ejection fraction (HFPEF or 'diastolic HF'). The search is current to January 2013.

Key results

We found 33 RCTs that included 4740 participants. The findings of this update are consistent with the previous (2010) version of this Cochrane review and show important benefits of exercise-based rehabilitation that include a reduction in the risk of hospital admissions

due to HF and improvements in health-related quality of life compared with not undertaking exercise. There was a high level of variation across studies in health-related quality of life outcome. While the majority of evidence was for exercise-based rehabilitation in people with HFREF, this update did identify a broader evidence base that included higher risk (New York Heart Association class IV) and older people, people with HFPEF and more programmes conducted in a home-based setting. We found no evidence to suggest that exercise training programmes cause harm in terms of an increase in the risk of death in either the short or longer term. A small body of economic evidence was identified indicating exercise-based rehabilitation to be cost-effective. Further evidence is needed to understand the effect of exercise training in people with HFPEF better and the costs and effects of exclusively home-based exercise rehabilitation programmes.

Quality of evidence

The general lack of reporting of methods in the included trial reports made it difficult to assess their methodological quality and thereby judge their risk of possible bias.

BACKGROUND

Description of the condition

People with heart failure (HF) present with a variety of symptoms most of which are non-specific (Watson 2000). The most frequently presenting symptom is exertional breathlessness. Other important symptoms are fatigue and lethargy in addition to swelling of the feet and ankles. There is no single diagnostic test for HF and diagnosis relies on clinical judgement based on a combination of history, physical examination and appropriate investigations. The symptoms and functional exercise capacity are used to classify the severity of HF, using the New York Heart Association (NYHA) classification (NYHA 1994), and to judge responsiveness to treatment. While diagnosis is based upon symptoms, disease severity can be quantified using objective measures, for example echocardiographic assessment of ejection fraction.

People with HF experience marked reductions in their exercise capacity, which has detrimental effects on their activities of daily living, health-related quality of life (HRQoL), and ultimately their hospital admission rate and mortality (WGCR 2001). While survival after HF diagnosis has improved (AHA 2014), HF has a poor prognosis as 30% to 40% of people diagnosed with HF die within one year although thereafter the mortality is less than 10% per year (AHA 2014). Hospital admission rates for HF in the US appear to have fallen between 1998 and 2008 (Chen 2011). However, in the UK, despite a progressive reduction in age-adjusted hospital admission rates since 1992 to 1993, admissions due HF are projected to rise by 50% over the next 25 years, largely due to the ageing of the population (NICE 2010). It is estimated that the total annual cost of HF to the UK National Health Service (NHS) is around GBP1 billion, or around 2% of the total UK NHS budget; approximately 70% of this total is due to the costs of hospitalisation (Editorial 2011; NICE 2010).

The prevalence and incidence of HF is steadily increasing, with approximately 825,000 new cases annually in the US (AHA 2014). While improved management of hypertension has reduced this condition as an aetiological factor in the development of HF, the increased survival rate from myocardial infarction has led to a subsequent increase in the number of cases of HF (Kostis 1997), as has increasing longevity in developed countries. Estimates of the prevalence of HF in the US range from 0.7% to 1.5% in adults aged 40 to 59 years; over 80 years of age the prevalence of HF is in the region of 8.6% to 11.5% (AHA 2014).

It has been increasingly recognised that HF has two subcategories. People with HF can be categorised as having impaired left ventricular contraction, which results in a reduced ejection fraction (less than 35% to 50%), known as HF with reduced ejection fraction (HFREF) or 'left ventricular dysfunction' or 'systolic HF'. The other category is HF with preserved ejection fraction (HFPEF) with an ejection fraction of greater than 35% to 50% and also known as 'diastolic HF' (Lam 2011; Owen 2006). Prognosis in HFPEF is better than HFREF. One meta-analysis reported a mortality of 32.1% in HFPEF versus 40.6% in HFREF (risk ratio (RR) 0.79) over a mean of 47 months' follow-up (Somaratne 2009). Although individuals with HFPEF are thought to contribute 54% of all people with HF, most trials to date of drug and medical device therapies have recruited only people with HFREF. This limited number of studies examining the effect of different pharmacological agents with proven use in HFREF has largely been disappointing in the HFPEF group (Holland 2011).

National and international evidence-based guidelines have been developed to help improve diagnosis and treatment for people with HF. These guidelines cover aetiology, prevention, diagnostic modalities and therapeutic interventions that increasingly in-

clude exercise rehabilitation (ACCF/AHA 2013; McMurray 2012; NICE 2010).

Description of the intervention

While there are many definitions of cardiac rehabilitation (CR), the following presents their combined key elements: "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 2012). A central component of CR is exercise training (Piepoli 1998). However, in addition to exercise, programmes are encouraged also provide risk factor and lifestyle education on risk factor management plus counselling and psychological support, so-called 'comprehensive CR' (Corra 2005).

Based on current evidence of clinical outcomes and costs, national and international guidelines on the management of HF including the American College of Cardiology/American Heart Association, European Society of Cardiology and National Institute for Health and Care Excellence (NICE) in the UK consistently recommend CR as an effective and safe intervention (ACCF/AHA 2013; McMurray 2012; NICE 2010). However, these guidelines are not fully implemented in practice and the current uptake of CR for HF appears to be suboptimal (Dalal 2012; Tierney 2011). A key driver of this poor uptake has shown to be that CR programmes are not offering rehabilitation to people with HF due to lack of resources and exclusion of HF from local commissioning agreements (Dalal 2012).

How the intervention works

The precise mechanism(s) through which exercise training benefits people with HF remains unclear. One explanation, applicable to people with Ischaemic causes of HF, is that exercise training improves myocardial perfusion by alleviating endothelial dysfunction, therefore 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). One meta-analysis by Haykowsky et al. demonstrated the benefits of exercise training on cardiac remodelling as measured by ejection fraction, end-diastolic volume and end-systolic volume (Haykowsky 2007). Regardless of cause, there are important neurohormonal and musculoskeletal abnormalities in HF. 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). Hambrecht et al. have demonstrated that regular physical activity in people with HF stimulates 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 2010. The first Cochrane systematic review of exercise-based interventions for HF in 2004 concluded that exercise training clearly improved short-term (up to one-year follow-up) exercise capacity compared with no exercise control (Rees 2004; Smart 2004). However, only one of the 29 included randomised controlled trials (RCTs) was powered to report hospitalisations and mortality. Few trials assessed HRQoL. Accepting the evidence for improvement in short-term exercise capacity, the updated 2010 Cochrane review focused on trials of follow-up of six-months or longer that reported clinical events (mortality, hospitalisation) or HRQoL (Davies 2010). The 2010 review of 19 RCTs (3647 participants) showed no difference between exercise and control in either short or long-term all-cause mortality, a reduction in HF-related hospitalisations (RR 0.72; 95% CI 0.52 to 0.99) and improvement in patient-reported HRQoL (standardised mean difference (SMD) 20.63; 95% CI 20.37 to 20.80) with exercise therapy. The majority of trials included in the 2010 review were in men at low-to-medium risk (NYHA class II to III). None of the trials included people with HFPEF and programmes delivered in a centre-based setting.

Using additional RCT evidence, since the 2010 Cochrane review, the aim of this update was to reassess the effectiveness of exercise-based rehabilitation on mortality, hospital admissions, morbidity and HRQoL of people with HF compared with no exercise training. In particular, we sought to identify additional evidence: 1. for those individuals poorly represented in previous reviews (i.e. older individuals, females and people with HFPEF), 2. for programmes specifically delivered in a home- or community-based setting and 3. on costs and cost-effectiveness.

OBJECTIVES

To determine the effectiveness of exercise-based rehabilitation on the mortality, hospitalisation admissions, morbidity and health-related quality of life for people with HF. Review inclusion criteria were extended to consider not only HF due to reduced ejection fraction (HFREF or 'systolic HF') but also HF due to preserved ejection fraction (HFPEF or 'diastolic HF').

METHODS

Criteria for considering studies for this review

Types of studies

RCTs of either a parallel group or cross-over design where the follow-up was at least six months post-randomisation.

Types of participants

Adults aged 18 years or older with HF.

We widened the inclusion criteria to include studies with individuals with HFPEF in addition to those with HFREF who were included in the previous versions of this review. We excluded studies that included participants who had previously received exercise rehabilitation.

Types of interventions

Exercise-based interventions either alone or as a component of comprehensive CR (defined as programmes including 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 include one or more of the following outcomes.

Primary outcomes

Mortality and safety: all-cause mortality, deaths due to HF and sudden death.

Hospital admission or re-hospitalisation, and whether this was due to HF.

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

Electronic searches

For the previous reviews (Davies 2010; Rees 2004), the review authors searched the Cochrane Controlled Trials Register (Issue 1, 2001; Issue 1, 2007), MEDLINE, EMBASE and CINAHL (1984 to January 2008) (see Appendix 1; Appendix 2). The search strategy developed in 2008 included broader terms as this search was part of review strategy that sought to identify evidence for CR that included an update of this review and exercise-based rehabilitation for coronary heart disease (Heran 2011), and home- versus centre-based CR (Taylor 2010).

This search was updated from the last version (2008) and included the Cochrane Central Register of Controlled Trials (CENTRAL) (Issue 1, 2013), MEDLINE (Ovid, January 2013, week 4 2013), MEDLINE In-Process (Ovid, 5 February 2013), EMBASE (Ovid, January 2013, week 5), CINAHL (EBSCOhost, 5 February 2013) and PsycINFO (Ovid, January 2013, week 5). A small addition to the search strategy was made to reflect the more recent use of the terms 'HFPEF' and 'HFREF'.

We searched conference proceedings on Web of Science (2008 to January 2013) and trial registers (Clinicaltrials.gov; Controlled-trials.com).

We limited searches to RCTs and applied filters to limit to humans and year 2008 onwards. We imposed no language or other limitations. We considered variations in terms used and the spelling of terms in different countries, so that studies were not missed by the search strategy. We designed the search strategies with reference to those of the previous systematic review (Davies 2010), and in accordance with the *Cochrane Handbook of Reviews of Interventions* (Higgins 2011) (see Appendix 3).

Searching other resources

We searched reference lists of all eligible trials and identified systematic reviews for additional studies.

Data collection and analysis

Selection of studies

Two review authors (VAS, RST) screened the references identified by the search strategy by title and abstract and discarded clearly irrelevant studies. For selection, 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 (VAS and RST) independently assessed them for eligibility based on the defined inclusion criteria. We resolved any disagreements by discussion. EJD, KR and RST undertook data study selection in previous review versions.

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), risk of bias (randomisation, blinding, attrition and control) and results. One review author (VAS) extracted data and a second review author (RST) checked entries. We contacted study

authors to seek clarification on issues of reporting or to obtain further outcome details. Excluded studies and reasons for their exclusion are detailed in the Characteristics of excluded studies table. EJD, KR and RST undertook data extraction in previous review versions.

Assessment of risk of bias in included studies

Factors considered included the quality of the random sequence generation and allocation concealment, incomplete outcome data, analysis by intention-to-treat, blinding (participants, personnel and outcome assessors) and selective outcome reporting (Higgins 2011). One review author (VAS) assessed the risk of bias in eligible trials and a second review author (RST) verified the decision. EJD, KR and RST undertook risk of bias in previous review versions.

Measures of treatment effect

We expressed dichotomous outcomes as RR and 95% CI for each study. For continuous variables, we compared net changes (i.e. exercise group minus control group to give differences) and calculated mean difference (MD) or SMD and 95% CI for each study. For each trial, we sought the mean change (and standard deviation (SD)) in outcome 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. For trials with more than one relevant intervention arm, we divided the number randomised in the control group by the number of intervention arms to obtain the denominator for data analysis. Where trials reported more than one HRQoL outcome, we included the first outcome reported in the paper in the meta-analysis. We tabulated all reported HRQoL outcomes at all follow-up times for each included study. We reported outcome results at two time points: 1. up to and including 12 months' follow-up and 2. longer than 12 months' follow-up. The latest follow-up was used in each of these time point analyses.

Assessment of heterogeneity

We explored heterogeneity among included studies qualitatively (by comparing the characteristics of included studies) and quantitatively (using the Chi^2 test of heterogeneity and the I^2 statistic). Where appropriate, we combined the results from included studies for each outcome to give an overall estimate of treatment effect.

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 (i.e. all-cause mortality, hospital admissions and HRQoL) (Egger 1997).

Data synthesis

We processed data in accordance with the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011). We used a fixed-effect meta-analysis except where we identified statistical heterogeneity (I^2 statistic greater than 50%), where we used a random-effects model.

Subgroup analysis and investigation of heterogeneity

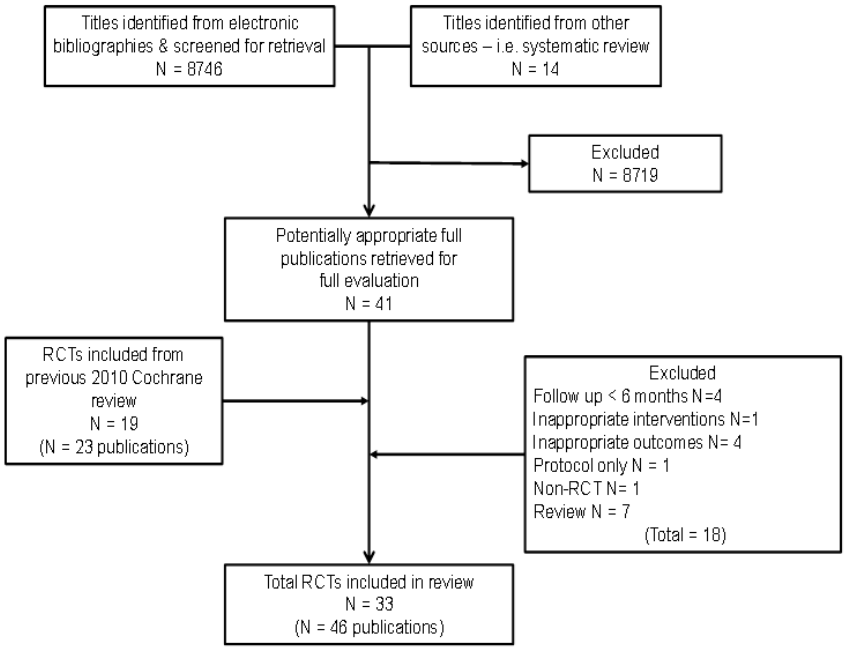
We explored the potential heterogeneity in exercise-based rehabilitation by two approaches: 1. within-trial subgroup analyses (supported by subgroup x intervention/control interaction terms) and 2. between-trial analyses using meta-regression. Meta-regression was used to examine the association between the effect of exercise on all-cause mortality, all hospitalisation and HRQoL (MLWHF or other measures) up to 12 months as these three outcomes contained the most trials. Specific study covariates included in the meta-regression included: mean per cent left ventricular ejection fraction (LVEF); dose of aerobic exercise (calculated as the overall number of weeks of training multiplied by the mean number of sessions per week multiplied by the 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 versus comprehensive); overall risk of bias ('low', i.e. absence of bias in five or more of eight of risk of bias items; 'high', i.e. absence of bias in fewer than five of eight of risk of bias items); single versus multicentre; and publication date. We added year of publication as an additional study level factor (pre versus post 2000) in order 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 covariates, meta-regression was limited to univariate analysis (Higgins 2011). The permute option in STATA was used to allow for multiple testing in meta-regression.

RESULTS

Description of studies

The 2004 and 2010 versions of this Cochrane review contributed eight (Rees 2004) and 19 trials (Davies 2010) to this latest update. Several trials from the 2004 review were excluded in the 2010 review as their follow-up was less than six months or they reported only exercise capacity outcomes. This 2014 update identified a further 14 trials. The study selection process is summarised in the QUORUM flow diagram shown in Figure 1.

Figure 1.



The included 33 trials randomised 4740 participants predominantly with HFREF and NYHA classes II and III. Four trials included a (undefined) proportion of people with HFPEF (Davidson 2010; Gary 2010 (comp); Gary 2010 (exalone); Nilsson 2008; Wall 2010). The majority of trials were small (26 trials had fewer than 100 participants) and single centre (30 trials), with one large trial contributing about 50% (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 87%), although there was evidence that more females were recruited in recent trials. Only four trials reported on ethnicity and 62% to 100% of the study population was white. Eleven trials reported follow-up in excess of 12 months (Austin 2005; Belardinelli 1999; Belardinelli 2012; Davidson 2010; Dracup 2007; HF ACTION 2009; McKelvie 2002; Mueller 2007; Myers 2000; Nilsson 2008; Wall 2010). Two trials had more than one exercise intervention arm. These two trials were treated as each contributing two separate comparative arms for the purpose of the meta-analysis (Gary 2010 (comp); Gary 2010 (exalone); Klocek 2005 (Const); Klocek 2005 (Prog)). All trials evaluated an aerobic intervention and 11 also included resistance training (Austin 2005; DANREHAB 2008; Dracup 2007; Jolly 2009; Jónsdóttir 2006a; Koukouvou 2004; McKelvie 2002; Norman 2012; Pozehl 2008; Witham 2005; Witham 2012). Exercise training was most commonly delivered in either an exclusively centre-based setting or a centre-based setting in combination with some home exercise sessions. Five studies were conducted in an exclusively home-based setting (Dracup 2007; Gary 2010 (comp); Gary 2010 (exalone); Jolly 2009; Passino 2006; Wall 2010). The dose of exercise training ranged widely across studies with session duration of 15 to 120 minutes, one to seven sessions/week, inten-

sity of 40% to 80% of maximal heart rate to 50% to 85% of maximal oxygen uptake (VO_2 max) to Borg rating of 12 to 18, over a period of 15 to 120 weeks. In addition to exercise training,12 trials included other ('comprehensive rehabilitation') elements that included education and psychological interventions (Bocalini 2008; DANREHAB 2008; Davidson 2010; Gary 2010 (exalone); Jolly 2009; Jónsdóttir 2006a; Mueller 2007; Myers 2000; Nilsson 2008; Pozehl 2008; Witham 2012).

Details of the studies included in the review are shown in the Characteristics of included studies table. Reasons for exclusion are presented in the Characteristics of excluded studies table. The status of ongoing trials are detailed in the Characteristics of ongoing studies table.

Risk of bias in included studies

The overall risk of bias was moderate. A number of trials (particularly those published prior to 2000) failed to give sufficient detail to assess their potential risk of bias (Figure 2; Figure 3). Details of generation and concealment of random allocation sequence and blinding of outcomes were particularly poorly reported. Only the studies of Austin 2005; DANREHAB 2008; HF ACTION 2009; Jolly 2009; McKelvie 2002; and Witham 2012 provided an adequate description of the randomisation process. Nevertheless, none of the studies had 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. Given the nature of an exercise intervention, is not possible to blind participants and carers. However, several studies reported blinding of outcome assessment (Davidson 2010; Gary 2010 (exalone); Gary 2010 (comp); HF ACTION 2009; McKelvie 2002, Koukouvou 2004; Nilsson 2008; Willenheimer 2001; Witham 2005; Yeh 2011). By not reporting co-intervention details for both exercise and control groups, some studies may be prone to performance bias (Belardinelli 1999; Giannuzzi 2003; Gielen 2003; Hambrecht 1995; Hambrecht 2000; Keteyian 1996; Klecha 2007; Klocek 2005 (Prog); Klocek 2005 (Const); McKelvie 2002; Nilsson 2008; Pozehl 2008). There was evidence of improvement in reporting and lower risk of bias in more recent trials.

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

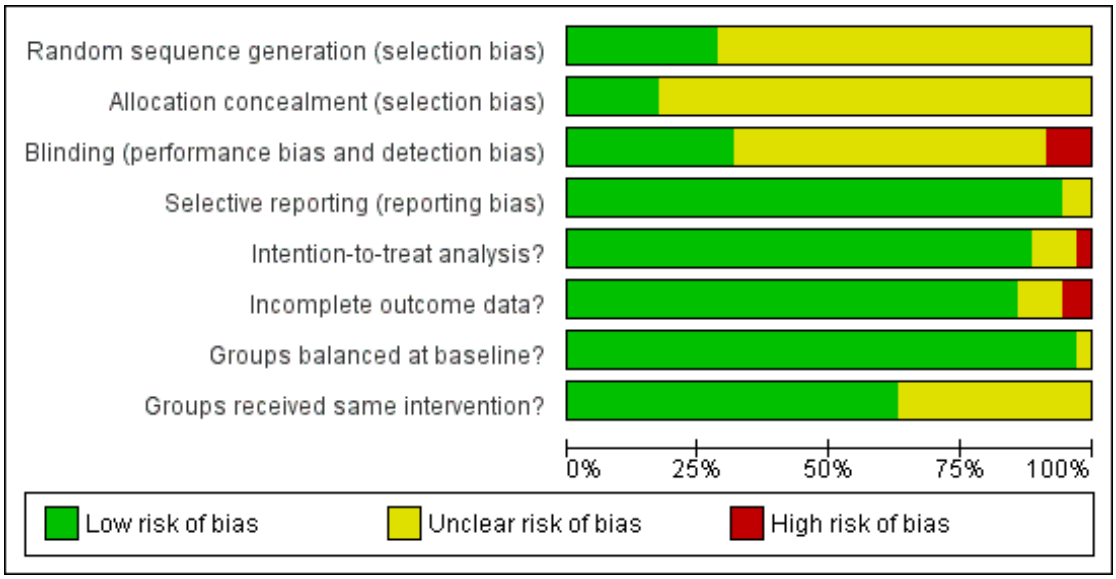
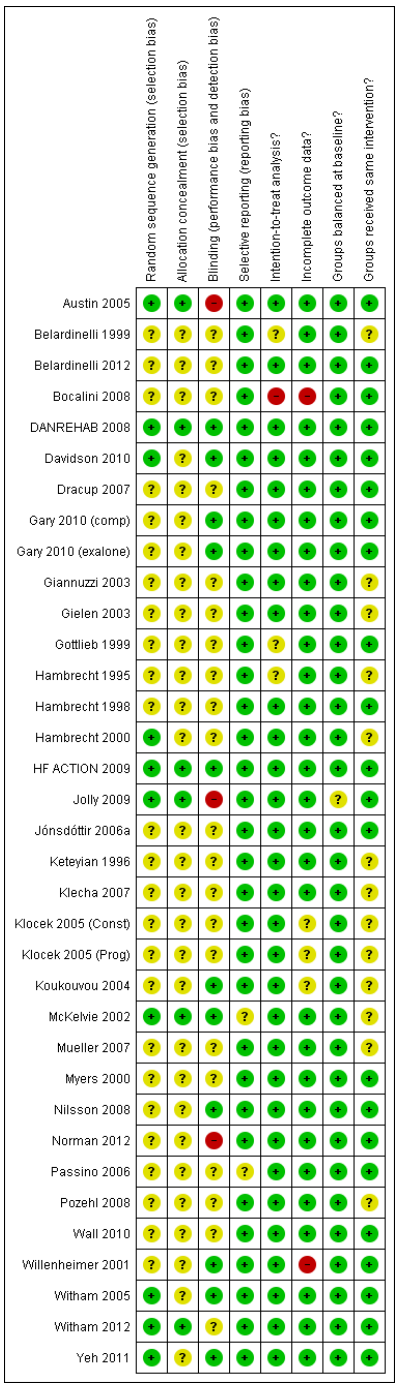


Figure 3. Methodological quality summary: review authors' judgements about each methodological quality item for each included study.



Effects of interventions

Mortality

Twenty-two studies reported all-cause mortality at up to 12-months' follow-up. The trials of Gielen 2003 and Klecha 2007 reported no deaths in either the exercise or control arm. There was no significant difference in pooled mortality up to 12 months' follow-up between groups (RR 0.93; 95% CI 0.69 to 1.27; P value = 0.59, I^2 = 0%; Chi^2 = 12.37, P value = 0.26, fixed-effect analysis) (Analysis 1.1). The studies of 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 (Belardinelli 2012), we obtained mortality data at 10 years by contacting the study authors. There was a trend towards a reduction in all-cause mortality when pooled across longest follow-up point of the six trials with more 12 months' follow-up (RR 0.88; 95% CI 0.75 to 1.02; P value = 0.07, I^2 = 34%; Chi^2 = 7.54, P value = 0.18, fixed-effect analysis) (Analysis 1.2). Studies did not consistently report deaths due to HF or sudden death.

Hospital admissions

There were reductions in the number of people experiencing hospital admissions with exercise compared with control up to 12 months' follow-up, all hospital admissions up to 12 months' follow-up (15 trials, RR 0.75; 95% CI 0.62 to 0.92; P value = 0.005, I^2 = 0%; Chi^2 = 11.71, P value = 0.55, fixed-effect analysis) (Analysis 1.3) and HF-specific admissions (12 trials, RR 0.61; 95% CI 0.46 to 0.80; P value = 0.002, I^2 = 34%; Chi^2 = 16.70, P value = 0.12) (Analysis 1.4). There was no difference in all hospital admissions in trials with more than 12 months' follow-up (5 trials, RR 0.92; 95% CI 0.66 to 1.29; P value = 0.63, I^2 = 63%; Chi^2 = 10.90, P value = 0.03, random-effects analysis) (Analysis 1.5)

Health-related quality of life

Nineteen out of the 33 included trials (20 comparisons) reported a validated HRQoL measure (see Table 1). The majority of studies reported disease-specific quality of life using the MLWHF, the HF ACTION 2009 trial using the Kansas City Cardiomyopathy Questionnaire (KCCQ). Generic HRQoL was also assessed using the EuroQoL (EQ-5D), SF-36, Psychological General Wellbeing index (PGWB), Patient's Global Assessment of Quality of Life (PGAQoL) and Spritzer's Quality of Life Index (QLI). The study by Gottlieb 1999 reported HRQoL values at follow-up for the exercise group but not the controls. Eleven of the 19 trials (58%) reported superior HRQoL at follow-up in people who exercised compared with controls and in no case was HRQoL score lower with exercise than control (see Table 1).

There was evidence of high levels of statistical heterogeneity in the exercise-control difference in MLWHF scores at follow-up across studies. When pooled across the 13 studies that reported the total MLWHF score up to 12 months' follow-up, there was a clinically important improvement with exercise (MD -5.8; 95% CI -9.2 to -2.4; P value = 0.0007, I^2 = 70%; Chi^2 = 40.24, P value < 0.0001, random-effects analysis) (Analysis 1.6). Pooling across all studies, regardless of the HRQoL measure used, there was also evidence of a significant improvement with exercise (19 trials [21 comparisons], SMD -0.46; 95% CI -0.66 to -0.26; P value < 0.0001, I^2 = 80%; Chi^2 = 93.86, P value < 0.0001, random-effects analysis) (Analysis 1.7). The three trials that reported MLWHF score at follow-up greater than 12 months also showed greater improvement compared with control (MD -9.5; 95% CI -17.5 to -1.5; P value < 0.0001, I^2 = 73%; Chi^2 = 7.33, P value < 0.02, random-effect analysis) (Analysis 1.8). Where studies reported more than one total HRQoL measure score, we selected the first cited score reported in the trial publication for meta-analysis to prevent double counting of a study; the inference of the SMD meta-analysis did not change when selecting the alternative HRQoL measure score.

Cost and cost-effectiveness

Three studies reported economic data, two undertaking a cost-effectiveness analysis (Flynn 2009; Georgiou 2001), and one reporting costs (Witham 2012) (see Table 2). Based on the Belardinelli trial (Belardinelli 1999), Georgiou and colleagues estimated an additional mean healthcare cost in the training group compared with controls of USD3227/person (Georgiou 2001). This cost was calculated 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. Using exponential survival modelling to 15.5 years, the estimated increment in life expectancy with exercise was 1.82 years/person compared with people in the control group and an incremental cost-effectiveness ratio of USD1773/life-year saved. The HF ACTION group estimated a mean gain in QALY of 0.03 at an additional mean cost of USD1161/person at 2.5 years' follow-up (Flynn 2009). Although an incremental cost-effectiveness ratio was not reported, the authors stated that there was a 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 the mean cost in the exercise group were lower (-GBP477.85/person) than 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 value 0.05 or less level.

Meta-regression

Predictors of all-cause mortality, hospitalisation and HRQoL intervention effects (12 months or less of follow-up) were examined using univariate meta-regression. No significant associations were seen on all-cause mortality, all hospitalisation and HRQoL at the P less than 0.05 level with the exception of risk of bias and setting for HRQoL (see Table 3). The HRQoL mean effect size for studies with a higher risk of bias was larger than for studies with lower risk of bias (MLWHF MD: high risk: -14.4 vs. low risk -4.2, P value = 0.04): and higher for single-centre studies (all HRQoL SMD: single centre: -0.90 vs. multicentre -0.35, P value = 0.04).

Within-trial subgroup analyses

Several studies 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 a cross-sectional association between particular participant characteristics and outcome (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 (Const); Klocek 2005 (Prog)). Two studies reported subgroup analyses where the methods were unclear (Pozehl 2008; Yeh 2011). Only the large HF ACTION trial undertook a pre-defined formal interaction tests of differences in intervention effects between subgroups. The HF ACTION authors reported no evidence of difference in the intervention effects as assessed on either the primary outcome (all-cause mortality or hospitalisation) or HRQoL (KCCQ overall score) across a number of participant-defined subgroups (see Table 4). The HF ACTION group also undertook a large post hoc observational analysis in those people assigned to exercise training (Keteyian 2012). This analysis showed that the volume of exercise undertaken by participants was associated with the risk for clinical events and moderate levels (3 to 7 MET-h per week) of exercise was needed to observe a clinical benefit.

Small-study bias

There was no evidence of funnel plot asymmetry for all-cause mortality (Egger test P value = 0.805) (Figure 4) or WLWHF (Egger test P value = 0.606) (Figure 5). The funnel plots for SMD HRQoL showed evidence of asymmetry (Egger test P value < 0.0001) (Figure 6).

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.

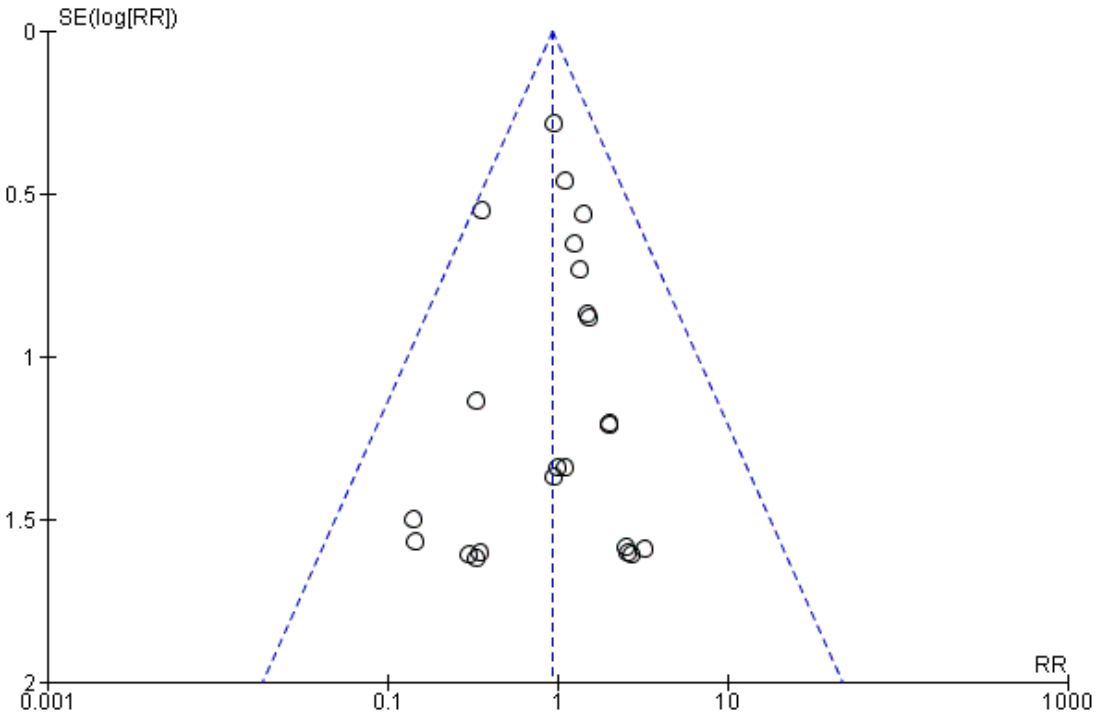


Figure 5. Funnel plot of comparison: 1 All exercise interventions versus usual care, outcome: 1.6 Health-related quality of life - Minnesota Living with Heart Failure (MLWHF) questionnaire up to 12 months' follow-up.

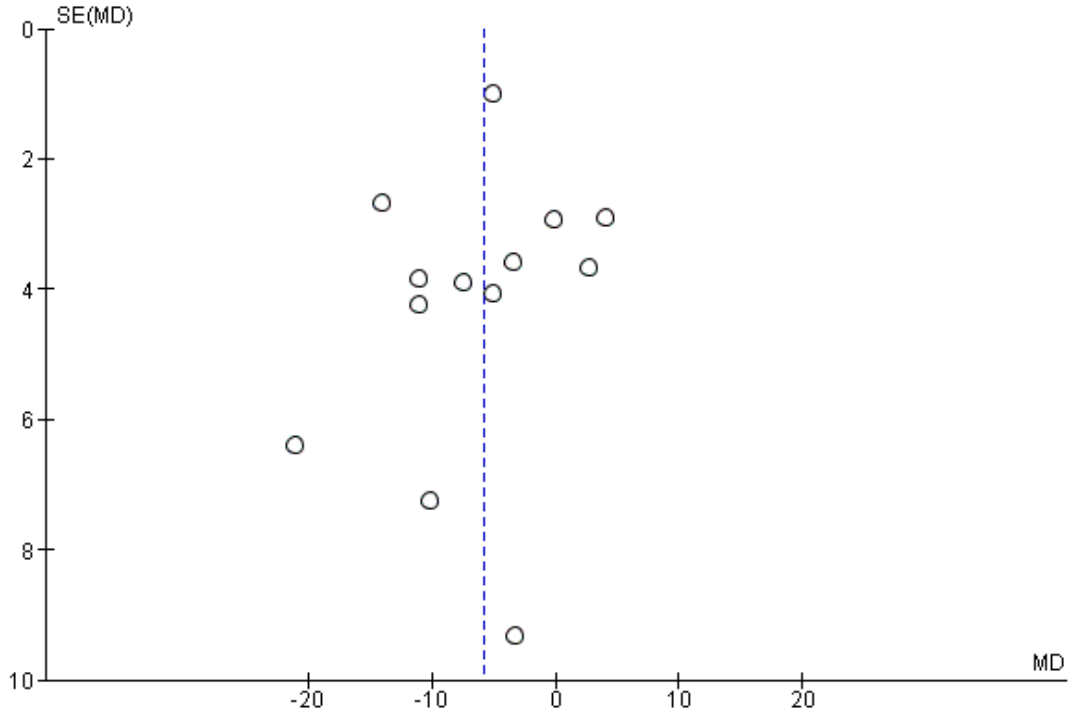
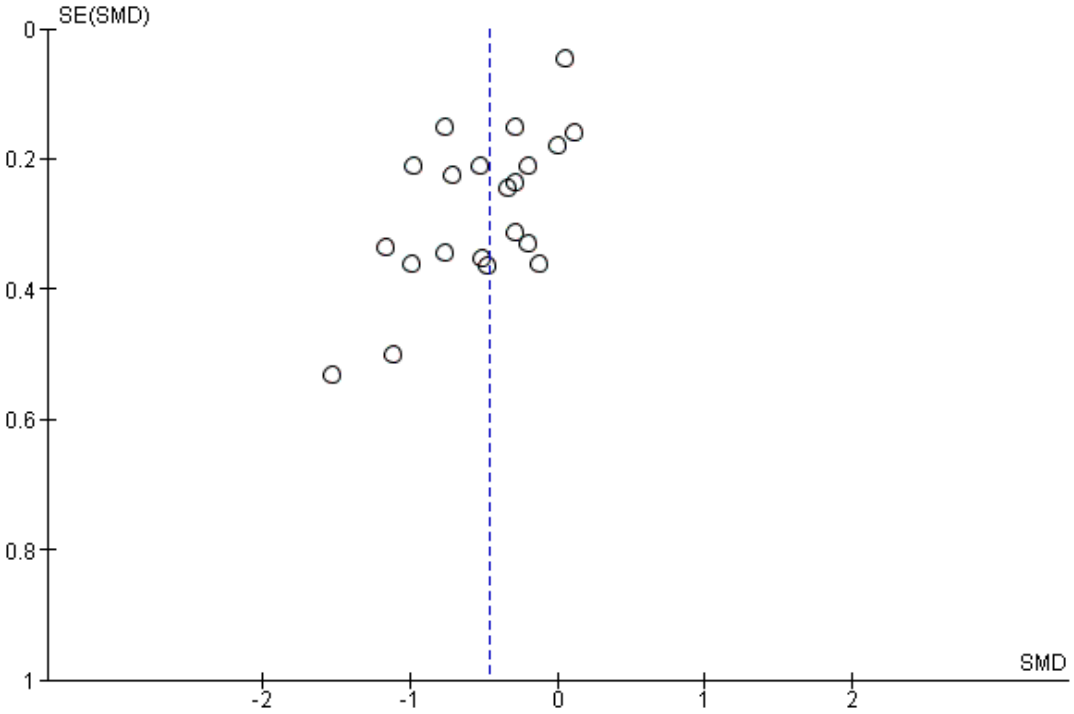


Figure 6. Funnel plot of comparison: 1 All exercise interventions versus usual care, outcome: 1.7 Health-related quality of life - Minnesota Living with Heart Failure (MLWHF) questionnaire and other scales.



DISCUSSION

Summary of main results

This update review shows that, when compared with no exercise control, exercise-based rehabilitation did not significantly impact on short-term (up to 12-months' follow-up) all-cause mortality. There was trend towards a reduction in all-cause mortality in trials with follow-up in excess of 12 months. We also found a reduction in hospitalisations related due to HF and higher levels of HRQoL following exercise training programmes compared with no exercise control. It is important to note that there was significant heterogeneity in our observations on HRQoL. Univariate meta-regression analysis shows that the benefits of exercise-based rehabilitation to be independent of participant age, gender, degree of left ventricular dysfunction, type of CR (exercise only versus comprehensive), mean dose of exercise intervention, length of follow-up, overall risk of bias and trial publication date. Whilst the majority of included participants in this review were HFREF and NYHA class II to III, more recent trials have recruited those who with HFPEF and NHYA IV and a greater proportion of females and older patients. Evidence from two trials support the cost-effectiveness of exercise-based rehabilitation.

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 the inclusion of more women, older age and people with HFPEF in recent trials, the findings of this updated review have potential greater external validity.

Quality of the evidence

The general lack of reporting of methods in the included RCT reports made it difficult to assess their methodological quality and thereby judge their risk of bias. There was evidence of large treatment effect for HRQoL outcomes in studies judged to be overall higher risk of bias compared with lower risk of bias studies, suggesting that risk of bias may be a major driver of the substantive statistical heterogeneity seen across trials in this outcome. There

appeared to be improvement in the quality of reporting in more recent trials.

Potential biases in the review process

We believe this is the most comprehensive systematic review to date of RCT-based evidence for the impact of exercise-based rehabilitation for people with HF. However, our review has some limitations. 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 of short-term follow-up so that the number of deaths and hospitalisations reported by most trials was small. Indeed, in many studies, we located event data in the trial descriptions of losses to follow-up and exclusions rather that as reported outcomes per se.

Agreements and disagreements with other studies or reviews

Based on an individual participant data pooled analysis, the ExTraMATCH Collaborative Group concluded that exercise training for HF significantly reduced overall mortality (hazard ratio 0.65; 95% CI 0.46 to 0.92) at mean follow-up of approximately two years (ExTraMatch 2004). The ExTraMATCH study was based on a limited bibliographic literature search (MEDLINE plus handsearching of selected leading cardiac journals), was limited to trials that reported survival data, and included unpublished data. Therefore, it has been difficult to verify the data and the comprehensiveness of this meta-analysis; in addition, several of the RCTs included in the Cochrane review were not included in the ExTraMATCH review. Re-analysis of the ExTraMATCH data using formal meta-analytic methods (taking account of outcome clustering at the trials level) has shown that the effect of exercise training was not statistically significant when compared with control (RR 0.88; 95% CI 0.70 to 1.10) (Gotzsche 2005).

The impact of exercise training on mortality in people with HF may depend on the length of follow-up and age of studies. While we found no improvement (or worsening) in overall survival with exercise compared with control in trials with short-term follow-up, there was a trend towards an improved survival with exercise in trials with follow-up beyond 12 months. More recent trials included in this review have been conducted in the era of optimal medical therapy. For example, at entry to the HF-ACTION trial, 94% of participants were receiving beta-blockers and angiotensin-receptor blockers or angiotensin-converting enzyme inhibitors (Whellan 2007). Forty-five per cent had an implantable cardioverter defibrillator or implanted biventricular pacemaker at the time of enrolment. Given the proven survival advantage of these medical treatments (Shekelle 2003), any incremental all-cause mortality benefit with exercise is likely to be small.

This update review found the exercise group scored on average 5.8 points higher than the control group at up 12 months' follow-up on the MLWHF questionnaire. A difference of four points or larger on the MLWHF questionnaire has been shown to represent a clinically important, meaningful difference for patients (McAlister 2004). The improvements in HRQoL seen with exercise training are in accordance with the previous systematic review of van Tol and colleagues (van Tol 2006), but not with that of Chien, which focused on home-based exercise training and concluded that exercise training compared with usual care or activity did not improve the HRQoL of people with HF (Chien 2008). Five studies included in this update review were conducted in an exclusively home-based setting (Dracup 2007; Gary 2010 (comp); Gary 2010 (exalone); Jolly 2009; Passino 2006; Wall 2010). Our meta-regression analysis showed no difference in the reduction in hospitalisations and improvement in HRQoL with exercise training between those studies based in a hospital versus home based setting.

AUTHORS' CONCLUSIONS

Implications for practice

This review shows that exercise rehabilitation provides important benefits by improving health-related quality of life and reducing heart failure (HF)-related hospitalisation in people predominantly with reduced left ventricular ejection fraction (HFREF or 'systolic HF') ranging from New York Heart Association (NYHA) class I to IV. We found no evidence to support that exercise training programmes increase (or decrease) the risk of death in the short term but there was trend towards reduced mortality in trials with follow-up beyond 12 months. The benefits of exercise training programmes appears to be independent of participant characteristics (e.g. age, gender, degree of left ventricular dysfunction) and the characteristics and setting of the exercise programmes. Programmes are typically based on aerobic exercise training with or without a resistance exercise element. Despite clinical guidelines stating their support of exercise-based rehabilitation in the management of HF, the provision and uptake of rehabilitation in HF remains poor. Future robust evidence of the economic value (costs and cost-effectiveness) of cardiac rehabilitation is likely to be important to encourage hospital and primary care providers to extend the current provision of exercise-based programmes for HF

Implications for research

The majority of trials in this review have investigated exercise training as a single intervention and against a no exercise control. However, in practice, exercise-based rehabilitation is often an adjunct to other HF management interventions, such as specialist HF nurse support or disease management programmes. While

trials have demonstrated the benefits of such HF management interventions alone, few trials have compared such interventions with and without adding a structured exercise training programme (Jolly 2009; Mudge 2011). This is an important clinical question for the future design of HF services, because the addition of an exercise programme adds considerably to staffing and equipment costs. Future clinical trials of exercise rehabilitation in HF also need to consider: the generalisability of trial populations (women, older people and people with HFPEF remain under-represented in trial populations); interventions to enhance the long-term maintenance of exercise training; and outcomes, costs and cost-effectiveness of exercise-based programmes delivered exclusively in a home-based setting.

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Dr Ann-Dorte Zwisler, Project Manager CopenHeart, Copenhagen, Denmark (DANREHAB 2008) - mortality and health-related quality of life data for people with HF.

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* *Indicates the major publication for the study*

CHARACTERISTICS OF STUDIES

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

Austin 2005

Methods	Parallel group RCT
Participants	**N Randomised:** 200 (exercise 100; control 100) **Diagnosis (% of participants):** *Aetiology:* ischaemic 77%; hypertension 15.5%; DCM 5.5%; other 2% *NYHA*: Class II 51.5%; Class III 48.5% *LVEF:* 40-35%: 16.5%; < 35-30%: 45%; < 30%: 38.5% **Case mix:** 100% as above **Age (yr):** exercise 71.9 (SD 6.3); control 71.8 (SD 6.8) **Male:** 43% **White:** not reported **Inclusion/exclusion criteria** *Inclusion:* age > 60 yr, NYHA Class II or III, and LVSD < 40%, confirmed by echocardiography *Exclusion:* diastolic dysfunction, significant co-morbidity preventing entry into study because of terminal disease or an 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 wk *Aerobic/resistance/mix:* aerobic endurance training and low resistance training/high repetitive muscular strength work *Frequency:* 2 sessions/wk (for 8 wk), 1 session/wk (16 wk) plus 3 sessions/wk at home *Duration:* 2.5 hr class (8 wk) and 1 hr class (next 16 wk) *Intensity:* not reported *Modality*: not reported *Setting:* hospital and home Other: none
Outcomes	HRQoL (MLWHFQ and EuroQol/EQ-5D); healthcare utilisation (length of stay of hospital, admissions arising from heart disease, prescribed HF medication); mortality
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)
Country and setting	UK Single centre
Follow-up	6 months and 5 yr (after randomisation)
Notes	
Risk of bias	

Austin 2005 (*Continued*)

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

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 (yr):** exercise 56 (SD 7); control 53 (SD 9) **Male:** 89% **White:** not reported **Inclusion/exclusion criteria** *Inclusion*: HF, LVEF < 40%, and 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, un-

Belardinelli 1999 (*Continued*)

	controlled hypertension, renal insufficiency (serum creatinine > 2.5 mg/dL), and orthopaedic or neurological limitations)
Interventions	**Exercise:** *Total duration:* 14 month; 8 wk supervised then 12 months maintenance *Aerobic/resistance/mix:* aerobic *Frequency:* 2-3 sessions/wk *Duration:* 40 min/session *Intensity:* 60% max VO_2 *Modality:* cycling *Setting:* hospital-based programme **Other:** all sessions were supervised by a cardiologist
Outcomes	HRQoL (MLWHFQ); mortality; morbidity; cost-effectiveness
Comparison	Standard medical care
Country and setting	Italy Single centre
Follow-up	14 and 26 months (after randomisation)
Notes	

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 methods, reported in results
Intention-to-treat analysis?	Unclear risk	Not reported
Incomplete outcome data?	Low risk	Losses to follow-up 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*"

Belardinelli 1999 (*Continued*)

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 (yr):** 59 (SD 14) **Male:** 78% **White:** not reported **Inclusion/exclusion criteria** *Inclusion:* clinical stability for 3 months before enrolment, LVEF < 40% and ability to exercise *Exclusion:* haemodynamically significant valvular heart disease, uncontrolled DM and hypertension, orthopaedic or neurological problems, and renal insufficiency (creatinine > 2.5 mg/dL)
Interventions	**Exercise:** *Total duration:* 10 yr; 8 wk supervised then 12 months maintenance *Aerobic/resistance/mix:* aerobic *Frequency:* 2-3 sessions/wk *Duration:* 40 min/session *Intensity:* 60% max VO_2 for first 2 months, and thereafter at 70% max VO_2 *Modality:* cycling *Setting*: Hospital and home-based **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 Exercises sessions held at the hospital were supervised by cardiologists. Authors emphasise that the supervised element was maintained over the 10 yr of follow-up
Outcomes	HRQoL (MLWHQ), mortality, morbidity (including hospitalisation), cost-effectiveness
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 of longer than 30 min. Authors advised control group participants to walk and perform usual physical activities
Country and setting	Italy Single centre
Follow-up	10 yr (every 12 months) (after randomisation)

Belardinelli 2012 (*Continued*)

Notes	Every 6 months, participants exercised at the hospital, and then they returned to a coronary club, where they exercised the rest of the year

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 methods, reported in results
Intention-to-treat analysis?	Low risk	"*All analysis were performed with an intention-to-treat principle*"
Incomplete outcome data?	Low risk	Losses to follow-up reported. Drop-out 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 control group decided to withdraw from 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 same interventions apart from CR intervention

Bocalini 2008

Methods	Parallel group RCT
Participants	**N Randomised:** 42 (exercise 22; control 20) **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:* $\leq$ 45% **Case mix:** 100% as above

	Age (yr): 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 wk before inclusion in the study, and compensated HF state at least 2 months prior *Exclusion:* age < 50 yr, 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 and a frequency in training protocol of < 80%
Interventions	**Exercise:** *Total duration:* 6 months *Aerobic/resistance/mix:* aerobic *Frequency:* 3 sessions/wk *Duration:* 90 min *Intensity:* target HR (50% of work in the max HR) *Modality:* walking on a treadmill *Setting*: not reported *Other*: relaxation and stretching exercises before and after every session
Outcomes	HRQoL (shortened version of World Health Organization Quality of Life questionnaire) , hospitalisation
Comparison	Usual medical therapy - individual dietary guidance and pharmacological therapy
Country and setting	Brazil Single-centre
Follow-up	6 months (after randomisation)
Notes	Initially randomised 53 participants, excluded data from participants who withdrew, lost to follow-up, etc. and hence 42 participants were analysed Although setting not reported, the exercise programme was described as “supervised”

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 methods reported in 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	"*…3 patients from the untrained group experienced an impairment of symptoms and were hospitalized*"
Groups balanced at baseline?	Low risk	Table 1 of the publication shows groups are well balanced
Groups received same intervention?	Low risk	"*All patients continued with pharmacological therapy and individual dietary guidance*"

DANREHAB 2008

Methods	Parallel group RCT
Participants	**N randomised:** 91 (exercise 45; control 46) **Age (yr):** exercise: median 66 (range 33-91); control median (range 29-94) **Male:** 90% **White:** not reported **Inclusion/exclusion criteria** *Inclusion:* present 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 wk *Aerobic/resistance/mix:* mix *Frequency:* 3 sessions/wk *Duration:* 90 min/session *Intensity:* 50% max HR *Modality:* not reported *Setting:* supervised centre-based plus home-based also encouraged to continue **Other:** the physical exercise was conducted as a mixture of endurance and strengthening training using various upper and lower body modalities easily implemented as activities that the participants could perform at home. CR included participant education, exercise training, dietary counselling, smoking cessation, psychosocial support, and risk factor management and clinical assessment. All components included theoretical and practical approaches followed by individual follow-up and feedback. The lifestyle intervention strategy was based on the stages of change model and self efficacy theory. The lifestyle intervention was designed as group intervention, but individual counselling was included

Outcomes	Primary: composite outcome measure included overall mortality, MI or acute first-time re-admission due to heart disease other than MI Secondary: collected data using an adapted standardised interview questionnaire and a postal questionnaire (e.g. SF-36, HADS), clinical examination and blood tests
Comparison	Usual care participants were offered follow-up treatment prescribed by the discharging physician either as outpatient control or by the general practitioner. The 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
Country and setting	Demark Single centre
Follow-up	12-months
Notes	HF subset of 770 participants randomised, other participants with coronary heart disease and were high risk but no disease. Randomisation stratified by indication

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 multi-block within-stratum method*"
Allocation concealment (selection bias)	Low risk	As above
Blinding (performance bias and detection bias) All outcomes	Low risk	"*Because of the nature of CR, the interventions were open to the investigators and the patients. Investigator independent outcome data from registries were chosen to ensure blinded assessment and outcome analysis*"
Selective reporting (reporting bias)	Low risk	All outcomes listed in methods reported in results
Intention-to-treat analysis?	Low risk	ITT analysis 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 (yr):** exercise 71.6 (SD not reported); control 73.9 (SD not reported) **Male:** 67% **White:** not reported **Inclusion/exclusion criteria** *Inclusion:* participants were of any age with a diagnosis of HF of any aetiology, and NYHA Class I-IV. All participants 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 wk *Aerobic/resistance/mix:* aerobic *Frequency:* 1 session/wk *Duration:* 30-50 min *Intensity:* not reported *Modality:* gymnasium: treadmills, stationary cycles, recumbent cycles Home-based: hall walks, stairs and sporting activities such as lawn bowls *Setting*: supervised gymnasium, home-based programme tailored to participant's need **Other:** also attended a nurse-coordinated CR clinic with emphasis of self-management. A group-based educational session was conducted for study participants and their families. Exercise group attended the nurse-co-ordinated CR clinic, where comprehensive assessment was performed by the physiotherapist, CR co-ordinator and occupational therapist
Outcomes	HRQoL (MLWHFQ), all-cause and cardiovascular-related hospital admission, mortality
Comparison	Information session and then usual medical care
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*"
Risk of bias	

Davidson 2010 (*Continued*)

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 described in methods reported
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	"*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*"
Groups received same intervention?	Low risk	Both groups appeared to receive same interventions apart from CR intervention

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-IV *LVEF:* 26.4 (SD 6.8) **Case mix:** 100% as above **Age (yr):** 54 (SD 12.5) **Male:** 71.7% **White:** 60.1 I**nclusion/exclusion criteria** *Inclusion*: English-speaking, age 18-80 yr, NYHA II-IV and LVSD with LVEF < 40% as documented by echocardiogram or radionuclide ventriculography within < 6 months, and sinus rhythm *Exclusion:* MI or recurrent angina within < 3 months, orthopaedic impediments to exercise, severe obstructive pulmonary disease with a forced expiratory volume < 1 L in 1 second as measured by spirometry, stenotic valvular disease as measured by echocardiogram,

Dracup 2007 (*Continued*)

	history of uncontrolled ventricular tachyarrhythmias (documented by electrophysiology study or 24-hr 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/wk *Duration:* 10-45 min *Intensity:* 40-60% 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…*"
Outcomes	HRQoL (MLWHFQ), mortality, hospitalisation
Comparison	Maintained usual level of daily activities. No exercise component
Country and setting	USA Single centre
Follow-up	6 and 12 months (after randomisation)
Notes	Home-based exercise programme Subgroup analysis reported: Evangelista 2010

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 methods reported
Intention-to-treat analysis?	Low risk	Although not reported as ITT analysis, groups did appear to be analysed according to original randomised allocation

Dracup 2007 (*Continued*)

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*"

Gary 2010 (comp)

Methods	Parallel group RCT
Participants	**N Randomised:** 28 (CBT 10; CBT and exercise 18) **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 (yr):** 65.8 (SD 13.5) **Male:** 41.9% **White:** not reported **Inclusion/exclusion criteria** *Inclusion:* 1. documented medical diagnosis of HF; 2. LVEF ≥ 15% documented within the last year by echocardiogram, cardiac catheterisation ventriculography or radionuclide ventriculography; 3. receiving therapy for HF according to guidelines published by the American College of Cardiology American Heart recommendations (angiotensin-converting enzyme inhibitors, diuretics, beta-blockers, angiotensin receptor blockers, hydralazine and nitrate combination, etc.); 4. Hamilton Rating Scale for Depression (HAM-D) score ≥ 11; 5. positive results on the Mini International Neuropsychiatric Interview (Mini) for minor or major depression and 6. DSM-IV diagnosis for depression for 14 days; or 7 days if history of major depressive disorder in the last 6 months. Participants also had to be 1. English speaking, 2. living independently (non-institutionalised)

Gary 2010 (comp) (*Continued*)

	within 100 miles of Atlanta, GA, 3. able to respond to questions appropriately, 4. able to hear adequately to respond to verbal questions, 5. not involved in any structured exercise programme or walking 3 times/wk for a minimum of 20 min, 6. not participating in any psychotherapy and 7. not hospitalised within the last 60 days *Exclusion:* 1. suicide ideation according to psychiatric assessment or Mini evaluation; 2. major psychiatric co-morbidity such as schizophrenia, personality disorder or dementia; 3. planned surgery; 4. not diagnosed with HF in the past 3 months; 5. renal insufficiency (serum creatinine >2.5 mg/dL); 6. uncontrolled hypertension; 7. acute bereavement or loss of significant other within the last month or currently involved in family crisis such as divorce; 8. any disorder interfering with independent ambulation; and 9. terminal illness such as cancer
Interventions	**Exercise:** *Total duration:* 12 wk *Aerobic/resistance/mix:* aerobic *Frequency:* 3 sessions/wk *Duration:* 30-45 min/session, max 1 hr *Intensity:* Borg < 15 ('moderate') *Modality:* walking *Setting*: home-based **Other**: exercise + CBT group also received 12 wk weekly 1-hr sessions of CBT for 12 wk. No other co-interventions mentioned
Outcomes	HRQoL (MLWHFQ) and mortality
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"
Country and setting	USA Single-centre
Follow-up	24 wk (after randomisation)
Notes	Exercise group participants had 12 weekly face-to-face home visits by 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 [dyspnea, 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*"

Risk of bias

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

Gary 2010 (comp) (*Continued*)

Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding (performance bias and detection bias) All outcomes	Low risk	"*Data collectors were blinded to group assignment*"
Selective reporting (reporting bias)	Low risk	Outcome described in methods are reported in results
Intention-to-treat analysis?	Low risk	Although not stated, CONSORT diagram suggests groups analysed according to initial randomised allocation
Incomplete outcome data?	Low risk	QUORUM diagram and details of losses to follow-up reported. In exercise group, 1 patient died and 3 withdrew at 24 wk. In usual care group, 2 participants and 1 participant withdraw at 12 and 24 wk, respectively. In combined CBT/exercise group 2 withdrew at 12 wk. 1 lost to follow-up and 1 withdrew at 24 wk. In CBT group, 1 withdrew at 12 wk and 24 wk. 1 died and 1 lost to follow-up at 24 wk
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 same care other that exercise and CBT interventions

Gary 2010 (exalone)

Methods	Parallel group RCT
Participants	**N Randomised:** 37 (exercise alone 20; control 17) CBT only group not included to this review **Diagnosis (% of participants):** *Aetiology:* not reported *NYHA:* Class II 43.3%; Class III 56.7% *LVEF:* ≥ 15% **Case mix:** 100% as above **Age (yr):** 65.8 (SD 13.5) **Male:** 41.9% **White:** not reported **Inclusion/exclusion criteria** *Inclusion:* 1. documented medical diagnosis of HF; 2. LVEF of ≥ 15% documented within the last year by echocardiogram, cardiac catheterisation ventriculography or radionuclide ventriculography; 3. receiving therapy for HF according to guidelines published by the American College of Cardiology American Heart recommendations (angiotensin-converting enzyme inhibitors, diuretics, beta-blockers, angiotensin receptor blockers, hydralazine and nitrate combination, etc.); 4. Hamilton Rating Scale for Depression (HAM-D) score ≥ 11; 5. positive results on the Mini International Neuropsychiatric Interview (Mini) for minor or major depression; and 6. DSM-IV diagnosis for

	depression for 14 days; or 7 days if history of major depressive disorder in the last 6 months. Participants also had to be 1. English speaking, 2. living independently (non-institutionalised) within 100 miles of Atlanta, GA, 3. able to respond to questions appropriately, 4. able to hear adequately to respond to verbal questions, 5. not involved in any structured exercise programme or walking 3 times/wk for a minimum of 20 min, 6. not participating in any psychotherapy, and 7. not hospitalised within the last 60 days *Exclusion:* 1. suicide ideation according to psychiatric assessment or Mini evaluation; 2. major psychiatric co-morbidity such as schizophrenia, personality disorder or dementia; 3. planned surgery; 4. not diagnosed with HF in the past 3 months; 5. renal insufficiency (serum creatinine >2.5 mg/dL); 6. uncontrolled hypertension; 7. acute bereavement or loss of significant other within the last month or currently involved in family crisis such as divorce; 8. any disorder interfering with independent ambulation; and 9. terminal illness such as cancer
Interventions	**Exercise:** *Total duration:* 12 wk *Aerobic/resistance/mix:* aerobic *Frequency:* 3 sessions/wk *Duration:* 30-45 min/session, max 1 hr *Intensity:* Borg < 15 ('moderate') *Modality:* walking *Setting:* home-based **Other:** none reported
Outcomes	HRQoL (MLWHFQ) and mortality
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."
Country and setting	USA Single-centre
Follow-up	24 wk
Notes	Exercise group participants had 12 weekly face-to-face home visits by 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 [dyspnea, 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*"

Risk of bias

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

Gary 2010 (exalone) (*Continued*)

Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding (performance bias and detection bias) All outcomes	Low risk	"*Data collectors were blinded to group assignment*"
Selective reporting (reporting bias)	Low risk	Outcome described in methods were reported in results
Intention-to-treat analysis?	Low risk	Although not stated, CONSORT diagram suggests groups analysed according to initial randomised allocation
Incomplete outcome data?	Low risk	QUORUM diagram and details of losses to follow-up reported. In exercise group, 1 participant died and 3 withdrew at 24 wk. In usual care group, 2 participants and 1 participant withdrew at 12 and 24 wk, respectively. In combined CBT/exercise group, 2 withdrew at 12 wk. 1 lost to follow-up and 1 withdrew at 24 wk. In CBT group, 1 withdrew at 12 wk and 24 wk. 1 died and 1 lost to follow-up at 24 wk
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 same care other that exercise and CBT interventions

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-III *LVEF:* exercise 25% (SD 4); control 25% (SD 4) **Case mix:** 100% **Age (yr):** exercise 60 (SD 7); control 61 (SD 7) **Male:** not reported **White:** not reported **Inclusion/exclusion criteria** *Inclusion*: 1. HF secondary to idiopathic DCM, ischaemic heart disease or valvular disease; 2. echocardiographic ejection fraction < 35%; 3. clinical stability for at least 3 months under optimised therapy; 4. NYHA functional Class II to III; 5. peak oxygen uptake (VO_2) < 20 mL/kg/min; and 6. 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 and inability to participate in a prospective study for any logistic reason

Interventions	**Exercise:** *Total duration:* 24 wk *Aerobic/resistance/mix:* aerobic *Frequency:* 3-5 sessions/wk *Duration:* 30 min *Intensity:* 60% peak VO_2 *Modality:* exercise cycle, daily brisk walk, callisthenic. In addition, requested to take brisk daily walk of > 30 min *Setting*: supervised cycling sessions at rehabilitation centre and unsupervised at home **Other:** not reported
Outcomes	Mortality and morbidity
Comparison	Educational support but no formal exercise protocol
Country and setting	Italy Multicentre (15 CR units)
Follow-up	6 months (after randomisation)
Notes	

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 reported in methods are reported
Intention-to-treat analysis?	Low risk	Although not stated, it is clear from CONSORT diagram that 2 groups were analysed according to ITT
Incomplete outcome data?	Low risk	45/45 (100%) exercise training group and 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*"

Giannuzzi 2003 (*Continued*)

Groups received same intervention?	Unclear risk	Not clearly stated if co-treatments (i.e. cardiovascular medication) in 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 (yr):** exercise 55 (SD 6); control 53 (SD 9) **Male:** 100% **White:** not reported I**nclusion/exclusion criteria** *Inclusion:* age < 70 yr with CHF (NYHA II to III) as result of DCM or IHD as assessed by cardiac catheterisation. All had clinical, radiological and echocardiographic signs of CHF and an LVEF 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 or musculoskeletal abnormalities precluding exercise training
Interventions	**Exercise:** *Total duration: 2* wk inpatient followed by 6 months as outpatient *Aerobic/resistance/mix:* aerobic *Frequency: 7* sessions/wk *Duration:* 20 min/session *Intensity:* 70% symptom limited VO_2 max *Modality:* cycle ergometers *Setting:* supervised sessions at hospital and home-based unsupervised sessions **Other:** expected to participate in 1 group training session (walking, callisthenics and non-competitive ball games) of 60 min each wk. Participants were asked to exercise for 20 min/day at home
Outcomes	Mortality
Comparison	Continued their sedentary lifestyle and remained on their individually tailored cardiac medication supervised by their private physicians
Country and setting	Switzerland Single centre
Follow-up	26 wk (after randomisation)
Notes	

Gielen 2003 (*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 methods are reported in 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 (yr):** exercise 67 (SD 7); control 64 (SD 10) **Male:** exercise 15/16 (94%); control 11/14 (79%); total 87% **White:** not reported **Inclusion/exclusion criteria** *Inclusion:* NYHA Class II-III for at least 3 months and were 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 session/wk *Duration:* 30 min *Intensity:* Borg 12-13 *Modality:* bike and treadmill *Setting*: supervised sessions at medical centre by a nurse or exercise physiologist **Other:** Care provided by specialist HF physician
Outcomes	HRQoL (MLWHFQ and MOS SF-36 questionnaire), mortality, morbidity
Comparison	Usual medical care **Other:** care provided by specialist HF physicians
Country and setting	USA Single centre
Follow-up	6 months (after randomisation)
Notes	MLWHF, MOS SF-36 results not reported for the control group

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 methods are reported
Intention-to-treat analysis?	Unclear risk	Not reported
Incomplete outcome data?	Low risk	Yes, QUORUM flow diagram reported Unclear how loss to follow-up, drop-out and cross-over 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"*

Gottlieb 1999 (*Continued*)

Groups received same intervention?	Low risk	*"Medical follow-up of both the control and intervention patients 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 (yr):** 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 a reduced fractional shortening < 30% assessed by echocardiography; willingness to participate in the study for the next 6 months; and a 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 (higher then Lown Class IVa), valvular heart disease, uncontrolled hypertension, peripheral vascular disease, COPD, and orthopaedic or other conditions precluding regular participation in exercise sessions
Interventions	**Exercise:** *Total duration:* 6 months *Aerobic/resistance/mix:* aerobic *Frequency:* 4-6 sessions/wk *Duration:* 10-60 min/session, 1 hr at home *Intensity:* 70% VO_2max *Modality:* cycling, walking, ball games and callisthenics *Setting:* first 3 wk supervised hospital-based training; thereafter home-based **Other:** none
Outcomes	Morbidity and mortality
Comparison	After discharge medical therapy continued and participants supervised by private physician
Country and setting	Germany Single centre
Follow-up	6 months (after randomisation)
Notes	

Hambrecht 1995 (*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 methods, reported in results
Intention-to-treat analysis?	Unclear risk	Not reported
Incomplete outcome data?	Low risk	Drop-outs and clinical events are fully reported for both groups. No imputation undertaken
Groups balanced at baseline?	Low risk	"*There were no significant differences in baseline variables between the training and control groups*"
Groups received same intervention?	Unclear risk	The exercise group had 3 wk of hospital stay, the control only 3 days. The control group follow-up with private physician. No comment on follow-up of 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 (yr):** exercise 54 (SD 9); control 56 (8) **Male:** 100% **White:** not reported **Inclusion/exclusion criteria** *Inclusion:* age < 70 yr, with CHF as a result of DCM or IHD, LVEF < 40% *Exclusion:* DM, hypertension, overt atherosclerotic PVD, hypercholesterolaemia, ventricular tachycardia, COPD and primary valvular disease
Interventions	**Exercise:** *Total duration:* 6 months *Aerobic/resistance/mix:* aerobic

	Frequency: 2-6 sessions/day *Duration:* 10-20 min/session *Intensity:* 70% VO_2 max *Modality:* bike ergometer *Setting*: supervised hospital-based sessions and unsupervised home-based sessions **Other:** not reported
Outcomes	Mortality
Comparison	**Description:** stayed on previous medication, continued sedentary lifestyle, and supervised by their private physicians
Country and setting	Germany Single centre
Follow-up	6 months (after randomisation)
Notes	

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 methods reported in results
Intention-to-treat analysis?	Low risk	It appears that groups are analysed according to original randomised allocation
Incomplete outcome data?	Low risk	Detailed description of losses to follow-up and drop-outs reported
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 [lett 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 (yr):** 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 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/wk *Duration:* 10-20/session *Intensity:* 70% of peak VO_2 *Modality:* cycle ergometer *Setting:* first 2 wk in hospital, remainder home based **Other:** plus group sessions 1 hr twice weekly, walking, ball games and callisthenics
Outcomes	Mortality
Comparison	Continued individually tailored cardiac medications, supervised by their physicians
Country and setting	Germany Single centre
Follow-up	6 months (after randomisation)
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**

Hambrecht 2000 (*Continued*)

Random sequence generation (selection bias)	Low risk	"*Patients were randomly assigned to either a training group or an inactive group sing 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 methods reported in results
Intention-to-treat analysis?	Low risk	Not reported
Incomplete outcome data?	Low risk	QUORUM diagram and details of losses to follow-up reported
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	The co-interventions in the control group 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 (yr):** exercise 59 (SD not reported); control 59 (SD not reported) **Male:** 72% **White:** 62% **Inclusion/exclusion criteria** *Inclusion:* LVEF < 35%, NYHA Class II-IV HF for the previous 3 months despite a 6-wk period of treatment, optimal HF therapy at stable doses for 6 wk before enrolment or documented rationale for variation, including intolerance, contraindication, participant preference and personal physicians judgement, sufficient stability, by investigator judgement, to begin an exercise programme *Exclusion:* (selected) age <18 yr, co-morbid disease or behavioural or other limitations that interfere with performing exercise training or prevent the completion of 1 yr of exercise training, major cardiovascular event or cardiovascular procedure, including implantable cardioverter defibrillator use and cardiac resynchronisation, within the previous 6 wk

HF ACTION 2009 (*Continued*)

Interventions	**Exercise:** *Total duration:* 30 months *Aerobic/resistance/mix:* aerobic *Frequency:* 3-5 sessions/wk *Duration:* 15-35 min/session *Intensity:* 60-70% of HR reserve *Modality:* cycling or walking *Setting:* First 36 sessions were supervised then advised to follow 5 day/wk home-based exercise programme **Other:** none reported
Outcomes	Mortality, hospitalisation, HRQoL (KCCQ), cost-effectiveness
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
Country and setting	USA Multicentre
Follow-up	Median 30.1 months (after randomisation)
Notes	Authors contacted for further details of outcome findings but no information provided

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 methods reported in results
Intention-to-treat analysis?	Low risk	
Incomplete outcome data?	Low risk	QUORUM diagram and details of losses to follow-up reported
Groups balanced at baseline?	Low risk	Table 1 of the publication shows 2 groups are well balanced

HF ACTION 2009 (*Continued*)

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 (yr):** 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 had a severity of at least NYHA group II in the previous 24 months. They had to have been clinically stable for 4 wk 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 trusts and not considered high-risk for a home-based exercise programme *Exclusion:* NYHA Class IV, MI or revascularisation within the past 4 months, hypotension, unstable angina, ventricular or symptomatic arrhythmias, obstructive abortive valvular disease, COPD, hypertrophic obstructive cardiomyopathy, severe musculoskeletal problems preventing exercise, and case-note reported dementia or current severe psychiatric disorder
Interventions	**Exercise:** *Total duration:* 6 months programme progressive with aim that participants achieved the following: *Aerobic/resistance/mix:* mix *Frequency:* 5 times/wk *Duration:* 20-30 min *Intensity:* 70% of peak VO_2 or Borg 12-13 *Modality:* aerobic and resistance elements (upper and lower limb exercises) *Setting:* first 3 sessions supervised centre-based followed by home-based programme with home-visits by nurse at 4, 10 and 20 wk and telephone support at 6, 15 and 24 wk. Intervention manual provided **Other:** specialist HF nurse care
Outcomes	HRQoL (MLWHFQ), composite of death, hospital admissions, generic quality of life (EQ-5D)
Comparison	Specialist HF nurse care
Country and setting	UK West-midlands, community

Follow-up	6- and 12-month follow-up (after randomisation)
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	"*An independent clinical trials unit using a computerized programme undertook randomization after each patient had consented and undergone the baseline tests and questionnaire*"
Allocation concealment (selection bias)	Low risk	"*An independent clinical trials unit using a computerized programme undertook randomization after each patient had consented and undergone the baseline tests and questionnaire*"
Blinding (performance bias and detection bias) All outcomes	High risk	"*…, the nurse undertaking the assessment was blinded to the treatment allocation of the patient, but owing to staffing issues, this occurred in only 62% of participants followed up at 6 months*"
Selective reporting (reporting bias)	Low risk	All of primary and majority of secondary outcomes described in methods reported Stated in 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	Drop-outs and clinical events are fully reported Outcome available for 161 (95%) participants at 6 months and 157 (92%) participants at 12 months. Non-imputed data reported and sensitivity analysis undertaken to examine 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 (yr):** 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, fulfil 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 and age > 80 yr
Interventions	**Exercise:** *Total duration*: 5 months *Aerobic/resistance/mix: m*ix *Frequency:* 2 sessions/wk *Duration:* 45 min *Intensity:* not reported *Modality:* cycling, free weights and elastic rubber-bands (Thera-bands) *Setting:* hospital outpatients, supervised by physiotherapists **Other:** training group had 3 educational lectures, about nutrition, physical activity and relaxation in addition to the exercise programme
Outcomes	Rehospitalisation and mortality
Comparison	Usual medical care (continued their previous level of physical activity, which varied from performing little physical activity up to taking a daily walk outdoors)
Country and setting	Iceland Single centre
Follow-up	12 and 28 months (after randomisation)
Notes	

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 methods reported in results
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	No losses to follow-up
Groups balanced at baseline?	Low risk	Table 2 of the publication suggests 2 groups are well balanced
Groups received same intervention?	Low risk	Yes, both groups appeared to receive same interventions apart from CR intervention

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 (yr):** 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 and 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, and current participation in a regular exercise programme (at least twice weekly)
Interventions	**Exercise:** *Total duration:* 24 wk *Aerobic/resistance/mix:* aerobic *Frequency:* 3 sessions/wk (rate of perceived exertion 12-14) *Duration:* 33 min *Intensity:* 60-80% peak HR *Modality:* treadmills, stationary cycles, rowing machines and arm ergometers **Setting:**outpatient clinic **Other:** none reported
Outcomes	Morality and hospital admissions

Keteyian 1996 (*Continued*)

Comparison	Usual medical care Participants were instructed to maintain their normal daily activity habits and not to begin an exercise regimen
Country and setting	North America Single centre
Follow-up	6 months (after randomisation)
Notes	Authors contacted for further details of outcome findings but no information provided. Each participant's physician was asked not to change drug regimen during the study, if possible

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 methods reported in 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*"

Keteyian 1996 (*Continued*)

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	The co-interventions in the control group 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: 28.5% (SD 5.2) **Case mix:** 100% as above **Age (yr):** 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 of > 6 months, clinically stable > 6 wk and LVEF < 35% *Exclusion:* uncontrolled arterial hypertension; history of major ventricular arrhythmias, acute coronary syndrome, percutaneous coronary intervention or brain event 3 months prior to the study; AF or other arrhythmia making it impossible to perform MRI; previous coronary artery bypass grafting; implantable cardiodefibrillator; permanent pacemaker or the presence of metal parts in the body; signs of osteoarticular dysfunction excluding participation in physical training; DM; COPD and anaemia
Interventions	**Exercise:** *Total duration:* 6 months *Aerobic/resistance/mix:* aerobic *Frequency:* 3 sessions/wk *Duration: 25* min/session *Intensity:* 80% predicted HR at VO_2 max *Modality:* cycling **Setting:** centre-based **Other:** none reported
Outcomes	Mortality
Comparison	Standard medical care only
Country and setting	Poland Single centre
Follow-up	26 wk (after randomisation)
Notes	

Klecha 2007 (*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 methods reported in results
Intention-to-treat analysis?	Low risk	Not implicit but numbers used suggest that groups analysed according to randomised allocation
Incomplete outcome data?	Low risk	No participants 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 (Const)

Methods	Parallel group RCT
Participants	**N Randomised:** 42 (exercise group A 14; control 14) **Diagnosis (% of participants):** *Aetiology:* ischaemic 100% *NYHA*: Class II/III exercise group A 55%; control 100% *LVEF: e*xercise group A: mean 33.6% (SD 3.6); control 33.2% (SD 3.8) **Case mix:** 100% as above **Age (yr):** exercise group A 54 (SD 7); 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 yr *Exclusion:* moderate or severe pulmonary disease, orthostatic blood pressure fall (> 20 mmHg), or with MI, unstable angina, heart surgery or coronary angioplasty within 3 months prior to inclusion as well as inability to perform bicycle training

Interventions	**Exercise:** *Total duration:* 6 months *Aerobic/resistance/mix:* aerobic *Frequency:* 3 sessions/wk *Duration:* group A - 20 min/session (4-min constant workload with 1 min rest repeated 5 times) *Intensity:* group A - 60% max HR *Modality:* cycle ergometer *Setting:* CR, outpatient unit under supervision of the physician and rehabilitation specialist **Other:** none reported
Outcomes	HRQoL (Psychological General Wellbeing Index)
Comparison	**Description:** controls were asked not to change their degree of physical activity during the study
Country and setting	Poland Single centre
Follow-up	26 wk (after randomisation)
Notes	

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 methods are reported in 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 presented on loss on loss to follow-up or drop-outs
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*

Klocek 2005 (Const) (*Continued*)

		groups A and B. Controls had lower total index than patients in group B"
Groups received same intervention?	Unclear risk	Details of co-interventions not reported although degree of follow-up was stated to be equivalent

Klocek 2005 (Prog)

Methods	Parallel group RCT
Participants	**N Randomised:** 42 (exercise group B 14; control 14) **Diagnosis (% of participants):** *Aetiology:* ischaemic 100% *NYHA*: Class II/III exercise group B 75%; control 100% *LVEF:* exercise group B: mean 34.2% (SD 4.2); control 33.2% (SD 3.8) **Case mix:** 100% as above **Age (yr):** 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 yr *Exclusion:* moderate or severe pulmonary disease, orthostatic blood pressure fall (> 20 mmHg), or with MI, unstable angina, heart surgery or coronary angioplasty within 3 months prior to inclusion as well as inability to perform bicycle training
Interventions	**Exercise:** *Total duration:* 6 months *Aerobic/resistance/mix:* aerobic *Frequency:* 3 sessions/wk *Duration:* group B: 25 min/session (exercise workload gradually increased after each 5-min training period to a total of 25 min) *Intensity:* group B: up to 75% max HR *Modality:* cycle ergometer *Setting:* CR, outpatient unit under supervision of the physician and rehabilitation specialist **Other:** none reported
Outcomes	HRQoL (Psychological General Wellbeing Index)
Comparison	Controls were asked not to change their degree of physical activity during the study
Country and setting	Poland Single centre
Follow-up	26 wk (after randomisation)
Notes	

Klocek 2005 (Prog) (*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	"*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 methods are reported in 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 presented on loss on loss to follow-up or drop-outs
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 not reported although degree of follow-up was stated to 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 (yr):** exercise 52 (SD 9); control 53 (SD 11) **Male:** 100% **White:** not reported **Inclusion/exclusion criteria** *Inclusion:*aetiology of CHF was either ischaemic heart disease or DCM. Diagnosis of CHF was 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/wk *Duration:* 60 min/session *Intensity:* 50-75% peak VO_2 *Modality:* cycle ergometer, walking or jogging, stair climber and step-aerobics Plus 'light' resistance exercise (not defined) *Setting:* supervised exercise training programme at institution **Other:** none reported
Outcomes	HRQoL (MLWHFQ and Spritzer Quality of Life Index)
Comparison	Not reported
Country and setting	Greece Single centre
Follow-up	6 months (after randomisation)
Notes	

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 methods are reported
Intention-to-treat analysis?	Low risk	Not stated explicitly but appear to analysed according to initial group allocation
Incomplete outcome data?	Unclear risk	Losses to follow-up, drop-outs not reported

Koukouvou 2004 (*Continued*)

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

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-III *LVEF:* < 40% **Case mix:** 100% as above **Age (yr):** exercise 64.8±1.1 (SD 10.5); control 66.1 (SD 9.4) **Male:** control 80; exercise 82 **White:** not reported **Inclusion/exclusion criteria** *Inclusion*: documented clinical signs and symptoms of HF; LVEF < 40%; NYHA Functional Class I-III; 6-min 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 mm Hg or diastolic blood pressure response > 15 mm Hg, systolic blood pressure response decrease of > 20 mm Hg after a 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 and 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: m*ix *Frequency:* 2 sessions/wk *Duration:* aerobic; 30 min/session *Intensity: a*erobic: 60-70% max HR. Resistance: 40% of 1-repetition maximum, with 10 repetitions for the arm exercises and 15 repetitions for the leg exercises, with an increase over 5 wk to an intensity of 60% of 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 set of free weights with instructions to continue training at home 3 times/wk for the remainder of the study **Setting:**Supervised for 3 months at rehabilitation centre and unsupervised for 9 months at home **Other:** none reported
Outcomes	HRQoL (MLWHFQ), mortality, composite of mortality and hospital admission for HF

McKelvie 2002 (*Continued*)

Comparison	Usual medical care. Control participants were not provided with a formal exercise prescription but were encouraged to continue their usual level of physical activity and were not discouraged from regular physical activity
Country and setting	Canada Multicentre
Follow-up	12 months (after randomisation)
Notes	

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*"
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 methods are reported in results
Intention-to-treat analysis?	Low risk	Although ITT analysis not reported, groups do appear to analysed according to 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 or sensitivity analysis undertaken to assess 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*"

McKelvie 2002 (*Continued*)

Groups received same intervention?	Unclear risk	"*All patients were reviewed monthly throughout the study*"

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 (yr):** 55 (SD 10) **Male:** 100% **White:** not reported **Inclusion/exclusion criteria** *Inclusion:* CHF documented by clinical, angiographic or echocardiographic criteria; and resting EF < 40% *Exclusion:* not reported
Interventions	**Exercise:** *Total duration:* 1 month *Aerobic/resistance/mix:* aerobic *Frequency:* 5 sessions/wk *Duration:* 30 min/session cycling, 90 min walking each day *Intensity:* Borg 12-14 (60-80% max HR) *Modality:* cycling and walking *Setting:* indoor cycling sessions were supervised directly by a medical resident and outdoor walking sessions were supervised by exercise physiologists **Other:** resided at the rehabilitation centre for 1 month. Programme component also included education and low-fat meals prepared daily by the centre's cook
Outcomes	Morbidity and mortality
Comparison	Usual medical care
Country and setting	Switzerland Single centre
Follow-up	6.2 yr (after randomisation)
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**

Mueller 2007 (*Continued*)

Random sequence generation (selection bias)	Unclear risk	Not reported
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding (performance bias and detection bias) All outcomes	Unclear risk	Not reported
Selective reporting (reporting bias)	Low risk	Outcomes described in the methods are reported in the results
Intention-to-treat analysis?	Low risk	ITT not stated explicitly. However, groups appear to analysed according to 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. 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 (yr):** 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

Myers 2000 (*Continued*)

Interventions	**Exercise:** *Total duration:* 2 months *Aerobic/resistance/mix:* aerobic *Frequency:* walking: 2 sessions/daily; cycling: 4 sessions/wk *Duration:* walking: 1 hr; cycling: 45 min *Intensity:* walking: not reported; cycling: 60-70% peak VO_2 *Modality:* walking and cycling *Setting:* centre based with supervised by physicians **Other:** exercise groups received education sessions and low-fat meals prepared 3 times daily
Outcomes	Hospitalisation and mortality
Comparison	Usual clinical follow-up
Country and setting	Switzerland Single-centre
Follow-up	2 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*"

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 methods reported in results
Intention-to-treat analysis?	Low risk	Although not explicit, participants appeared to be analysed according to initial random allocation
Incomplete outcome data?	Low risk	Lost to follow-up 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*"

Myers 2000 (*Continued*)

Groups received same intervention?	Low risk	Yes, both groups appeared to receive same interventions apart from 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 (yr):** 70.1 (SD 7.9) **Male:** 79% **White:** not reported **Inclusion/exclusion criteria** *Inclusion:* stable CHF and a LVEF < 40% or ≥ 40% with clinical symptoms of diastolic HF *Exclusion:* acute MI within 4 wk; unstable angina pectoris; serious rhythm disturbance; symptomatic PVD; severe CPOD, with a forced expiratory vital capacity < 50% of expected measured by spirometry; 6-min walking distance > 550 m; and work load on the cycle ergometer test > 110 watts, significant co-morbidities that would prevent entry into the study due to terminal disease or an inability to exercise (e.g. severe musculoskeletal disorder, advanced valvular disease) or were in long-term care establishments
Interventions	**Exercise:** *Total duration:* 4 months *Aerobic/resistance/mix:* aerobic *Frequency:* 2 sessions/wk *Duration:* 50 min *Intensity:* 15-18 on Borg scale *Modality:* fast walking, side stepping and leg lifts in combination with overhead arm reaches *Setting:* hospital outpatient department **Other:** 15-30 min counselling for participants in exercise group with CHF nurse (4 hr in total)
Outcomes	HRQoL (MLWHFQ) and mortality
Comparison	The control group was not provided with exercise prescriptions and encouraged to continue their usual levels of physical activity
Country and setting	Norway Single centre
Follow-up	12 months (after randomisation)
Notes	All training sessions were supervised by physiotherapist, a specialist in heart rehabilitation

Nilsson 2008 (*Continued*)

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 methods reported in results
Intention-to-treat analysis?	Low risk	"*Intention-to-treat analyses were performed*"
Incomplete outcome data?	Low risk	35/40 (88%) exercise training group and 37/40 (93%) control group available at 12 months
Groups balanced at baseline?	Low risk	Table 1 of the publication suggests no difference 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 (yr):** exercise 57 (SD 12); control 63 (SD 15) **Male:** 57.5% **White:** not reported **Inclusion/exclusion criteria** *Inclusion:* age $\geq$ 21 yr, with HF; orientated to person, place and time; able to speak and read English; resting LVEF $\leq$ 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, and participation in an aerobic exercise programme during the past 12 months

Interventions	**Exercise:** *Total duration:* 24 wk *Aerobic/resistance/mix:* mix *Frequency:* aerobic 3 days/wk, resistance 2 days/wk *Duration:* aerobic: 30 min/session (30 min warm-up); resistance: 8-10 exercises (upper and lower extremity) performed for 1 set of 10-15 repetitions *Intensity:* aerobic: 40-70% HR reserve, or Borg 11-14; resistance: not reported *Modality:* aerobic: not reported; resistance: weight machines, free weights or elastic bands based on their exercise performance *Setting:* 3 wk: supervised; 21 wk: hospital's wellness centre or home **Other:** group meetings that addressed the same education topics as the control group but in addition included information on problem-solving barriers to exercise, relapse management and symptoms experienced during exercise
Outcomes	HRQoL (KCCQ), SF-36 and mortality
Comparison	"*Attention control*" Instructions to continue with their normal level of activity. No instructions were given to withhold or stop activity
Country and setting	USA Single centre
Follow-up	24 wk (after randomisation)
Notes	Study conducted in 2 sequential 12-wk phases Phase 1: separate weekly group meetings of both groups during wk 1-3, then separate biweekly meetings during wk 4-12 Phase 2: following the groups for an additional 12 wk 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

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 methods reported in results

Norman 2012 (*Continued*)

Intention-to-treat analysis?	Low risk	Not stated but groups analysed according to randomised allocation
Incomplete outcome data?	Low risk	Due to mortality and drop out KCCQ scores available in 37 patients (88%) at 24 wk
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 only difference between groups was 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 (yr):** 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 diseases, and severe pulmonary or renal disease * baseline data only available for 85 participants
Interventions	**Exercise:** *Total duration:* 9 months *Aerobic/resistance/mix:* aerobic *Frequency:* > 3 sessions/wk *Duration:* 30 min/session *Intensity:* 65% max VO_2 *Modality:* cycle *Setting:* home-based **Other:** not reported
Outcomes	HRQoL (MLWHFQ) Morbidity
Comparison	Not reported
Country and setting	Italy Not reported

Passino 2006 (*Continued*)

Follow-up	9 months (after randomisation)	
Notes		
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 blinded
Selective reporting (reporting bias)	Unclear risk	Not reported
Intention-to-treat analysis?	Low risk	Although ITT not stated, groups appeared to be analysed according to original randomisation
Incomplete outcome data?	Low risk	Outcomes described in methods reported in results
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 (yr):** exercise 66.3 (SD 9.6); control 66 (SD 12.6) **Male:** 90% **White:** 100% **Inclusion/exclusion criteria** *Inclusion:* able to speak and read English; stable NYHA Class II-IV no change in medical therapy for 30 days; resting LVEF < 40% measured by echocardiography or gated

	equilibrium radionuclide angiography; medical diagnosis of HF either ischaemic or non-ischaemic; and standard pharmacological therapy for HF (diuretics, angiotensin-converting enzyme inhibitors and beta-blockers) *Exclusion:* participation in a formal exercise programme < 30 days prior to this study; clinical evidence decompensated HF; and 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 wk *Aerobic/resistance/mix:* mix *Frequency:* 3 sessions/wk *Duration:* 30 min aerobic, 20 min resistance *Intensity:* 60-85% max VO_2, 12-14 Borg scale *Modality:* aerobic: treadmill, stationary bike, rower, arm ergometer; resistance: light upper-body exercises (military press, biceps curl and lateral deltoid raises) and lower-body exercises (knee extension, side hip raise and hip extension) with 1-10 lb hand and ankle weights. Wall push-ups, abdominal curl-ups, pelvic tilts, or a combination *Setting:* first 12 wk at the hospital and remaining sessions were unsupervised at rehabilitation centre **Other:** strategies from social learning theory (goal-setting, feedback and problem-solving guidance) utilised to facilitate, improve adherence to the training programme
Outcomes	Mortality
Comparison	Usual medical care
Country and setting	USA Single centre
Follow-up	6 months (after randomisation)
Notes	

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 methods are reported in results

Pozehl 2008 (*Continued*)

Intention-to-treat analysis?	Low risk	Although not stated, groups appear to analysed according to 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

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); control 2.13 (SE 0.13) *LVEF:* ≤ 60% **Case mix:** as above **Age (yr):** exercise 69 (SD 4.44); control 70 (SD 4.05) **Male:** 58% **White:** 100% **Inclusion/exclusion criteria** *Inclusion:* 1. a diagnosis of NYHA Class I-III congestive HF, 2. an EF ≤ 60%, 3. systolic dysfunction, 4. physician approval and 5. the ability to complete a minimum of 3 min of a modified Bruce-protocol stress test *Exclusion:* failure to meet any of the inclusion criteria, inability to speak English or having noticeable cognitive impairment
Interventions	**Exercise:** *Total duration:* 12 months *Aerobic/resistance/mix:* aerobic *Frequency:* 3 sessions/wk *Duration:* > 15 min *Intensity:* not reported *Modality:* treadmill Lifestyler® treadmill provided for 1 year of in-home use, 3 supervised exercise sessions at hospital with CR specialist. Weekly in-home exercise visits with CR specialist, Month 1. Monthly in-home exercise visits with CR specialist, Months 2-12. Also received comprehensive disease management programme **Setting:** 3 hospital based and the remainder at home **Other:** not reported
Outcomes	Disease-specific HRQoL (Chronic Heart Failure Questionnaire), mortality

Wall 2010 (*Continued*)

Comparison	Comprehensive disease management - by dedicated case manager (participant education on nutrition, medications, and disease management; an oximetry assessment; and constant monitoring of symptomatic changes and disease status
Country and setting	USA Single-centre
Follow-up	12 months (after randomisation)
Notes	

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 methods reported
Intention-to-treat analysis?	Low risk	Although not stated, it is clear from CONSORT diagram that 2 groups were analysed according to ITT
Incomplete outcome data?	Low risk	QUORUM flow diagram report suggests 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 (yr):** exercise 64 (SD 5); control 64 (SD 9) **Male:** exercise 73%; control 70% **White:** not reported **Inclusion/exclusion criteria** *Inclusion:* 1. 8 points on Boston heart failure criteria; 2. LVEF 0.45 at the most recent radionuclide or echocardiographic examination (not older than 1 year at inclusion) and 3. age 75 yr *Exclusion:* 1. change of clinical status or medication (or both) within 4 wk prior to inclusion; 2. MI, heart surgery or coronary angioplasty within 3 months prior to inclusion; 3. inability to perform a bicycle test; 4. 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); 5. pulmonary disease judged to be the main exercise-limiting factor or peak expiratory flow rate < 50% of the age- and sex-adjusted reference value, or both; 6. NYHA Class IV and 7. clinically significant aortic stenosis
Interventions	**Exercise:** *Total duration:* 4 months *Aerobic/resistance/mix:* aerobic/interval *Frequency:* 2-3 sessions/wk *Duration:* 15 min/session increasing to 45 min/session *Intensity:* 80% peak VO_2, or 15 on Borg score *Modality:* cycle ergometry *Setting:* group sessions supervised by physiotherapist **Other:** none
Outcomes	HRQoL (Patient's Global Assessment of Quality of Life), mortality
Comparison	Control participants were asked not to 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
Country and setting	Sweden Single centre
Follow-up	10 months (after randomisation)
Notes	

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

Willenheimer 2001 (*Continued*)

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 methods reported in results
Intention-to-treat analysis?	Low risk	Although ITT not implicit, it appears that groups are analysed according to original randomised allocation
Incomplete outcome data?	High risk	Outcome available in only 43/54 (80%) participants randomised at 10 months' follow-up. No imputation or sensitivity analysis undertaken to assess effect of loss to follow-up. Authors state 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 (yr):** exercise 80 (SD 6); control 81 (SD 4) **Male:** 55% **White:** not reported **Inclusion/exclusion criteria** *Inclusion:* age ≥ 70 yr 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, or people currently undergoing physiotherapy or rehabilitation
Interventions	**Exercise:** *Total duration:* 6 months *Aerobic/resistance/mix:* mix *Frequency:* 2-3 sessions/wk *Duration:* 20 min *Intensity:* Borg 11-13 *Modality:* walking and wrist/ankle weights

	Setting: 3 months; hospital based by senior physiotherapist, 3 months; home-based After 3 months of supervised training, participants in the exercise group were asked to continue performing exercises at home 2 or 3 times/wk with the aid of video or audio cassette with demonstrations, instructions and music. No face-to-face contact with the physiotherapist during this period **Other:** not reported
Outcomes	A disease specific health-related quality-of-life (Guyatt chronic heart failure questionnaire), mortality, hospitalisation
Comparison	Usual medical care
Country and setting	UK Single centre
Follow-up	6 months (after randomisation)
Notes	

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 methods are reported in results
Intention-to-treat analysis?	Low risk	It appeared that groups were analysed according to initial random allocation from QUORUM diagram
Incomplete outcome data?	Low risk	75/82 (91%) and 68/82 (83%) available at 3 and 6 months' follow-up, respectively
Groups balanced at baseline?	Low risk	Table 1 of the publication shows groups are well balanced
Groups received same intervention?	Low risk	Yes, both group appeared to receive usual medical care and 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 (yr):** 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 yr with a confirmed diagnosis of HF due to LVSD (NYHA Class II and III) and a history of symptoms and signs of congestive HF *Exclusion:* wheelchair bound, unwilling or unable to give informed, had aortic stenosis with peak gradient > 30 mmHg, experienced sustained ventricular tachycardia or ventricular fibrillation outside the context of an acute MI, and currently (within the past month) had unstable angina or AF with a ventricular rate of > 100/min
Interventions	**Exercise:** *Total duration:* 24 wk *Aerobic/resistance/mix:* mix *Frequency:* 2 sessions/wk *Duration:* ≤ 60 min *Intensity:* not reported *Modality:* home; walking ***Setting:*** hospital and home* **Other:** cognitive and behavioural techniques were incorporated into first 8-wk hospital-based rehabilitation. Resistance training with elasticised bands
Outcomes	Disease-specific HRQoL (MLWHFQ), HRQoL (EuroQoL-5D), mortality, hospital admission, cost
Comparison	Usual medical care (given a booklet with general advice on diet, exercise and lifestyle). Not discouraged from exercising if they were already in the habit of doing so
Country and setting	UK Single-centre
Follow-up	24 wk (after randomisation)
Notes	*8 wk in hospital delivered by experienced physiotherapist, 16-wk home-based (telephoned every 2 wk for 8 wk by the physiotherapists, then monthly for the final 8 wk)

Risk of bias

Bias	Authors' judgement	Support for judgement

Witham 2012 (*Continued*)

Random sequence generation (selection bias)	Low risk	"*Using off-site telephone randomization service, randomization was performed without stratification and with block sizes between 8 and 16, depending on the size of each planned exercise class*"
Allocation concealment (selection bias)	Low risk	"*…the project coordinator passed the participants' details to the research physiotherapist who obtained group allocation, ensuring that the project coordinator remained blind to group assignments*"
Blinding (performance bias and detection bias) All outcomes	Unclear risk	Not reported
Selective reporting (reporting bias)	Low risk	All outcomes described in methods reported in results
Intention-to-treat analysis?	Low risk	Analyses were by ITT
Incomplete outcome data?	Low risk	89/104 (86%) and 87/104 (83%) available for follow-up at 8 and 24 wk, respectively
Groups balanced at baseline?	Low risk	Table 1 of the publication suggests no difference between the 2 groups
Groups received same intervention?	Low risk	It appeared that both groups received same care expect 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 (yr):** exercise 68.1 (SD 11.9); control 66.6 (SD 12.1) **Male:** 64% **White:** 86% **Inclusion/exclusion criteria** *Inclusion:* EF < 40% or lower in past 2 yr, stable medical regimen, NYHA Class I-III HF *Exclusion:* unstable angina, MI or major surgery in past 3 months; history of cardiac arrest in the past 6 months, history of cardiac resynchronisation 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 the 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 ≤ 24); inability to speak English and regular practice of Tai Chi

Interventions	**Exercise:** *Total duration:* 12 wk *Aerobic/resistance/mix:* aerobic *Frequency:* 2 sessions/wk (for 12 wk) and encouraged to practice at home at least 3 times/wk *Duration:* 1 hr class (30 min warm-up) *Intensity:* not reported *Modality:* Tai Chi movements 1. Wk 2-5: warm-up + raising the power, withdraw and push 2. Wk 6-9: 1 + grasp sparrow's tail, brush knee twist step 3. Wk 10-12: 2 + wave hands like clouds Participants were given 45-min instructional videotape that outlined the exercises presented in class as an aid to practice Participants also received same educational pamphlets used in education (control) group with a brief (< 5 min) explanation towards end of 1 Tai Chi session weekly *Setting:* centre-based and home-based **Other:** none reported
Outcomes	HRQoL (MLWHFQ), mortality, hospital admission
Comparison	Education group ('attention control'): nurse practitioner lead education session (same duration and frequency as the Tai Chi group classes) Participants were asked not to start Tai Chi classes during the study
Country and setting	USA Multisite
Follow-up	12 wk and 6 months (after randomisation)
Notes	Single blind

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 methods reported in results

Yeh 2011 (*Continued*)

Intention-to-treat analysis?	Low risk	All participants were included in the analysis regardless of their attendance
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

AF: atrial fibrillation; bpm: beats/minute; CBT: cognitive behavioural therapy; CHF: chronic heart failure; CONSORT: CONsolidated Standards of Reporting Trials; COPD: chronic obstructive pulmonary disease; CR: cardiac rehabilitation; DCM: dilated cardiomyopathy; DM: diabetes mellitus; DSM-IV: Diagnostic and Statistical Manual of Mental Disorders, 4th Edition; EF: ejection fraction; HADS: Hospital Anxiety and Depression Scale; HF: heart failure; hr: hour; HR: heart rate; HRQoL: health-related quality of life; ITT: intention to treat; KCCQ: Kansas City Cardiomyopathy Questionnaire; LVEF: left ventricular ejection fraction; LVSD: left ventricular systolic dysfunction; max: maximum; MI: myocardial infarction; min: minute; MOS: Medical Outcomes Survey; MLWHFQ: Minnesota Living with Heart Failure Questionnaire; MRI: magnetic resonance imaging; NYHA: New York Heart Association; PVD: peripheral vascular disease; RCT: randomised controlled trial; SD: standard deviation; SE: standard error; SF-36: 36-item Short Form; VO_2: oxygen consumption; wk: week; yr: year.

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

Study	Reason for exclusion
Adamopoulos 2001	Relevant outcomes not reported
Alves 2012	Relevant outcomes not reported
Barrow 2008	< 6 months' follow-up
Belardinelli 2005	< 6 months' follow-up
Briffa 2005	Not heart failure
Brotons 2009	Not exercise-based cardiac rehabilitation intervention
Chang 2005	Relevant outcomes not reported
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
Deng 2006	Relevant outcomes not reported
Dingli 2002	Relevant outcomes not reported
Edelmann 2011	< 6 months' follow-up
Erbs 2003	Relevant outcomes not reported
Erbs 2010	Relevant outcomes not reported
ExTraMATCH 2004	Meta-analysis
Franco 2006	< 6 months' follow-up
Gary 2004	Relevant outcomes not reported
Gary 2007	< 6 months' follow-up
Haykowsky 2007	Meta-analysis
Inglis 2006	Exercise advice only
Jolly 2007	Protocol only
Jónsdóttir 2006b	< 6 months' follow-up
Kiilavuori 1999	Relevant outcomes not reported
Kitzman 2010	< 6 months' follow-up
Kobayashi 2003	Relevant outcomes not reported
Korzeniowska-Kubacka 2010	Not a randomised controlled trial
Lloyd-Williams 2002	Meta-analysis
Meyer 2005	Relevant outcomes not reported
Molloy 2006	Relevant outcomes not reported
Mudge 2011	Protocol
Myers 2001	Relevant outcomes not reported
Myers 2002	Relevant outcomes not reported

(*Continued*)

Myers 2007	Relevant outcomes not reported
Niebauer 2005a	Relevant outcomes not reported
Niebauer 2005b	Relevant outcomes not reported
Oka 2000	Relevant outcomes not reported
Owen 2000	< 6 months' follow-up
Parnell 2002	< 6 months' follow-up
Passino 2008	Relevant outcomes not reported
Ponikowski 1997	< 6 months' follow-up
Pozehl 2003	< 6 months' follow-up
Pu 2001	Relevant outcomes not reported
Sabelis 2004	Relevant outcomes not reported
Sarullo 2006	< 6 months' follow-up
Selig 2004	< 6 months' follow-up
Senden 2005	Relevant outcomes not reported
Smart 2004	Meta-analysis
Smart 2007	< 6 months' follow-up
Stewart 1998	Exercise advice only
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
Vasiliauskas 2007	Relevant outcomes not reported
Wielenga 1998	< 6 months' follow-up

(*Continued*)

Williams 2007	Relevant outcomes not reported
Wisløff 2007	< 6 months' follow-up
Yeh 2004	< 6 months' follow-up
Zhang 2003	< 6 months' follow-up
Zhao 2005	Relevant outcomes not reported

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

ISRCTN86879094

Trial name or title	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)
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 1. Combined outcome score (modified 'Packer score', Packer 2001). This combined score classifies participants as: 1 (worsened), 0 (unchanged) or +1 (improved) Secondary 1. 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') 2. Change in echocardiographic parameters of diastolic function (left atrial volume index, Grad 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 and 12 months 3. Change in quality of life (SF-36, Minnesota Living with Heart Failure Questionnaire, Hospital Anxiety and Depression Scale) after 6 and 12 months 4. Change in ventilatory efficacy (VE/VCO_2) and submaximal exercise capacity (anaerobic threshold, 6-min walk distance) after 6 and 12 months 5. Change in neurohumoral activation (N-terminal pro brain natriuretic peptide) after 6 and 12 months 6. Safety and tolerability of training intervention 7. Gender aspects of all primary and secondary endpoints
Starting date	1 September 2011

ISRCTN86879094 (*Continued*)

Contact information	Dr Frank Edelmann: fedelmann@med.uni-goettingen.de
Notes	Trial still recruiting. Recruitment completion expected in 2014 (author email reply 21 July 2013)

Mudge ongoing

Trial name or title	The Exercise Joins Education: Combined Therapy to Improve Outcomes in Newly-discharged Heart Failure (EJECTION-HF)
Methods	RCT
Participants	350 recently hospitalised people with HF with impaired and preserved left ventricular systolic function
Interventions	Supervised exercise training programme and disease management programme vs. disease management programme alone
Outcomes	Primary outcome 1. proportion of participants who have died or been re-admitted for any cause within 12 months of enrolment Secondary outcomes at 6 and 12 months 1. Depressive symptoms measured using the Geriatric Depression Scale and the Hare-Davis Cardiac Depression Scale 2. Functional status measured using a standardised 6-min walk test, hand-held dynamometry as a measure of grip strength and activities of daily living using standardised questions 3. Cognitive status using Folstein's Mini-Mental Status Examination 4. Quality of life using the Assessment of Quality of Life instrument 5. Sleep quality using the Pittsburgh Sleep Quality Index (in a subset of participants) 6. Healthcare use including hospital admissions and outpatient and emergency department attendances obtained from the hospital information systems
Starting date	Not reported (150 recruited at time of publication) *"Enrolment will be completed in 2013"*
Contact information	Corresponding author: telephone: +61 7 36360854, fax: +61 7 36360272, Email: Alison_Mudge@health.qld.gov.au Internal Medicine and Aged Care, Royal Brisbane and Women's Hospital, Butterfield St, Herston, Queensland 4029 Australia
Notes	Trial completed recruiting. Publication of primary outcomes expected in late 2014 (author email reply 29 July 2013)

NCT00012883

Trial name or title	Home Walking Exercise (HWE) Training in Advanced Heart Failure
Methods	RCT
Participants	79 participants with stable HF in the past 3 months
Interventions	12-week nurse-managed progressive home walking exercise protocol versus usual activity
Outcomes	Pre- and post-study assessment of: Functional status (peak VO_2 and ventilatory threshold via complete physical examination, 6-min walk test and a Heart Failure Functional Status Inventory), quality of life (Cardiac Quality of Life Index, SF-36, and Dyspnea-Fatigue Index with global rating of symptoms) and autonomic tone (norepinephrine (noradrenaline) and heart rate variability)
Starting date	December 2001
Contact information	Teresita E Corvera-Tindel, PhD RN MN, VA Greater Los Angeles Health Care System, USA
Notes	Contact email sent - no reply

NCT00013221

Trial name or title	Exercise Effect on Aerobic Capacity and QOL in Heart Failure
Methods	RCT
Participants	About 84 participants with left LVEF $\leq$ 40%. Stable HF
Interventions	Exercise group: 36 weeks of exercise training Control group: weekly visits with a nurse for 12 weeks
Outcomes	At 12 weeks, exercise capacity (peak VO_2) and HRQoL (SF-36)
Starting date	Not reported
Contact information	Eileen G Collins, PhD RN, Edward Hines Jr. VA Hospital, USA
Notes	Contact email sent - no reply (as of 20 September 2013)

NCT01033591

Trial name or title	Exercise for Patients with Heart Failure in Primary Care: the EFICAR
Methods	RCT
Participants	Inclusion criteria: • Age $\geq$ 18 years

NCT01033591 (*Continued*)

	• Diagnosis of HF on the basis of signs and symptoms (Framingham criteria) and evidence of structural heart alterations detected by echocardiography. Echocardiography scanning guarantees that we are dealing with participants with HF avoiding confounding clinical factors • LVEF < 45% • NYHA functional Class II-IV, or Stages B and C of the American Heart Association, in a stable situation for at least the previous 4 weeks, with no changes in baseline functional status, no signs of congestion or changes in weight faster than 2 kg in 3 days • Receiving optimal treatment with angiotensin-converting enzyme inhibitors, angiotensin II receptor antagonists, beta-blockers, diuretics and aldosterone antagonists at stable doses for the previous 4 weeks, as long as there are no justified contraindications for their use, and meeting the clinical practice guidelines of the European Society of Cardiology 600 participant target
Interventions	Experimental: exercise supervised exercise + optimised treatment according to the European Society of Cardiology guidelines No intervention: control optimised treatment according to the European Society of Cardiology guidelines
Outcomes	Primary outcomes: 1. Change in HRQoL (SF-36 and Minnesota Living with Heart Failure Questionnaire) Secondary outcomes: 1. Change in functional capacity (6-min walking test) 2. Cardiac structural changes (B-type natriuretic peptide) 3. Muscle strength (dynamometer) 4. Body composition (fat and muscular weight) All at 12 months
Starting date	January 2011
Contact information	Contact: Dr Gonzalo Grandes
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 Trial still recruiting. Recruitment completion expected June 2014 (author email reply 20 July 2013)

HF: heart failure; HRQoL: health-related quality of life; LVEF: left ventricular ejection fraction; NYHA: New York Heart Association; min: minute; RCT: randomised controlled trial; SF-36: 36-item Short Form; VCO_2: carbon dioxide consumption; VE: ventilatory efficiency; VO_2: oxygen consumption.

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 to12 months' follow-up	25	1871	Risk Ratio (M-H, Fixed, 95% CI)	0.93 [0.69, 1.27]
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	15	1328	Risk Ratio (M-H, Fixed, 95% CI)	0.75 [0.62, 0.92]
4 Hospital admission heart failure only	12	1036	Risk Ratio (M-H, Fixed, 95% CI)	0.61 [0.46, 0.80]
5 Hospital admission more than 12 months' follow-up	5	2722	Risk Ratio (M-H, Random, 95% CI)	0.92 [0.66, 1.29]
6 Health-related quality of life - MLWHF up to 12 months' follow-up	13	1270	Mean Difference (IV, Random, 95% CI)	-5.83 [-9.21, -2.44]
7 Health-related quality of life - MLWHF and other scales	21	3240	Std. Mean Difference (IV, Random, 95% CI)	-0.46 [-0.66, -0.26]
8 Health-related quality of life - MLWHF 12 months' follow-up	3	329	Mean Difference (IV, Random, 95% CI)	-9.49 [-17.48, -1.50]

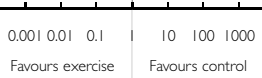
Analysis 1.1. Comparison 1 All exercise interventions versus usual care, Outcome 1 All-cause mortality up to12 months' follow-up.

Review: Exercise-based rehabilitation for heart failure

Comparison: 1 All exercise interventions versus usual care

Outcome: 1 All-cause mortality up to12 months' follow-up

Study or subgroup	Exercise n/N	Control n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Austin 2005	5/100	4/100		5.3 %	1.25 [0.35, 4.52]
DANREHAB 2008	4/45	3/46		3.9 %	1.36 [0.32, 5.75]
Davidson 2010	4/53	11/52		14.8 %	0.36 [0.12, 1.05]
Dracup 2007	9/87	8/86		10.7 %	1.11 [0.45, 2.75]
Gary 2010 (comp)	0/18	1/19		1.9 %	0.35 [0.02, 8.09]
Gary 2010 (exalone)	1/20	0/17		0.7 %	2.57 [0.11, 59.30]
Giannuzzi 2003	0/45	1/45		2.0 %	0.33 [0.01, 7.97]
Gielen 2003	0/10	0/10			Not estimable
Gottlieb 1999	1/17	1/16		1.4 %	0.94 [0.06, 13.82]
Hambrecht 1995	1/12	0/10		0.7 %	2.54 [0.11, 56.25]
Hambrecht 1998	1/10	1/10		1.3 %	1.00 [0.07, 13.87]
Hambrecht 2000	3/36	2/37		2.6 %	1.54 [0.27, 8.69]
Jolly 2009	7/84	5/85		6.6 %	1.42 [0.47, 4.29]
Keteyian 1996	0/21	1/19		2.1 %	0.30 [0.01, 7.02]
Klecha 2007	0/25	0/25			Not estimable
McKelvie 2002	19/90	20/91		26.5 %	0.96 [0.55, 1.68]
Myers 2000	1/12	0/13		0.6 %	3.23 [0.14, 72.46]
Nilsson 2008	2/40	1/40		1.3 %	2.00 [0.19, 21.18]
Norman 2012	1/22	0/20		0.7 %	2.74 [0.12, 63.63]
Pozehl 2008	0/15	1/6		2.8 %	0.15 [0.01, 3.16]
Wall 2010	1/9	1/10		1.3 %	1.11 [0.08, 15.28]
Willenheimer 2001	3/27	2/27		2.7 %	1.50 [0.27, 8.28]
Witham 2005	1/41	3/41		4.0 %	0.33 [0.04, 3.07]
Witham 2012	2/53	1/54		1.3 %	2.04 [0.19, 21.81]
Yeh 2011	0/50	3/50		4.7 %	0.14 [0.01, 2.70]



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Study or subgroup	Exercise n/N	Control n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Total (95% CI)	**942**	**929**		**100.0 %**	**0.93 [0.69, 1.27]**
Total events: 66 (Exercise), 70 (Control)					
Heterogeneity: Chi^2 = 12.60, df = 22 (P = 0.94); I^2 =0.0%					
Test for overall effect: Z = 0.43 (P = 0.67)					
Test for subgroup differences: Not applicable					

Analysis 1.2. Comparison 1 All exercise interventions versus usual care, Outcome 2 All-cause mortality more than 12 months' follow-up.

Review: Exercise-based rehabilitation for heart failure

Comparison: 1 All exercise interventions versus usual care

Outcome: 2 All-cause mortality more than 12 months' follow-up

Study or subgroup	Exercise n/N	Control n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Austin 2005	31/100	38/100		13.6 %	0.82 [0.56, 1.20]
Belardinelli 1999	9/50	20/49		7.2 %	0.44 [0.22, 0.87]
Belardinelli 2012	4/63	10/60		3.7 %	0.38 [0.13, 1.15]
HF ACTION 2009	189/1159	198/1171		70.5 %	0.96 [0.80, 1.16]
J nsd ttir 2006a	2/21	2/22		0.7 %	1.05 [0.16, 6.77]
Mueller 2007	9/25	12/25		4.3 %	0.75 [0.39, 1.46]
Total (95% CI)	**1418**	**1427**		**100.0 %**	**0.88 [0.75, 1.02]**
Total events: 244 (Exercise), 280 (Control)					
Heterogeneity: Chi^2 = 7.54, df = 5 (P = 0.18); I^2 =34%					
Test for overall effect: Z = 1.69 (P = 0.092)					
Test for subgroup differences: Not applicable					

Analysis 1.3. Comparison 1 All exercise interventions versus usual care, Outcome 3 Hospital admission up to 12 months' follow-up.

Review: Exercise-based rehabilitation for heart failure

Comparison: 1 All exercise interventions versus usual care

Outcome: 3 Hospital admission up to 12 months' follow-up

Study or subgroup	Exercise n/N	Control n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Austin 2005	9/100	19/100		12.4 %	0.47 [0.23, 1.00]
Bocalini 2008	0/22	3/20		2.4 %	0.13 [0.01, 2.38]
Davidson 2010	23/53	36/52		23.7 %	0.63 [0.44, 0.90]
Dracup 2007	35/87	37/86		24.3 %	0.94 [0.66, 1.33]
Giannuzzi 2003	2/45	1/45		0.7 %	2.00 [0.19, 21.28]
Gielen 2003	1/10	0/10		0.3 %	3.00 [0.14, 65.90]
Hambrecht 1995	0/12	1/10		1.1 %	0.28 [0.01, 6.25]
Jolly 2009	16/84	20/85		13.0 %	0.81 [0.45, 1.45]
J nsd ttir 2006a	2/21	5/22		3.2 %	0.42 [0.09, 1.93]
Keteyian 1996	0/21	1/19		1.0 %	0.30 [0.01, 7.02]
Klecha 2007	0/25	0/25			Not estimable
Passino 2006	0/44	2/41		1.7 %	0.19 [0.01, 3.78]
Witham 2005	10/41	11/41		7.2 %	0.91 [0.43, 1.90]
Witham 2012	13/53	10/54		6.5 %	1.32 [0.64, 2.75]
Yeh 2011	2/50	4/50		2.6 %	0.50 [0.10, 2.61]
Total (95% CI)	**668**	**660**		**100.0 %**	**0.75 [0.62, 0.92]**

Total events: 113 (Exercise), 150 (Control)

Heterogeneity: Chi^2 = 11.71, df = 13 (P = 0.55); I^2 =0.0%

Test for overall effect: Z = 2.79 (P = 0.0052)

Test for subgroup differences: Not applicable

Analysis 1.4. Comparison 1 All exercise interventions versus usual care, Outcome 4 Hospital admission heart failure only.

Review: Exercise-based rehabilitation for heart failure

Comparison: 1 All exercise interventions versus usual care

Outcome: 4 Hospital admission heart failure only

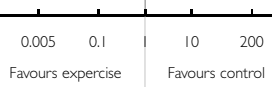
Study or subgroup	Exercise n/N	Control n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Belardinelli 1999	5/50	14/49		14.5 %	0.35 [0.14, 0.90]
Belardinelli 2012	8/63	25/60		26.3 %	0.30 [0.15, 0.62]
Dracup 2007	35/87	37/86		38.3 %	0.94 [0.66, 1.33]
Giannuzzi 2003	2/45	1/45		1.0 %	2.00 [0.19, 21.28]
Hambrecht 1995	0/12	1/10		1.7 %	0.28 [0.01, 6.25]
Jolly 2009	4/84	2/85		2.0 %	2.02 [0.38, 10.75]
J nsd ttir 2006a	0/21	3/22		3.5 %	0.15 [0.01, 2.73]
Mueller 2007	2/25	3/25		3.1 %	0.67 [0.12, 3.65]
Myers 2000	0/12	2/13		2.5 %	0.22 [0.01, 4.08]
Passino 2006	0/44	2/41		2.7 %	0.19 [0.01, 3.78]
Willenheimer 2001	0/23	3/27		3.3 %	0.17 [0.01, 3.07]
Witham 2012	1/53	1/54		1.0 %	1.02 [0.07, 15.87]
Total (95% CI)	**519**	**517**		**100.0 %**	**0.61 [0.46, 0.80]**

Total events: 57 (Exercise), 94 (Control)

Heterogeneity: Chi^2 = 16.70, df = 11 (P = 0.12); I^2 =34%

Test for overall effect: Z = 3.52 (P = 0.00044)

Test for subgroup differences: Not applicable



Analysis 1.5. Comparison 1 All exercise interventions versus usual care, Outcome 5 Hospital admission more than 12 months' follow-up.

Review: Exercise-based rehabilitation for heart failure

Comparison: 1 All exercise interventions versus usual care

Outcome: 5 Hospital admission more than 12 months' follow-up

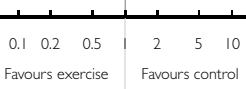
Study or subgroup	Exercise n/N	Control n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
Austin 2005	53/100	38/100		31.0 %	1.39 [1.02, 1.90]
Belardinelli 1999	5/50	14/49		9.7 %	0.35 [0.14, 0.90]
HF ACTION 2009	729/1159	760/1171		41.9 %	0.97 [0.91, 1.03]
J nsd ttir 2006a	7/21	11/22		13.9 %	0.67 [0.32, 1.39]
Mueller 2007	2/25	3/25		3.5 %	0.67 [0.12, 3.65]
Total (95% CI)	**1355**	**1367**		**100.0 %**	**0.92 [0.66, 1.29]**

Total events: 796 (Exercise), 826 (Control)

Heterogeneity: $Tau^2 = 0.07$; $Chi^2 = 10.90$, df = 4 (P = 0.03); $I^2 = 63\%$

Test for overall effect: Z = 0.48 (P = 0.63)

Test for subgroup differences: Not applicable



Analysis 1.6. Comparison 1 All exercise interventions versus usual care, Outcome 6 Health-related quality of life - MLWHF up to 12 months' follow-up.

Review: Exercise-based rehabilitation for heart failure

Comparison: 1 All exercise interventions versus usual care

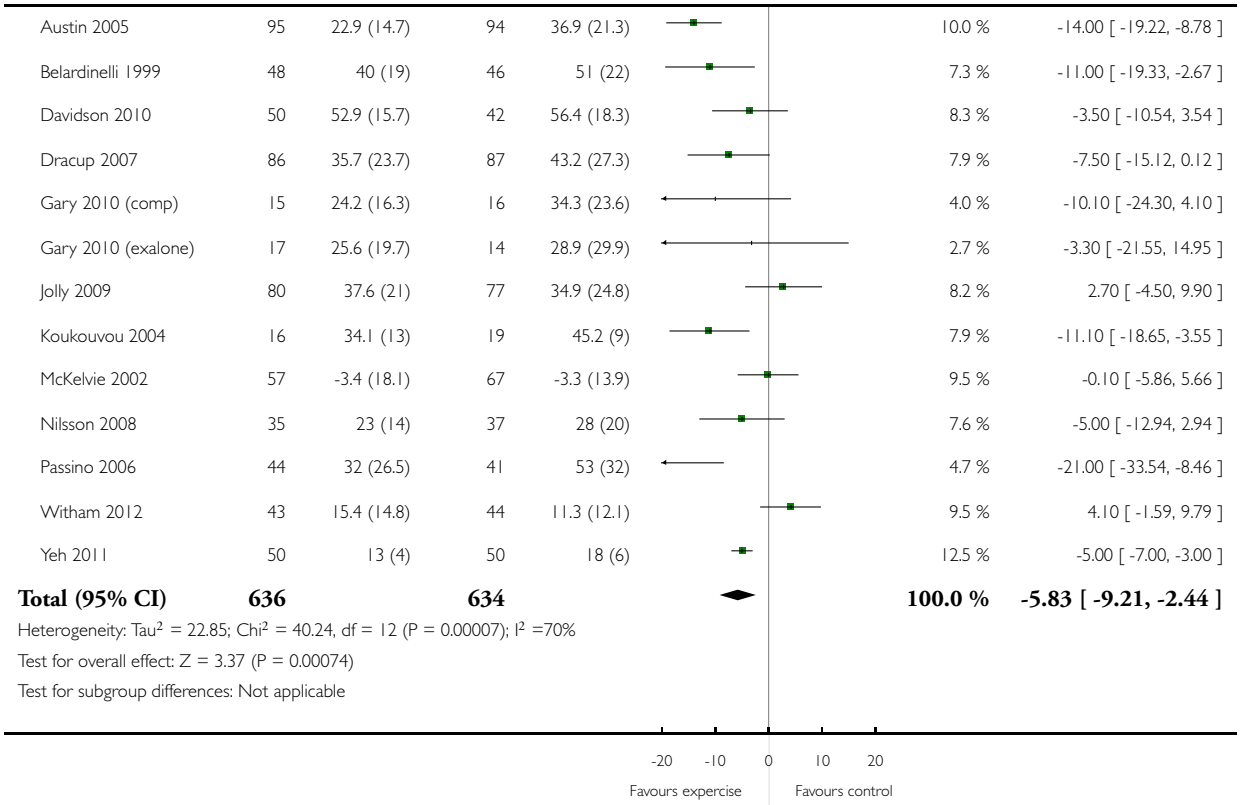
Outcome: 6 Health-related quality of life - MLWHF up to 12 months' follow-up

Study or subgroup	Exercise		Control		Mean Difference	Weight	Mean Difference
	N	Mean(SD)	N	Mean(SD)	IV,Random,95% CI		IV,Random,95% CI
Austin 2005	95	22.9 (14.7)	94	36.9 (21.3)		10.0 %	-14.00 [-19.22, -8.78]
Belardinelli 1999	48	40 (19)	46	51 (22)		7.3 %	-11.00 [-19.33, -2.67]
Davidson 2010	50	52.9 (15.7)	42	56.4 (18.3)		8.3 %	-3.50 [-10.54, 3.54]
Dracup 2007	86	35.7 (23.7)	87	43.2 (27.3)		7.9 %	-7.50 [-15.12, 0.12]
Gary 2010 (comp)	15	24.2 (16.3)	16	34.3 (23.6)		4.0 %	-10.10 [-24.30, 4.10]
Gary 2010 (exalone)	17	25.6 (19.7)	14	28.9 (29.9)		2.7 %	-3.30 [-21.55, 14.95]
Jolly 2009	80	37.6 (21)	77	34.9 (24.8)		8.2 %	2.70 [-4.50, 9.90]
Koukouvou 2004	16	34.1 (13)	19	45.2 (9)		7.9 %	-11.10 [-18.65, -3.55]
McKelvie 2002	57	-3.4 (18.1)	67	-3.3 (13.9)		9.5 %	-0.10 [-5.86, 5.66]
Nilsson 2008	35	23 (14)	37	28 (20)		7.6 %	-5.00 [-12.94, 2.94]
Passino 2006	44	32 (26.5)	41	53 (32)		4.7 %	-21.00 [-33.54, -8.46]
Witham 2012	43	15.4 (14.8)	44	11.3 (12.1)		9.5 %	4.10 [-1.59, 9.79]
Yeh 2011	50	13 (4)	50	18 (6)		12.5 %	-5.00 [-7.00, -3.00]
Total (95% CI)	**636**		**634**			**100.0 %**	**-5.83 [-9.21, -2.44]**

Heterogeneity: $Tau^2 = 22.85$; $Chi^2 = 40.24$, df = 12 (P = 0.00007); $I^2 = 70\%$

Test for overall effect: Z = 3.37 (P = 0.00074)

Test for subgroup differences: Not applicable



Analysis 1.7. Comparison 1 All exercise interventions versus usual care, Outcome 7 Health-related quality of life - MLWHF and other scales.

Review: Exercise-based rehabilitation for heart failure

Comparison: 1 All exercise interventions versus usual care

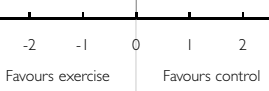
Outcome: 7 Health-related quality of life - MLWHF and other scales

Study or subgroup	Exercise N	Mean(SD)	Control N	Mean(SD)	Std. Mean Difference IV,Random,95% CI	Weight	Std. Mean Difference IV,Random,95% CI
Austin 2005	95	22.9 (14.7)	94	36.9 (21.3)		6.2 %	-0.76 [-1.06, -0.47]
Belardinelli 1999	48	40 (19)	46	51 (22)		5.5 %	-0.53 [-0.94, -0.12]
Bocalini 2008	22	-87 (4)	20	-81 (6)		4.0 %	-1.17 [-1.83, -0.51]
DANREHAB 2008	19	-42.7 (9.1)	15	-37.4 (11.4)		3.8 %	-0.51 [-1.20, 0.18]
Davidson 2010	50	52.9 (15.7)	42	56.4 (18.3)		5.5 %	-0.20 [-0.62, 0.21]
Dracup 2007	86	35.7 (23.7)	87	43.2 (27.3)		6.2 %	-0.29 [-0.59, 0.01]
Gary 2010 (comp)	15	24.2 (16.3)	16	34.3 (23.6)		3.7 %	-0.48 [-1.20, 0.23]
Gary 2010 (exalone)	17	25.6 (19.7)	14	28.9 (29.9)		3.7 %	-0.13 [-0.84, 0.58]
HF ACTION 2009	906	72.39 (20.46)	850	71.24 (21.48)		7.1 %	0.05 [-0.04, 0.15]
Jolly 2009	80	37.6 (21)	77	34.9 (24.8)		6.1 %	0.12 [-0.20, 0.43]
J nsd ttir 2006a	21	-47.55 (8.7)	20	-44.1 (14.04)		4.2 %	-0.29 [-0.91, 0.32]
Klocek 2005 (Const)	14	-109 (23.5)	7	-71.7 (23.5)		2.4 %	-1.52 [-2.57, -0.48]
Klocek 2005 (Prog)	14	-99 (23.5)	7	-71.7 (23.5)		2.6 %	-1.12 [-2.10, -0.13]
Koukouvou 2004	16	34.1 (13)	19	45.2 (9)		3.7 %	-0.99 [-1.69, -0.28]
McKelvie 2002	57	-3.4 (18.1)	67	-3.3 (13.9)		5.9 %	-0.01 [-0.36, 0.35]
Nilsson 2008	35	23 (14)	37	28 (20)		5.2 %	-0.29 [-0.75, 0.18]
Norman 2012	19	-81 (18.2)	18	-77.9 (11.6)		4.1 %	-0.20 [-0.84, 0.45]
Passino 2006	44	32 (26.5)	41	53 (32)		5.3 %	-0.71 [-1.15, -0.27]
Willenheimer 2001	20	-0.7 (0.8)	17	0 (1)		3.9 %	-0.76 [-1.44, -0.09]
Witham 2005	36	-69 (13)	32	-65 (10)		5.1 %	-0.34 [-0.82, 0.14]
Yeh 2011	50	13 (4)	50	18 (6)		5.5 %	-0.97 [-1.39, -0.56]
Total (95% CI)	**1664**		**1576**			**100.0 %**	**-0.46 [-0.66, -0.26]**

Heterogeneity: $Tau^2 = 0.14$; $Chi^2 = 94.85$, df = 20 (P<0.00001); $I^2 = 79\%$

Test for overall effect: Z = 4.58 (P < 0.00001)

Test for subgroup differences: Not applicable

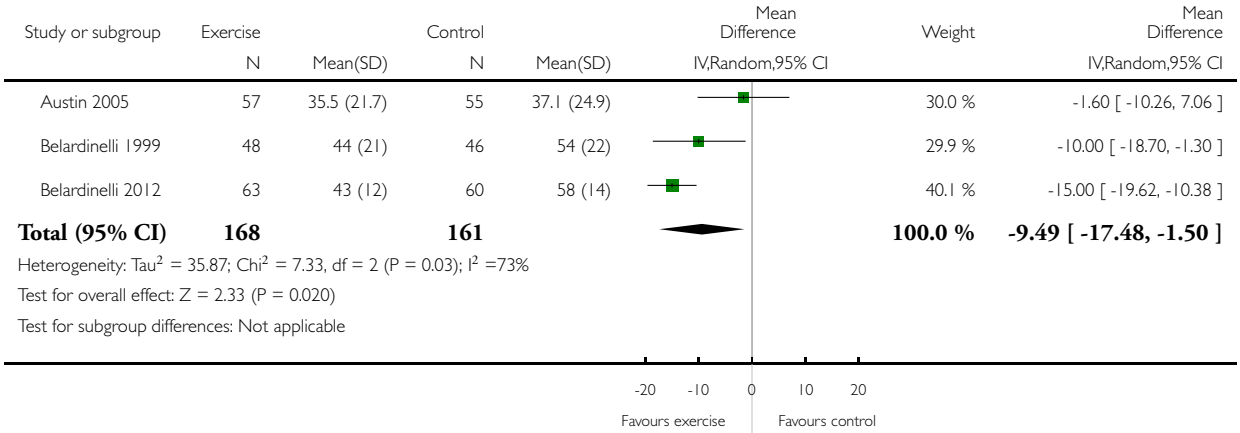


Analysis 1.8. Comparison 1 All exercise interventions versus usual care, Outcome 8 Health-related quality of life - MLWHF 12 months' follow-up.

Review: Exercise-based rehabilitation for heart failure

Comparison: 1 All exercise interventions versus usual care

Outcome: 8 Health-related quality of life - MLWHF 12 months' follow-up



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
Austin (2005/8)	6 months 5 years	MLWHF Physical Emotional Total EQ-5D MLWHF Physical Emotional Total EQ-5D	20.4 (12.2) vs. 12.6 (9.7) ; P value < 0.0001* 8.0 (7.1) vs. 4.4 (10.4); P value < 0.01* 36.9 (24.0) vs. 22.9 (17. 8); P value < 0.001* 0.58 (0.19) vs. 0.70 (0. 16); P value < 0.0001* 19.3 (23.5) vs. 18.3 (11. 2); P value = 0.66* 7.6 (7.1) vs. 7.4 (6.5); P	Exercise > Control Exercise > Control Exercise > Control Exercise > Control Exercise = Control Exercise = Control Exercise = Control Exercise = Control

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

			value = 0.88* 37.1 (24.9) vs. 35.5 (21.7); P value = 0.72* 0.58 (0.22) vs. 0.64 (0.19); P value = 0.12*	
Belardinelli (1999)	15 months 29 months	MLWHF total	52 (20) vs. 39 (20); P value < 0.001 54 (22) vs. 44 (21); P value < 0.001	Exercise > Control Exercise > Control
DANREHAB (2008)	12 months	SF-36 PCS MCS	37.4 (11.4) vs. 42.7 (9.1) *; P value = 0.14 50.5 (10.0) vs. 49.7 (8.8) *; P value = 0.81	Exercise = Control Exercise = Control
Davidson (2010)	12 months	MLWHF total	56.4 (18.3) vs. 52.9 (15.7); P value = 0.33	Exercise = Control
Dracup (2007)	6 months	MLWHF Physical Emotional Total	19.4 (11.5) vs. 16.1 (10.0); P value = 0.04* 10.5 (7.4) vs. 7.8 (6.6); P value = 0.01* 43.2 (26.5) vs. 35.7 (23.7); P value = 0.05	Exercise > Control Exercise > Control Exercise > Control
Gary (2010) Comp	6 months	MLWHF total	34.3 (23.6) vs. 24.2 (16.3); P value = 0.18*	Exercise = Control
Gary (2010) Exer	6 months	MLWHF total	28.9 (29.9) vs. 25.6 (19.7); P value = 0.71*	Exercise = Control
Gottlieb (1999)	6 months	MLWHF Total MOS PF RL 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)	3 months	KCCQ+	5.21 (95% CI 4.42 to 6.00) vs. 3.28 (2.48 to 4.09); P value < 0.001	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 value = 0.30 0.62 (0.32) vs. 0.66 (0.24); P value = 0.004 34.9 (24.8) vs. 37.6 (21.0); P value = 0.80	Exercise = Control Exercise > Control Exercise = Control Exercise = Control

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

			0.69 (0.28) vs. 0.68 (0.21); P value = 0.07	
Jónsdóttir (2006)	6 months	Icelandic Quality of Life Questionnaire	4.10 (14.04) vs. 47.55 (8.7); P value = 0.34	Exercise = Control
Klocek (2005)	6.5 months	PGWB total	99.0 vs. 109.0 (training group A) vs. 71.7 (training group B); P value < 0.01	Exercise > Control
Koukouvou (2004)	6 months	MLWHF total Spritzer QLI total	34.1 (13.0) vs. 45.1 (9.9); P value = 0.05* 7.1 (1.1) vs. 9.1 (1.1); P value < 0.0001*	Exercise > Control Exercise > Control
McKelvie (2002)	12 months	MLWHF total+	-3.3 (13.9) vs. -3.4 (18.1); P value = 0.98	Exercise = Control
Nilsson (2008)	12 months	MLWHF total	28 (20) vs. 22 (12); P value = 0.003	Exercise > Control
Norman (2012)	6 months	KCCQ	77.9 (11.6) vs. 81.0 (18.2); P value = 0.78	Exercise = Control
Passino (2006)	9.75 months	MLWHF total	53 (32) vs. 32 (26.5); P value < 0.0001*	Exercise > Control
Willenheimer (2001)	10 months	PGAQoL	0 (1) vs. 0.7 (0.9); P value = 0.023	Exercise > Control
Witham (2005)	6 months	GCHFQ	69 (13) vs. 65 (10); P value = 0.48	Exercise = Control
Yeh (2011)	12 months	MLWHF total	18 (6) vs. 13 (4); P value < 0.0001	Exercise > Control

*P values calculated by authors of this paper; +: change in outcome from baseline.
GCHFQ: Guyatt chronic heart failure questionnaire; GH: General health; KCCQ: Kansas City Cardiomyopathy Questionnaire; MCS: mental component score; MLWHF: Minnesota Living with Heart Failure questionnaire; MOS: Medical Outcomes Study; NR: not reported; PCS: physical component score; PF: physical functioning; PGAQoL: Patient's Global Assessment of Quality of life; PGWB: Psychological General Wellbeing Index; QLI: Quality of Life Index; RL: role limitation; SF-36: 36-item Short Form.
Exercise = Control: no statistically significant difference (P value > 0.05) in HRQoL between exercise and control groups at follow-up.
Exercise > Control: statistically significant (P value ≤ 0.05) higher HRQoL in exercise compared to control group at follow-up.
Exercise < Control: statistically significant (P value ≤ 0.05) lower HRQoL in exercise versus control group at follow-up.

Table 2. Costs and cost-effectiveness

Author (year)	Georgiou (2001)	HF-ACTION Reed (2010)	Witham (2012)
Year of costs	1998	2008	2010
Country	US	US	UK
Currency	USD	USD	GBP
Intervention cost			
Mean costs/participant	USD4563	USD 6482 (SD 4884)	GBP474.75
Costs considered	Staffing, space rental, equipment, participant's lost wages	Staffing, participant time, travel, parking	Staffing, equipment, staff and participant travel
Cost-effectiveness			
Follow-up period	15.5 years	Mean 2.5 years	6 months
Total mean healthcare cost/participant (exercise)	USD5282*	USD57,338 (SD 81,343)+	GBP1888.24 (SD 3111)
Total mean healthcare costs/participant (control)	USD2055*	USD56,177 (SD 92,749)+	GBP1943.93 (SD 4551)
Incremental healthcare costs	3227*	USD1161 (95% CI -6205 to 8404)	GBP-447.85 (95% CI -1696.00 to 931.00)
Additional healthcare costs considered	Hospitalisations	Medication, procedures, outpatient visits, emergency visits, hospitalisations, tests	Inpatient and outpatient admissions, primary care contacts, medication
Mean healthcare benefit (exercise)	10.24 life years	2.02 QALYs (SD 1.00)	-
Mean healthcare benefit (control)	7.96 life years	1.99 QALYS (SD 1.01)	-
Incremental mean healthcare benefit	1.82 life years*	0.03 (95% CI -0.06 to 0.11)	-
Incremental cost-effectiveness ratio	USD1773 per life year saved	Not reported	-

CI: confidence interval; GBP: GB pounds; 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*
Mean left ventricular ejection fraction (%)	0.39	0.26	0.42	0.82
Mean age (years)	0.29	0.93	0.09	0.88
Sex (% male)	0.54	0.16	-	0.69
Type of rehabilitation (exercise only vs. comprehensive)	0.76	0.77	0.23	0.28
Type of exercise (aerobic training alone vs. aerobic plus resistance training)	0.74	0.56	0.28	0.54
Exercise dose (number of weeks x number of sessions/week x mean duration of session in hours)	0.15	0.80	0.15	0.28
Exercise setting I (hospital only, home only, both hospital and home)	0.23	0.11	0.85	0.23
Exercise setting II (single centre vs. multicentre)	0.94	0.70	0.14	0.01
Publication date	0.54	0.54	0.46	0.60
Risk of bias*	0.40	0.57	0.04	0.08

*'low' risk of bias trial: absence of bias in > 5 out 8 of risk of bias items vs. 'high' risk of trial: absence of bias in < 5 out 8 items.
HRQoL: health-related quality of life; MLWHF: Minnesota Living with Heart Failure questionnaire.

Table 4. Within trial subgroup analyses

Author (year)	Outcome(s)	Subgroup(s)	Results (P value)	Data analysis methods
HF ACTION (O'Connor, 2009)	Composite primary end point of all-cause mortality or hospitalisation, median follow-up 30 months	Age (≤ 70 yr vs. > 70 yr), gender (males vs. females), race (white vs. non-white), heart failure aetiology (ischaemic vs. non-ischaemic), baseline LVEF (≤ 25% vs. > 25%), baseline NYHA (Class II vs. Class III/IV) , previous revascularisation, 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 value > 0. 05)	Interaction test on hazard ratio
HF ACTION (Flynn, 2009)	KCCQ overall score up to 36 months	Age, LVEF (≤ 25% or > 25%), previous revascularisation (coronary artery bypass graft surgery or percutaneous coronary intervention, or no previous revascularisation) , history of MI, and KCCQ overall summary score at baseline (0-50, 50-75 or 75-100)	No significant subgroup interactions (P value > 0. 05)	Interaction test
HF ACTION Keteyian (2012)	All-cause mortality or hospitalisation and cardiovascular mortality or HF hospitalisation at median follow-up 28.2 months	Exercise volume defined as metabolic equivalent [MET]-hr per week i.e. product of exercise intensity (where 1 MET is 3.5 mL VO_2/ kg/min) and the hours of exercise/ week	Exercise volume was logarithmic predictor (P value = 0.03) for all-cause mortality or hospitalisation. For cardiovascular mortality or heart failure hospitalisation, exercise volume was a significant (P value < 0.001) linear and logarithmic predictor Moderate exercise volumes of 3-5 MET-hr and 5-7 MET-hr/week were associated with reductions in subsequent risk that exceeded 30%	Regression-based methods (based only on exercise group data)

ACE: angiotensin-converting enzyme; hr: hour; KCCQ: Kansas City Cardiomyopathy Questionnaire; LVEF: left ventricular ejection fraction; MET: metabolic equivalent; MI: myocardial infarction; NYHA: New York Heart Association; VO_2: oxygen consumption; yr: year.

APPENDICES

Appendix 1. Search strategy 2001

Cochrane Controlled Trials Register (2001, Issue 2)
1. HEART-FAILURE-CONGESTIVE*:ME
2. (HEART and FAILURE)
3. (CARDIAC and FAILURE)
4. ((#1 or #2) or #3)
5. REHABILITATION*:ME
6. EXERCISE*:ME
7. EXERCISE-THERAPY*:ME
8. SPORTS*:ME
9. PHYSICAL-EDUCATION-AND-TRAINING*:ME
10. EXERTION*:ME
11. REHABILITAT*
12. (PHYSICAL* near FIT)
13. (PHYSICAL* near FITNESS)
14. (PHYSICAL near TRAIN*)
15. (PHYSICAL* near ACTIVIT*)
16. (TRAIN* near STRENGTH*)
17. (TRAIN* near AEROBIC*)
18. (AEROBIC* near EXERCISE*)
19. KINESIOTHERAP*
20. (EXERCISE* near TRAIN*)
21. ((((((((((((((#5 or #6) or #7) or #8) or #9) or #10) or #11) or #12) or #13) or #14) or #15) or #16) or #17) or #18) or #19) or #20)
22. (#4 and #21)

Appendix 2. Search strategies 2008

CENTRAL on The Cochrane Library 2007, Issue 4

#1MeSH descriptor Myocardial Ischemia explode all trees
#2(myocard* NEAR isch*mi*)
#3isch*mi* NEAR heart
#4MeSH descriptor Coronary Artery Bypass explode all trees
#5coronary
#6MeSH descriptor Coronary Disease explode all trees
#7MeSH descriptor Myocardial Revascularization explode all trees
#8MeSH descriptor Myocardial Infarction explode all trees
#9myocard* NEAR infarct*
#10heart NEAR infarct*

#11MeSH descriptor Angina Pectoris explode all trees
#12angina
#13MeSH descriptor Heart Failure, Congestive explode all trees
#14heart and (failure or attack)
#15MeSH descriptor Heart Diseases explode all trees
#16heart and disease*
#17myocard*
#18cardiac*
#19CABG
#20PTCA
#21stent* AND (heart or cardiac*)
#22MeSH descriptor Heart Bypass, Left explode all trees
#23MeSH descriptor Heart Bypass, Right explode all trees
#24(#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23)
#25MeSH descriptor Rehabilitation Centers, this term only
#26MeSH descriptor Exercise Therapy explode all trees
#27MeSH descriptor Sports, this term only
#28MeSH descriptor Exertion explode all trees
#29rehabilitat*
#30(physical* NEAR (fit* or train* or therap* or activit*))
#31MeSH descriptor Exercise explode all trees
#32(train*) near (strength* or aerobic or exercise*)
#33((exercise* or fitness) NEAR/3 (treatment or intervent* or program*))
#34MeSH descriptor Rehabilitation explode all trees
#35MeSH descriptor Patient Education explode all trees
#36(patient* NEAR/3 educat*)
#37((lifestyle or life-style) NEAR/3 (intervent* or program* or treatment*))
#38MeSH descriptor Self Care explode all trees
#39MeSH descriptor Ambulatory Care explode all trees
#40MeSH descriptor Psychotherapy explode all trees
#41psychotherap*
#42psycholog* NEAR intervent*
#43relax*
#44MeSH descriptor Mind-Body and Relaxation Techniques explode all trees
#45MeSH descriptor Counseling explode all trees
#46counsel*ing
#47MeSH descriptor Cognitive Therapy explode all trees
#48MeSH descriptor Behavior Therapy explode all trees
#49(behavio*r*) NEAR/4 (modif* or therap* or rehab* or change)
#50MeSH descriptor Stress, Psychological explode all trees
#51stress NEAR manage*
#52cognitive* NEAR therap*
#53MeSH descriptor Meditation explode all trees
#54meditat*
#55MeSH descriptor Anxiety, this term only
#56(manage*) NEAR (anxiety or depres*)
#57CBT
#58hypnotherap*
#59goal NEAR/3 setting
#60(psycho-educat*) or (psychoeducat*)
#61motivat* NEAR interv*
#62MeSH descriptor Psychopathology explode all trees

#63psychopathol*
#64MeSH descriptor Autogenic Training explode all trees
#65autogenic*
#66self near (manage* or care or motivat*)
#67distress*
#68psychosocial* or psycho-social
#69MeSH descriptor Health Education explode all trees
#70(nutrition or diet or health) NEAR education
#71heart manual
#72(#25 OR #26 OR #27 OR #28 OR #29 OR #30 OR #31 OR #32 OR #33 OR #34 OR #35 OR #36 OR #37)
#73(#38 OR #39 OR #40 OR #41 OR #42 OR #43 OR #44 OR #45 OR #46 OR #47 OR #48 OR #49 OR #50 OR #51 OR #52 OR #53 OR #54 OR #55 OR #56 OR #57 OR #58 OR #59 OR #60 OR #61 OR #62 OR #63 OR #64 OR #65 OR #66 OR #67 OR #68 OR #69 OR #70 OR #71)
#74(#72 OR #73)
#75(#74 AND #24)

MEDLINE DIALOG to WEEK 1 2008

1. SEARCH: MYOCARDIAL-ISCHEMIA#.DE.
2. SEARCH: MYOCARD$4 NEAR (ISCHAEMI$2 OR ISCHEMI$2)
3. SEARCH: (ISCHAEMI$2 OR ISCHEMI$2) NEAR HEART
4. SEARCH: CORONARY-ARTERY-BYPASS#.DE.
5. SEARCH: CORONARY.TI,AB.
6. SEARCH: CORONARY-DISEASE#.DE.
7. SEARCH: MYOCARDIAL-REVASCULARIZATION#.DE.
8. SEARCH: MYOCARDIAL-INFARCTION#.DE.
9. SEARCH: MYOCARD$5 NEAR INFARCT$5
10. SEARCH: HEART NEAR INFARCT$5
11. SEARCH: ANGINA-PECTORIS#.DE.
12. SEARCH: ANGINA.TI,AB.
13. SEARCH: HEART-FAILURE-CONGESTIVE#.DE.
14. SEARCH: HEART NEAR FAILURE
15. SEARCH: 1 OR 2 OR 3 OR 4 OR 5 OR 6 OR 7 OR 8 OR 9 OR 10 OR 11 OR 12 OR 13 OR 14
16. SEARCH: HEART-DISEASES#.DE.
17. SEARCH: (HEART NEAR DISEASE$2).TI,AB.
18. SEARCH: MYOCARD$5.TI,AB.
19. SEARCH: CARDIAC$2.TI,AB.
20. SEARCH: CABG
21. SEARCH: PTCA
22. SEARCH: STENT$4 AND (HEART OR CARDIAC$4)
23. SEARCH: HEART-BYPASS-LEFT#.DE. OR HEART-BYPASS-RIGHT#.DE.
24. SEARCH: 16 OR 17 OR 18 OR 19 OR 20 OR 21 OR 22 OR 23
25. SEARCH: REHABILITATION-CENTERS.DE.
26. SEARCH: EXERCISE-THERAPY#.DE.
27. SEARCH: REHABILITATION.W..DE.
28. SEARCH: SPORTS#.W..DE.
29. SEARCH: EXERTION#.W..DE.
30. SEARCH: EXERCISE#.W..DE.
31. SEARCH: REHABILITAT$5.TI,AB.
32. SEARCH: PHYSICAL$4 NEAR (FIT OR FITNESS OR TRAIN$5 OR THERAP$5 OR ACTIVIT$5)
33. SEARCH: TRAIN$5 NEAR (STRENGTH$3 OR AEROBIC OR EXERCIS$4)
34. SEARCH: (EXERCISE$4 OR FITNESS) NEAR (TREATMENT OR INTERVENT$4 OR PROGRAM$2 OR THERAPY)
35. SEARCH: PATIENT-EDUCATION#.DE.

36. SEARCH: PATIENT$2 NEAR EDUCAT$4
37. SEARCH: (LIFESTYLE OR LIFE-STYLE) NEAR (INTERVENT$5 OR PROGRAM$2 OR TREATMENT$2)
38. SEARCH: SELF-CARE.DE.
39. SEARCH: SELF NEAR (MANAGE$5 OR CARE OR MOTIVAT$5)
40. SEARCH: AMBULATORY-CARE.DE.
41. SEARCH: PSYCHOTHERAPY#.W..DE.
42. SEARCH: PSYCHOTHERAP$2.TI,AB.
43. SEARCH: PSYCHOLOG$5 NEAR INTERVENT$5
44. SEARCH: RELAX$6.TI,AB.
45. SEARCH: RELAXATION-TECHNIQUES#.DE. OR MIND-BODY-AND-RELAXATION-TECHNIQUES#.DE.
46. SEARCH: COUNSELING#.W..DE.
47. SEARCH: (COUNSELLING OR COUNSELING).TI,AB.
48. SEARCH: COGNITIVE-THERAPY#.DE.
49. SEARCH: BEHAVIOR-THERAPY#.DE.
50. SEARCH: (BEHAVIOR$4 OR BEHAVIOUR$4) NEAR (MODIFY OR MODIFICAT$4 OR THERAP$2 OR CHANGE)
51. SEARCH: STRESS-PSYCHOLOGICAL#.DE.
52. SEARCH: STRESS NEAR MANAGEMENT
53. SEARCH: COGNITIVE NEAR THERAP$2
54. SEARCH: MEDITAT$4
55. SEARCH: MEDITATION#.W..DE.
56. SEARCH: ANXIETY#.W..DE.
57. SEARCH: MANAGE$5 NEAR (ANXIETY OR DEPRES$5)
58. SEARCH: CBT.TI,AB.
59. SEARCH: HYPNOTHERAP$5
60. SEARCH: GOAL NEAR SETTING
61. SEARCH: GOAL$2 NEAR SETTING
62. SEARCH: PSYCHO-EDUCAT$5 OR PSYCHOEDUCAT$5
63. SEARCH: MOTIVAT$5 NEAR (INTERVENTION OR INTERV$3)
64. SEARCH: PSYCHOPATHOLOGY#.W..DE.
65. SEARCH: PSYCHOPATHOL$4.TI,AB.
66. SEARCH: PSYCHOSOCIAL$4.TI,AB.
67. SEARCH: DISTRESS$4.TI,AB.
68. SEARCH: HEALTH-EDUCATION#.DE.
69. SEARCH: HEALTH NEAR EDUCATION
70. SEARCH: HEART ADJ MANUAL
71. SEARCH: AUTOGENIC-TRAINING#.DE.
72. SEARCH: AUTOGENIC$5.TI.AB.
73. SEARCH: 25 OR 26 OR 27 OR 28 OR 29 OR 30 OR 31 OR 32 OR 33 OR 34 OR 35 OR 36 OR 37 OR 38
74. SEARCH: 39 OR 40 OR 41 OR 42 OR 43 OR 44 OR 45 OR 46 OR 47 OR 48 OR 49 OR 50 OR 51 OR 52 OR 53 OR 54 OR 55 OR 56 OR 57 OR 58 OR 59 OR 60 OR 61 OR 62 OR 63 OR 64 OR 65 OR 66 OR 67 OR 68 OR 69 OR 70 OR 71 OR 72
75. SEARCH: 15 OR 24
76. SEARCH: 73 or 74
77. SEARCH: 75 AND 76
78. SEARCH: RANDOMIZED-CONTROLLED-TRIALS#.DE.
79. SEARCH: PT=RANDOMIZED-CONTROLLED-TRIAL
80. SEARCH: PT=CONTROLLED-CLINICAL-TRIAL
81. SEARCH: CONTROLLED-CLINICAL-TRIALS#.DE.
82. SEARCH: RANDOM-ALLOCATION#.DE.
83. SEARCH: DOUBLE-BLIND-METHOD#.DE.
84. SEARCH: SINGLE-BLIND-METHOD#.DE.
85. SEARCH: (RANDOM$ OR PLACEBO$).TI,AB.
86. SEARCH: ((SINGL$3 OR DOUBL$3 OR TRIPL$3 OR TREBL$3) NEAR (BLIND$3 OR MASK$3)).TI,AB.

87. SEARCH: RESEARCH-DESIGN#.DE.
88. SEARCH: PT=CLINICAL-TRIAL#
89. SEARCH: CLINICAL-TRIALS#.DE.
90. SEARCH: (CLINIC$3 ADJ TRIAL$2).TI,AB.
91. SEARCH: 77 AND 90
92. SEARCH: (ANIMALS NOT HUMANS).SH.
93. SEARCH: 91 NOT 92
94. SEARCH: LIMIT 93 TO 2001-DATE

EMBASE DIALOG to WEEK 1 2008

1. HEART-DISEASE#.DE.
2. (MYOCARD$4 NEAR (ISCHAEMI$2 OR ISCHEMI$2)).TI,AB.
3. ((ISCHAEMI$2 OR ISCHEMI$2) NEAR HEART).TI,AB.
4. CORONARY-ARTERY-DISEASE#.DE.
5. TRANSLUMINAL-CORONARY-ANGIOPLASTY#.DE.
6. (CORONARY NEAR (DISEASE$2 OR BYPASS$2 OR THROMBO$5 OR ANGIOPLAST$2)).TI,AB.
7. HEART-INFARCTION#.DE.
8. (MYOCARD$4 NEAR INFARCT$5).TI,AB.
9. (HEART NEAR INFARC$5).TI,AB.
10. HEART-MUSCLE-REVASCULARIZATION#.DE.
11. ANGINA-PECTORIS#.DE.
12. ANGINA.TI,AB.
13. CONGESTIVE-HEART-FAILURE#.DE.
14. (HEART NEAR FAILURE).TI,AB.
15. 1 OR 2 OR 3 OR 4 OR 5 OR 6 OR 7 OR 8 OR 9 OR 10 OR 11 OR 12 OR 13 OR 14
16. (HEART NEAR DISEASE$2).TI,AB.
17. CARDIAC$2.TI,AB.
18. CABG.TI,AB.
19. PTCA.TI,AB.
20. STENT$4.TI,AB. AND HEART.TI,AB.
21. EXTRACORPOREAL-CIRCULATION#.DE.
22. 16 OR 17 OR 18 OR 19 OR 20 OR 21
23. 15 OR 22
24. PSYCHOTHERAPY#.W..DE.
25. PSYCHOTHERAP$2.TI,AB.
26. PSYCHOLOG$5 NEAR INTERVENT$5
27. RELAX$6.TI,AB.
28. RELAXATION-TRAINING#.DE.
29. COUNSELING#.W..DE.
30. (COUNSELLING OR COUNSELING).TI,AB.
31. (BEHAVIOR$4 OR BEHAVIOUR$4) NEAR (MODIFY OR MODIFICAT$4 OR THERAPY$2 OR CHANGE)
32. STRESS-MANAGEMENT#.DE.
33. STRESS NEAR MANAGEMENT
34. MEDITATION#.W..DE.
35. MEDITAT$5.TI,AB.
36. MANAGE$5 NEAR (ANXIETY OR DEPRES$5)
37. CBT.TI,AB.
38. HYPNOTHERAP$2.TI,AB.
39. GOAL$2 NEAR SETTING
40. PSYCHO-EDUCAT$5 OR PSYCHOEDUCAT$5
41. MOTIVAT$5 NEAR INTERVENT$6
42. PSYCHOSOCIAL-CARE#.DE. OR PSYCHOSOCIAL-REHABILITATION#.DE.

43. PSYCHOSOCIAL.TI,AB.
44. HEALTH-EDUCATION#.DE.
45. HEALTH NEAR EDUCATION
46. HEART ADJ MANUAL
47. AUTOGENIC-TRAINING#.DE.
48. AUTOGENIC.TI,AB.
49. REHABILITATION#.W..DE.
50. REHABILITATION-CENTER#.DE.
51. REHABIL$.TI,AB.
52. SPORT#.W..DE.
53. KINESIOTHERAPY#.W..DE.
54. EXERCISE#.W..DE.
55. PHYSIOTHERAPY#.W..DE.
56. PHYSICAL$4 NEAR (FIT OR FITNESS OR TRAIN$5 OR THERAP$5 OR ACTIVIT$5)
57. TRAIN$5 NEAR (STRENGTH$3 OR AEROBIC OR EXERCIS$4)
58. (EXERCISE$4 OR FITNESS) NEAR (TREATMENT OR INTERVENT$4 OR PROGRAM$2 OR THERAPY)
59. AEROBIC$4 NEAR EXERCISE$4
60. (KINESIOTHERAPY OR PHYSIOTHERAPY).TI,AB.
61. PATIENT-EDUCATION#.DE.
62. PATIENT$2 NEAR EDUCAT$4
63. (LIFESTYLE OR LIFE ADJ STYLE OR LIFE-STYLE) NEAR (INTERVENT$5 OR PROGRAM$2 OR TREATMENT$2)
64. SELF-CARE#.DE.
65. SELF NEAR (MANAGE$5 OR CARE OR MOTIVAT$5)
66. AMBULATORY-CARE#.DE.
67. PSYCHO-EDUCAT$5 OR PSYCHOEDUCAT$5
68. MOTIVAT$5 NEAR INTERVENT$6
69. PSYCHOSOCIAL-CARE#.DE. OR PSYCHOSOCIAL-REHABILITATION#.DE.
70. PSYCHOSOCIAL.TI,AB.
71. HEALTH-EDUCATION#.DE.
72. HEALTH NEAR EDUCATION
73. HEART ADJ MANUAL
74. AUTOGENIC-TRAINING#.DE.
75. AUTOGENIC.TI,AB.
76. PSYCHO-EDUCAT$5 OR PSYCHOEDUCAT$5
77. MOTIVAT$5 NEAR INTERVENT$6
78. PSYCHOSOCIAL-CARE#.DE. OR PSYCHOSOCIAL-REHABILITATION#.DE.
79. PSYCHOSOCIAL.TI,AB.
80. HEALTH-EDUCATION#.DE.
81. HEALTH NEAR EDUCATION
82. HEART ADJ MANUAL
83. 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41 or
42 or 43 or 44 or 45 or 46 or 47 or 48 or 49
84 50 OR 51 OR 52 OR 53 OR 54 OR 55 OR 56 OR 57 OR 58 OR 59 OR 60 OR 61 OR 62 OR 63 OR 64 OR 65 OR
66 OR 67 OR 68 OR 69 OR 70 OR 71 OR 72 OR 73 OR 74 OR 75 OR 76 OR 77 OR 78 OR 79 OR 80 OR 81 OR 82
85. 83 OR 84
86. (RANDOM$ OR PLACEBO$).TI,AB.
87. (SINGL$4 OR DOUBLE$4 OR TRIPLE$4 OR TREBLE$4).TI,AB. AND (BLIND$4 OR MASK$4).TI,AB.
88. (CONTROLLED ADJ CLINICAL ADJ TRIAL).TI,AB.
89. RANDOMIZED-CONTROLLED-TRIAL#.DE.
90. 1 OR 2 OR 3 OR 4
91. 23 AND 85
92. 91 AND 92
93. LIMIT 92 TO 2001-2008

CINAHL DIALOG to WEEK 1 2008

1. ((MYOCARD$4 OR HEART) NEAR (ISCHAEMI$2 OR ISCHEMI$2)).TI,AB.
2. CORONARY.TI,AB.
3. ((MYOCARD$4 OR HEART) NEAR INFARC$5).TI,AB.
4. ANGINA.TI,AB.
5. (HEART NEAR FAILURE).TI,AB.
6. (HEART NEAR DISEAS$2).TI,AB.
7. CARDIAC$2.TI,AB.
8. CABG
9. PTCA
10. STENT$4.TI,AB. AND (HEART OR CARDIAC$4).TI,AB.
11. MYOCARDIAL-ISCHEMIA#.DE.
12. MYOCARDIAL-INFARCTION#.DE.
13. CORONARY-ARTERY-BYPASS#.DE.
14. CORONARY-DISEASE#.DE.
15. CARDIAC-PATIENTS#.DE.
16. MYOCARDIAL-DISEASES#.DE.
17. MYOCARDIAL-REVASCULARIZATION#.DE.
18. HEART-DISEASES#.DE.
19. CARDIOVASCULAR-DISEASES#.DE.
20. HEART-FAILURE-CONGESTIVE#.DE.
21. ANGINA-PECTORIS#.DE.
22. 1 OR 2 OR 3 OR 4 OR 5 OR 6 OR 7 OR 8 OR 9 OR 10 OR 11 OR 12 OR 13 OR 14 OR 15 OR 16 OR 17 OR 18 OR 19 OR 20 OR 21
23. REHABILITATION#.W..DE.
24. SPORTS#.W..DE.
25. EXERCISE#.W..DE.
26. PHYSICAL-ACTIVITY#.DE.
27. MUSCLE-STRENGTHENING#.DE.
28. AEROBIC-EXERCISES#.DE.
29. PHYSICAL-FITNESS#.DE.
30. PATIENT-EDUCATION#.DE.
31. THERAPEUTIC-EXERCISE#.DE.
32. REHABILITAT$5.TI,AB.
33. (PHYSICAL$4 NEAR (FIT OR FITNESS OR TRAIN$4 OR THERAP$5 OR ACTIVIT$4)).TI,AB.
34. (TRAIN$4 NEAR (STRENGTH$3 OR AEROBIC OR EXERCIS$4)).TI,AB.
35. ((EXERCISE$4 OR FITNESS) NEAR (TREATMENT OR INTERVENT$4 OR PROGRAM$2 OR THERAPY)).TI,AB.
36. (PATIENT$2 NEAR EDUCAT$4).TI,AB.
37. ((LIFESTYLE OR LIFE-STYLE) NEAR (INTERVENT$5 OR PROGRAM$2 OR TREATMENT$2)).TI,AB.
38. SELF-CARE#.DE.
39. (SELF NEAR (MANAGE$5 OR CARE OR MOTIVAT$5)).TI,AB.
40. AMBULATORY-CARE#.DE.
41 AEROBIC.TI,AB.
42. RESISTANCE ADJ TRAIN$4
43. MUSCLE ADJ STRENGTH$5
44. AEROBIC.TI,AB.
45. RESISTANCE ADJ TRAIN$4
46. MUSCLE ADJ STRENGTH$5
47. PSYCHOTHERAPY#.W..DE.
48. PSYCHOTHERAP$2.TI,AB.
49. (PSYCHOLOG$5 NEAR INTERVENT$5).TI,AB.
50. RELAX.TI,AB.

51. RELAXATION-TECHNIQUES#.DE.
52. (COUNSELLING OR COUNSELING).TI,AB.
53. COUNSELING#.W..DE.
54. ((BEHAVIOR$4 OR BEHAVIOUR$4) NEAR (MODIFY OR MODIFICAT$4 OR THERAP$2 OR CHANGE)).TI,AB.
55. STRESS-MANAGEMENT#.DE.
56. (STRESS NEAR MANAG$5).TI,AB.
57. (COGNITIVE NEAR THERAP$2).TI,AB.
58. MEDITATION#.W..DE.
59. MEDITAT$5.TI,AB.
60. ANXIETY#.W..DE.
61. (MANAGE$5 NEAR (ANXIETY OR DEPRESS$5)).TI,AB.
62. CBT.TI,AB.
63. HYPNOTHERAP$5.TI,AB.
64. (GOAL$2 NEAR SETTING).TI,AB.
65. (PSYCHO-EDUCAT$5 OR PSYCHOEDUCAT$5).TI,AB.
66. (MOTIVAT$5 NEAR (INTERV$3 OR INTERVENT$5)).TI,AB.
67. PSYCHOSOCIAL$4.TI,AB.
68. HEALTH-EDUCATION#.DE.
69. (HEALTH NEAR EDUCAT$5).TI,AB.
70. HEART ADJ MANUAL
71. AUTOGENIC$3.TI,AB.
72. 23 OR 24 OR 25 OR 26 OR 27 OR 28 OR 29 OR 30 OR 31 OR 32 OR 33 OR 34 OR 35 OR 36 OR 37 OR 38 OR 39 OR 40 OR 41 OR 42 OR 43 OR 44 OR 45 OR 46
73. 47 OR 48 OR 49 OR 50 OR 51 OR 52 OR 53 OR 54 OR 55 OR 56 OR 57 OR 58 OR 59 OR 60 OR 61 OR 62 OR 63 OR 64 OR 65 OR 66 OR 67 OR 68 OR 69 OR 70 OR 71
74. 72 OR 73
75. 22 AND 74
76. PT=CLINICAL-TRIAL
77. CLINICAL-TRIALS#.DE.
78. (RANDOM$5 OR PLACEBO$2).TI,AB.
79. (SINGL$ OR DOUBLE$ OR TRIPLE$ OR TREBLE$).TI,AB. AND (BLIND$ OR MASK$).TI,AB.
80. CONTROLLED ADJ CLINICAL ADJ TRIALS
81. 76 OR 77 OR 78 OR 79 OR 80
82. 75 AND 81
83. LIMIT 82 TO 2001-2008

PsycINFO DIALOG TO JAN WEEK 1

1. SEARCH: HEART-DISORDERS#.DE.
2. SEARCH: MYOCARDIAL-INFARCTIONS.DE.
3. SEARCH: ISCHEMIA#.W..DE.
4. SEARCH: HEART-SURGERY.DE.
5. SEARCH: ANGIOPLASTY
6. SEARCH: HEART ADJ BYPASS
7. SEARCH: CORONARY.TI,AB.
8. SEARCH: (ISCHEMI$3 OR ISCHAEMI$3).TI,AB.
9. SEARCH: (MYOCARD$5 NEAR INFARCT$5).TI,AB.
10. SEARCH: (HEART NEAR (INFARC$5 OR FAILURE OR ATTACK)).TI,AB.
11. SEARCH: ANGINA.TI,AB.
12. SEARCH: (HEART NEAR DISEASE$2).TI,AB.
13. SEARCH: MYOCARD$5.TI,AB.
14. SEARCH: CARDIAC$4.TI,AB.
15. SEARCH: CABG.TI,AB.

16. SEARCH: PTCA.TI,AB.
17. SEARCH: 1 OR 2 OR 3 OR 4 OR 5 OR 6 OR 7 OR 8 OR 9 OR 10 OR 11 OR 12 OR 13 OR 14 OR 15 OR 16
18. SEARCH: PHYSICAL-ACTIVITY#.DE.
19. SEARCH: SPORTS#.W..DE.
20. SEARCH: PHYSICAL-EDUCATION.DE.
21. SEARCH: HEALTH-BEHAVIOR#.DE.
22. SEARCH: PHYSICAL-FITNESS.DE.
23. SEARCH: (PHYSICAL ADJ EDUCATION).TI,AB.
24 SEARCH: EXERTION.TI,AB.
25. SEARCH: REHABILITAT$6.TI,AB.
26. SEARCH: (PHYSICAL NEAR (FIT$5 OR TRAIN$5 OR THERAP$5 OR ACTIVIT$4)).TI,AB.
27. SEARCH: (TRAIN$4 NEAR (STRENGTH$4 OR AEROBIC OR EXERCISE$2)).TI,AB.
28. SEARCH: ((EXERCISE$3 OR FITNESS) NEAR (TREATMENT OR INTERVENT$4 OR PROGRAM$4 OR THERAP$2)).TI,AB.
29. SEARCH: (PATIENT WITH EDUCATION).TI,AB.
30. SEARCH: CLIENT-EDUCATION#.DE.
31. SEARCH: HEALTH-PROMOTION#.DE.
32. SEARCH: ((LIFESTYLE OR LIFE-STYLE) NEAR (INTERVENT$5 OR PROGRAM$2 OR TREATMENT$2)).TI,AB.
33. SEARCH: OUTPATIENT-TREATMENT#.DE.
34. SEARCH: 18 OR 19 OR 20 OR 21 OR 22 OR 23 OR 24 OR 25 OR 26 OR 27 OR 28 OR 29 OR 30 OR 31 OR 32 OR 33
35. SEARCH: PSYCHOTHERAPY#.W..DE.
36 SEARCH: PSYCHOTHERAP$2.TI,AB.
37 SEARCH: TREATMENT#.W..DE.
38 SEARCH: (PSYCHOLOG$4 NEAR INTERVENT$5).TI,AB.
39 SEARCH: COUNSELING#.W..DE.
40 SEARCH: COPING-BEHAVIOR#.DE.
41 SEARCH: MEDITATION.W..DE.
42 SEARCH: AUTOGENIC-TRAINING.DE.
43 SEARCH: HEALTH-EDUCATION#.DE.
44. SEARCH: RELAX$6.TI,AB.
45. SEARCH: (COUNSELLING OR COUNSELING).TI,AB.
46. SEARCH: ((BEHAVIOUR OR BEHAVIOR) NEAR (MODIF$5 OR THERAP$5 OR REHABILIT$5 OR CHANGE)).TI,AB.
47. SEARCH: (STRESS NEAR MANAGE$5).TI,AB.
48. SEARCH: MEDITAT$5.TI,AB.
49. SEARCH: (MANAGE$5 NEAR (ANXIETY OR DEPRES$5)).TI,AB.
50. SEARCH: (CBT OR COGNITIV$2 NEAR THERAP$3).TI,AB.
51. SEARCH: HYPNOTHERAP$3.TI,AB.
52. SEARCH: (PSYCHO-EDUCAT$6 OR PSYCHOEDUCAT$6).TI,AB.
53. SEARCH: (MOTIVAT$5 NEAR INTERVENT$5).TI,AB.
54. SEARCH: (SELF NEAR MANAG$6).TI,AB.
55. SEARCH: AUTOGENIC$3.TI,AB.
56. SEARCH: (GOAL NEAR SETTING).TI,AB.
57. SEARCH: (HEALTH NEAR EDUCATION).TI,AB.
58. SEARCH: (HEART ADJ MANUAL).TI,AB.
59. SEARCH: 35 OR 36 OR 37 OR 38 OR 39 OR 40 OR 41 OR 42 OR 43 OR 44 OR 45 OR 46 OR 47 OR 48 OR 49 OR 50 OR 51 OR 52 OR 53 OR 54 OR 55 OR 56 OR 57 OR 58
60. SEARCH: 17 AND (34 OR 59)
61. SEARCH: (RANDOM$5 OR PLACEBO$5).TI,AB.
62. SEARCH: (DOUBLE$4 OR SINGLE$4 OR TRIPLE$4).TI,AB. AND (BLIND$4 OR MASK OR SHAM$4 OR DUMMY).TI,AB.
63. SEARCH: RCT.TI,AB.
64. SEARCH: AT=TREATMENT$

65. SEARCH: 61 OR 62 OR 63 OR 64
66. SEARCH: 60 AND 66
67. SEARCH: LIMIT 66 TO YRS=2001-2008

ISI Proceedings, search date 1 April 2008

# 7 807 #5 and #6
Databases=STP Timespan=2001-2008
# 6 29,517 TS=(rehab* or educat*)
Databases=STP Timespan=2001-2008
# 5 52,687 #4 OR #3 OR #2 OR #1
Databases=STP Timespan=2001-2008
# 4 27,506 TS=(angina or cardiac* or PTCA or CABG)
Databases=STP Timespan=2001-2008
# 3 11,226 TS=((heart) SAME (infarct* or isch?emia or failure or attack))
Databases=STP Timespan=2001-2008
# 2 12,618 TS=((coronary* or heart*) SAME (by?pass or disease*))
Databases=STP Timespan=2001-2008
# 1 11,809 TS=((myocard*) SAME (isch?emia or infarct* or revasculari?*))
Databases=STP Timespan=2001-2008

Appendix 3. Search strategies 2013

CENTRAL on *The Cochrane Library 2013, Issue 1*

1. MeSH descriptor: [Myocardial Ischemia] explode all trees
2. (myocard* near isch*mi*):ti or (myocard* near isch*mi*):ab
3. (isch*mi* near heart):ti or (isch*mi* near heart):ab
4. MeSH descriptor: [Coronary Artery Bypass] explode all trees
5. (coronary):ti or (coronary):ab
6. MeSH descriptor: [Coronary Disease] explode all trees
7. MeSH descriptor: [Myocardial Revascularization] explode all trees
8. MeSH descriptor: [Myocardial Infarction] explode all trees
9. (myocard* near infarct*):ti or (myocard* near infarct*):ab
10. (heart near infarct*):ti or (heart near infarct*):ab
11. MeSH descriptor: [Angina Pectoris] explode all trees
12. (angina):ti or (angina):ab
13. MeSH descriptor: [Heart Failure] explode all trees
14. (heart and (failure or attack)):ti or (heart and (failure or attack)):ab
15. (Heart diseases):ti or (Heart diseases):ab
16. MeSH descriptor: [Heart Diseases] explode all trees
17. (heart and (disease*)):ti or (heart and (disease*)):ab
18. (myocard*):ti or (myocard*):ab
19. (cardiac*):ti or (cardiac*):ab
20. (CABG):ti or (CABG):ab
21. (PTCA):ti or (PTCA):ab
22. (stent* and (heart or cardiac*)):ti or (stent* and (heart or cardiac*)):ab
23. MeSH descriptor: [Heart Bypass, Left] explode all trees
24. (HFNEF or HFPEF or HFREF or "HF NEF" or "HF PEF" or "HF REF"):ti or (HFNEF or HFPEF or HFREF or "HF NEF" or "HF PEF" or "HF REF"):ab
25. (#1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10 or #11 or #12 or #13 or #14 or #15 or #16 or #17 or #18 or #19 or # 20 or #21 or #22 or #23 or #24)
26. MeSH descriptor: [Rehabilitation Centers] this term only

27. MeSH descriptor: [Exercise Therapy] explode all trees
28. MeSH descriptor: [Sports] this term only
29. MeSH descriptor: [Physical Exertion] explode all trees
30. (rehabilitat*):ti or (rehabilitat*):ab
31. (physical* near (fit* or train* or therap* or activit*)):ti or (physical* near (fit* or train* or therap* or activit*)):ab
32. MeSH descriptor: [Exercise] explode all trees
33. (train*) near (strength* or aerobic or exercise*):ti or (train*) near (strength* or aerobic or exercise*):ab
34. ((exercise* or fitness) near/3 (treatment or intervent* or program*)):ti or ((exercise* or fitness) near/3 (treatment or intervent* or program*)):ab
35. MeSH descriptor: [Rehabilitation] explode all trees
36. MeSH descriptor: [Patient Education as Topic] this term only
37. (patient* near/3 educat*):ti or (patient* near/3 educat*):ab
38. ((lifestyle or life-style) near/3 (intervent* or program* or treatment*)):ti or ((lifestyle or life-style) near/3 (intervent* or program* or treatment*)):ab
39. MeSH descriptor: [Self Care] explode all trees
40. MeSH descriptor: [Ambulatory Care] explode all trees
41. MeSH descriptor: [Psychotherapy] explode all trees
42. (psychotherap*):ti or (psychotherap*):ab
43. (psycholog* near intervent*):ti or (psycholog* near intervent*):ab
44. (relax*):ti or (relax*):ab
45. MeSH descriptor: [Mind-Body Therapies] explode all trees
46. ((Mind or Body) and (Relaxation Techniques)):ti or ((Mind or Body) and (Relaxation Techniques)):ab
47. MeSH descriptor: [Counseling] explode all trees
48. (counseling or counselling):ti or (counseling or counselling):ab
49. MeSH descriptor: [Cognitive Therapy] explode all trees
50. MeSH descriptor: [Behavior Therapy] explode all trees
51. ((behavio*r*) near/4 (modif* or therap* or rehab* or change)):ti or ((behavio*r*) near/4 (modif* or therap* or rehab* or change)):ab
52. MeSH descriptor: [Stress, Psychological] explode all trees
53. (stress near manage*):ti or (stress near manage*):ab
54. (cognitive* near therap*):ti or (cognitive* near therap*):ab
55. MeSH descriptor: [Meditation] explode all trees
56. (meditat*):ti or (meditat*):ab
57. MeSH descriptor: [Anxiety] this term only
58. ((manage*) near (anxiety or depres*)):ti or ((manage*) near (anxiety or depres*)):ab
59. (CBT):ti or (CBT):ab
60. (hypnotherap*):ti or (hypnotherap*):ab
61. (goal near/3 (setting)):ti or (goal near/3 (setting)):ab
62. ((psycho-educat*) or (psychoeducat*)):ti ((psycho-educat*) or (psychoeducat*)):ab
63. (motivat* near (interv*)):ti or (motivat* near (interv*)):ab
64. MeSH descriptor: [Psychopathology] explode all trees
65. (psychopathol*):ti or (psychopathol*):ab
66. MeSH descriptor: [Autogenic Training] explode all trees
67. (autogenic*):ti or (autogenic*):ab
68. (self near (manage* or care or motivat*)):ti or (self near (manage* or care or motivat*)):ab
69. (distress*):ti or (distress*):ab
70. (psychosocial* or psycho-social):ti or (psychosocial* or psycho-social):ab
71. MeSH descriptor: [Health Education] explode all trees
72. (nutrition or diet or health near (education)):ti or (nutrition or diet or health near (education)):ab
73. (heart manual):ti or (heart manual):ab
74. (#26 or #27 or #28 or #29 or #30 or #31 or #32 or #33 or #34 or #35 or #36 or #37)
75. (#38 or #40 or #41 or #42 or #43 or #44 or #45 or #46 or #47 or #48 or #49 or #50 or #51 or #52 or #53 or #54 or #55 or #56 or #57 or #58 or #59 or #60 or #61 or #62 or #63 or #64 or #65 or #66 or #67 or #68 or #69 or #70 or #71 or #72 or #73)

76. (#74 or #75)
77. (#76 and #25)
78. #77 from 2008, in Trials

MEDLINE(R) Ovid 1946 to January week 4 2013

1. exp Myocardial Ischemia/
2. (myocard$4 adj5 (ischaemi$2 or ischemi$2)).ti,ab.
3. ((ischaemi$2 or ischemi$2) adj5 heart).ti,ab.
4. exp Coronary Artery Bypass/
5. coronary.ti,ab.
6. exp Coronary Disease/
7. exp Myocardial Revascularization/
8. Myocardial Infarction/
9. (myocard$5 adj5 infarct$5).ti,ab.
10. (heart adj5 infarct$5).ti,ab.
11. exp Angina Pectoris/
12. angina.ti,ab.
13. exp Heart Failure/
14. (heart adj5 failure).ti,ab.
15. (HFNEF or HFPEF or HFREF or "HF NEF" or "HF PEF" or "HF REF").ti,ab.
16. or/1-15
17. exp Heart Diseases/
18. (heart adj5 disease$2).ti,ab.
19. myocard$5.ti,ab.
20. cardiac$2.ti,ab.
21. CABG.ti,ab.
22. PTCA.ti,ab.
23. (stent$4 and (heart or cardiac$4)).ti,ab.
24. Heart Bypass, Left/ or exp Heart Bypass, Right/
25. or/17-24
26. *Rehabilitation Centers/
27. exp Exercise Therapy/
28. *Rehabilitation/
29. exp Sports/
30. Physical Exertion/ or exertion.ti,ab.
31. exp Exercise/
32. rehabilitat$5.ti,ab.
33. (physical$4 adj5 (fit or fitness or train$5 or therap$5 or activit$5)).ti,ab.
34. (train$5 adj5 (strength$3 or aerobic or exercise$4)).ti,ab.
35. ((exercise$4 or fitness) adj5 (treatment or intervent$4 or programs$2 or therapy)).ti,ab.
36. Patient Education as Topic/
37. (patient$2 adj5 educat$4).ti,ab.
38. ((lifestyle or life-style) adj5 (intervent$5 or program$2 or treatment$2)).ti,ab.
39. *Self Care/
40. (self adj5 (manage$5 or care or motivate$5)).ti,ab.
41. *Ambulatory Care/
42. exp Psychotherapy/
43. psychotherap$2.ti,ab.
44. (psycholog$5 adj5 intervent$5).ti,ab.
45. relax$6.ti,ab.
46. exp Relaxation Therapy/ or exp Mind-Body Therapies/
47. exp Counseling/
48. (counselling or counseling).ti,ab.

49. exp Cognitive Therapy/
50. exp Behavior Therapy/
51. ((behavior$4 or behaviour$4) adj5 (modify or modificat$4 or therap$2 or change)).ti,ab.
52. *Stress, Psychological/
53. (stress adj5 management).ti,ab.
54. (cognitive adj5 therap$2).ti,ab.
55. meditat$4.ti,ab.
56. *Meditation/
57. exp Anxiety/
58. (manage$5 adj5 (anxiety or depress$5)).ti,ab.
59. CBT.ti,ab.
60. hypnotherap$5.ti,ab.
61. (goal adj5 setting).ti,ab.
62. (goal$2 adj5 setting).ti,ab.
63. (psycho-educat$5 or psychoeducat$5).ti,ab.
64. (motivat$5 adj5 (intervention or interv$3)).ti,ab.
65. Psychopathology/
66. psychopathol$4.ti,ab.
67. psychosocial$4.ti,ab.
68. distress$4.ti,ab.
69. exp Health Education/
70. (health adj5 education).ti,ab.
71. (heart adj5 manual).ti,ab.
72. Autogenic Training/
73. autogenic$5.ti,ab.
74. or/26-39
75. or/40-73
76. 16 or 25
77. 74 or 75
78. 76 and 77
79. randomized controlled trial/
80. randomized controlled trial.pt.
81. controlled clinical trial.pt.
82. controlled clinical trial/
83. Random Allocation/
84. Double-Blind Method/
85. single-blind method/
86. (random$ or placebo$).ti,ab.
87. ((singl$3 or doubl$3 or tripl$3 or trebl$3) adj5 (blind$3 or mask$3)).ti,ab.
88. exp Research Design/
89. Clinical Trial.pt.
90. exp clinical trial/
91. (clinic$3 adj trial$2).ti,ab.
92. or/79-91
93. 78 and 92
94. (Animals not Humans).sh.
95. 93 not 94
96. limit 95 to yr="2008 -Current"

MEDLINE In-Process and Other Non-Indexed Citations Ovid 5 February 2013

1. (myocard$4 adj5 (ischaemi$2 or ischemi$2)).ti,ab.
2. ((ischaemi$2 or ischemi$2) adj5 heart).ti,ab.
3. coronary.ti,ab.

4. (myocard$5 adj5 infarct$5).ti,ab.
5. (heart adj5 infarct$5).ti,ab.
6. angina.ti,ab.
7. (heart adj5 failure).ti,ab.
8. (HFNEF or HFPEF or HFREF or "HF NEF" or "HF PEF" or "HF REF").ti,ab.
9. or/1-8
10. (heart adj5 disease$2).ti,ab.
11. myocard$5.ti,ab.
12. cardiac$2.ti,ab.
13. CABG.ti,ab.
14. PTCA.ti,ab.
15. (stent$4 and (heart or cardiac$4)).ti,ab.
16. or/10-15
17. Physical Exertion/ or exertion.ti,ab.
18. rehabilitat$5.ti,ab.
19. (physical$4 adj5 (fit or fitness or train$5 or therap$5 or activit$5)).ti,ab.
20. (train$5 adj5 (strength$3 or aerobic or exercise$4)).ti,ab.
21. ((exercise$4 or fitness) adj5 (treatment or intervent$4 or programs$2 or therapy)).ti,ab.
22. (patient$2 adj5 educat$4).ti,ab.
23. ((lifestyle or life-style) adj5 (intervent$5 or program$2 or treatment$2)).ti,ab.
24. (self adj5 (manage$5 or care or motivate$5)).ti,ab.
25. psychotherap$2.ti,ab.
26. (psycholog$5 adj5 intervent$5).ti,ab.
27. relax$6.ti,ab.
28. (counselling or counseling).ti,ab.
29. ((behavior$4 or behaviour$4) adj5 (modify or modificat$4 or therap$2 or change)).ti,ab.
30. (stress adj5 management).ti,ab.
31. (cognitive adj5 therap$2).ti,ab.
32. meditat$4.ti,ab.
33. (manage$5 adj5 (anxiety or depress$5)).ti,ab.
34. CBT.ti,ab.
35. hypnotherap$5.ti,ab.
36. (goal adj5 setting).ti,ab.
37. (goal$2 adj5 setting).ti,ab.
38. (psycho-educat$5 or psychoeducat$5).ti,ab.
39. (motivat$5 adj5 (intervention or interv$3)).ti,ab.
40. psychopathol$4.ti,ab.
41. psychosocial$4.ti,ab.
42. distress$4.ti,ab.
43. (health adj5 education).ti,ab.
44. (heart adj5 manual).ti,ab.
45. autogenic$5.ti,ab.
46. or/17-45
47. 9 or 16
48. 46 and 47
49. (random$ or placebo$).ti,ab.
50. ((singl$3 or doubl$3 or tripl$3 or trebl$3) adj5 (blind$3 or mask$3)).ti,ab.
51. (clinic$3 adj trial$2).ti,ab.
52. 49 or 50 or 51
53. 48 and 52
54. limit 53 to yr="2008 -Current"

EMBASE Ovid 1980 to 2013 week 5

1. exp heart disease/
2. (myocard$4 adj5 (ischaemi$2 or ischemi$2)).ti,ab.
3. ((ischaemi$2 or ischemi$2) adj5 heart).ti,ab.
4. exp coronary artery disease/
5. transluminal coronary angioplasty/
6. (coronary adj5 (disease$2 or bypass$2 or thrombo$5 or angioplasty$2)).ti,ab.
7. exp heart infarction/
8. (myocard$5 adj5 infarct$5).ti,ab.
9. (heart adj5 infarct$5).ti,ab.
10. heart muscle revascularization/
11. exp Angina Pectoris/
12. angina.ti,ab.
13. exp congestive heart failure/
14. (heart adj5 failure).ti,ab.
15. (HFNEF or HFPEF or HFREF or "HF NEF" or "HF PEF" or "HF REF").ti,ab.
16. or/1-15
17. (heart adj5 disease$2).ti,ab.
18. cardiac$2.ti,ab.
19. CABG.ti,ab.
20. PTCA.ti,ab.
21. (stent$4 and heart).ti,ab.
22. exp extracorporeal circulation/
23. or/17-22
24. 16 or 23
25. *Psychotherapy/
26. psychotherapy$2.ti,ab.
27. (psycholog$5 adj5 intervent$5).ti,ab.
28. relax$6.ti,ab.
29. relaxation training/
30. *counselling/
31. (counselling or counseling).ti,ab.
32. ((behavior$4 or behaviour$4) adj5 (modify or modificat$4 or therap$2 or change)).ti,ab.
33. stress management/
34. (stress adj5 management).ti,ab.
35. *Mediation/
36. meditat$5.ti,ab.
37. (manage$5 adj5 (anxiety or depress$5)).ti,ab.
38. CBT.ti,ab.
39. hypnotherap$2.ti,ab.
40. (goal$2 adj5 setting).ti,ab.
41. (psycho-educat$5 or psychoeducat$5).ti,ab.
42. (motivat$5 adj5 intervent$6).ti,ab.
43. exp psychosocial care/ or exp psychosocial rehabilitation/
44. psychosocial.ti,ab.
45. exp health education/
46. (health adj5 education).ti,ab.
47. (heart adj5 manual).ti,ab.
48. autogenic training/
49. autogenic.ti,ab.
50. *Rehabilitation/
51. rehabilitation center/
52. rehabil$.ti,ab.
53. exp Sport/

54. exp Kinesiotherapy/
55. exp Exercise/
56. exp Physiotherapy/
57. (physical$4 adj5 (fit or fitness or train$5 or therap$5 or activit$5)).ti,ab.
58. (train$5 adj5 (strength$3 or aerobic or exercise$4)).ti,ab.
59. ((exercise$4 or fitness) adj5 (treatment or intervent$4 or programs$2 or therapy)).ti,ab.
60. (aerobic$4 adj5 exercise$4).ti,ab.
61. (kinesiotherapy or physiotherapy).ti,ab.
62. patient education/
63. (patient$2 adj5 educat$4).ti,ab.
64. ((((lifestyle or life) adj1 style) or life-style) adj5 (intervent$5 or program$2 or treatment$2)).ti,ab.
65. exp self care/
66. (self adj5 (manage$5 or care or motivate$5)).ti,ab.
67. exp ambulatory care/
68. (psycho-educat$5 or psychoeducat$5).ti,ab.
69. (motivat$5 adj5 intervent$6).ti,ab.
70. psychosocial care/ or psychosocial rehabilitation/
71. psychosocial.ti,ab.
72. exp health education/
73. (health adj5 education).ti,ab.
74. (heart adj5 manual).ti,ab.
75. autogenic training/
76. autogenic$5.ti,ab.
77. (psycho-educat$5 or psychoeducat$5).ti,ab.
78. (motivat$5 adj5 intervent$6).ti,ab.
79. psychosocial care/ or psychosocial rehabilitation/
80. psychosocial.ti,ab.
81. exp health education/
82. (health adj5 education).ti,ab.
83. (heart adj5 manual).ti,ab.
84. or/25-50
85. or/51-83
86. 84 or 85
87. (random$ or placebo$).ti,ab.
88. ((singl$4 or doubl$4 or tripl$4 or trebl$4) adj5 (blind$4 or mask$4)).ti,ab.
89. (controlled adj1 clinical adj1 trial).ti,ab.
90. randomized controlled trial/
91. or/87-90
92. 24 and 86
93. 91 and 92
94. (animal$ not human$).sh,hw.
95. 93 not 94
96. limit 95 to yr="2008 -Current"

PsycINFO Ovid 1806 to January week 5 2013

1. exp heart disorders/
2. *Myocardial Infarctions/
3. exp Ischemia/
4. *Heart Surgery/
5. angioplasty.ti,ab.
6. (heart adj1 bypass).ti,ab.
7. coronary.ti,ab.
8. (ischemi$3 or ischaemi$3).ti,ab.

9. (myocard$5 adj5 infarct$5).ti,ab.
10. (heart adj5 (infarct$5 or failure or attack)).ti,ab.
11. angina.ti,ab.
12. (heart adj5 disease$2).ti,ab.
13. myocard$5.ti,ab.
14. cardiac$4.ti,ab.
15. CABG.ti,ab.
16. PTCA.ti,ab.
17. (HFNEF or HFPEF or HFREF or "HF NEF" or "HF PEF" or "HF REF").ti,ab.
18. or/1-17
19. exp Physical Activity/
20. exp Sports/
21. *Physical Education/
22. exp Health Behavior/
23. *Physical Fitness/
24. (physical adj1 education).ti,ab.
25. exertion$6.ti,ab.
26. rehabilitat$6.ti,ab.
27. (physical adj5 (fit$5 or train$5 or therap$5 or activit$4)).ti,ab.
28. (train$4 adj5 (strength$4 or aerobic or exercise$2)).ti,ab.
29. ((exercise$3 or fitness) adj5 (treatment or intervent$4 or program$4 or therap$2)).ti,ab.
30. patient with education.ti,ab.
31. exp Client Education/
32. exp Health Promotion/
33. ((lifestyle or life-style) adj5 (intervent$5 or program$2 or treatment$2)).ti,ab.
34. exp Outpatient Treatment/
35. or/19-34
36. exp Psychotherapy/
37. psychotherapy$2.ti,ab.
38. exp Treatment/
39. (psycholog$4 adj5 intervent$5).ti,ab.
40. exp Counseling/
41. exp Coping Behavior/
42. *Meditation/
43. *Autogenic Training/
44. exp Health Education/
45. relax$6.ti,ab.
46. (counselling or counseling).ti,ab.
47. ((behavior or behaviour) adj5 (modif$5 or therap$5 or rehabilit5 or change)).ti,ab.
48. (stress adj5 management).ti,ab.
49. meditat$5.ti,ab.
50. (manage$5 adj5 (anxiety or depress$5)).ti,ab.
51. ((cbt or cognitive$2) adj5 therap$3).ti,ab.
52. hypnotherap$3.ti,ab.
53. (psycho-educat$6 or psychoeducat$6).ti,ab.
54. (motivat$5 adj5 intervent$5).ti,ab.
55. (self adj5 manag$6).ti,ab.
56. autogenic$3.ti,ab.
57. (goal adj5 setting).ti,ab.
58. (health adj5 education).ti,ab.
59. (heart adj1 manual).ti,ab.
60. or/36-59
61. 18 and (35 or 60)

62. (random$5 or placebo$5).ti,ab.
63. ((single$4 or double$4 or triple$4) and (blind$4 or mask or sham$4 or dummy)).ti,ab.
64. RCT.ti,ab.
65. or/62-64
66. 61 and 65
67. limit 66 to yr="2008 -Current"

CINAHL EBSCOhost, search date 5 February 2013

1. TI((myocard* N5 ischaemi*) or (myocard* N5 ischemi*) or (heart N5 ischaemi*) or (heart N5 ischemi*)) OR AB((myocard* N5 ischaemi*) or (myocard* N5 ischemi*) or (heart N5 ischaemi*) or (heart N5 ischemi*))
2. TI(coronary) or AB(coronary)
3. TI((myocard* N5 infarc*) or (heart N5 infarc*)) or AB((myocard* N5 infarc*) or (heart N5 infarc*))
4. TI(angina) OR AB(angina)
5. TI(heart N5 failure) or AB(heart N5 failure)
6. TI(heart N5 diseas*) or AB(heart N5 diseas*)
7. TI(cardiac) or AB(cardiac)
8. TI(CABG) or AB(CABG)
9. TI(PTCA) or AB(PTCA)
10. TI(Stent* and (heart or cardiac*)) or AB(Stent* and (heart or cardiac*))
11. (MH "Myocardial Ischemia+")
12. (MH "Myocardial Infarction+")
13. (MH "Coronary Artery Bypass+")
14. (MH "Coronary Disease+")
15. TI(cardiac N5 patient*) or AB(cardiac N5 patient*)
16. TI(Cardiomyopathies) or AB(Cardiomyopathies)
17. (MH "Myocardial Revascularization+")
18. (MH "Heart Diseases+")
19. (MH "Cardiovascular Diseases+")
20. (MH "Heart Failure+")
21. (MH "Angina Pectoris+")
22. TI(HFNEF or HFPEF or HFREF or "HF NEF" or "HF PEF" or "HF REF") or AB(HFNEF or HFPEF or HFREF or "HF NEF" or "HF PEF" or "HF REF")
23. S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7 OR S8 OR S9 OR S10 OR S11 OR S12 OR S13 OR S14 OR S15 OR S16 OR S17 OR S18 OR S19 OR S20 OR S21 OR S22
24. (MM "Rehabilitation")
25. (MM "Sports")
26. (MM "Physical Activity")
27. (MH "Muscle Strengthening+")
28. (MH "Aerobic Exercises+")
29. (MH "Physical Fitness+")
30. (MH "Patient Education+")
31. (MH "Therapeutic Exercise+")
32. TI(rehabilitat*) or AB(rehabilitat*)
33. TI((physical* N5 fit) or (physical N5 fitness) or (physical N5 train*) or (physical N5 therap*) or (physical N5 activit*)) or AB((physical* N5 fit) or (physical N5 fitness) or (physical N5 train*) or (physical N5 therap*) or (physical N5 activit*))
34. TI((train N5 strength) or (train N5 aerobic) or (train N5 exercis*)) or AB((train N5 strength) or (train N5 aerobic) or (train N5 exercis*))
35. TI((exercise N5 treatment) or (fitness N5 treatment) or (exercise N5 intervent*) or (fitness N5 intervent*) or (exercise N5 program*) or (fitness N5 program) or (exercise N5 therapy) or (fitness N5 therapy)) or AB((exercise N5 treatment) or (fitness N5 treatment) or (exercise N5 intervent*) or (fitness N5 intervent*) or (exercise N5 program*) or (fitness N5 program) or (exercise N5 therapy) or (fitness N5 therapy))
36. TI(patient* N5 educat*) or AB(patient* N5 educat*)

37. TI ((lifestyle N5 intervent*) or (life-style N5 intervent*) or (lifestyle N5 program*) or (life-style N5 program*) or (lifestyle N5 treatment) or (life-style N5 treatment)) OR AB ((lifestyle N5 intervent*) or (life-style N5 intervent*) or (lifestyle N5 program*) or (life-style N5 program*) or (lifestyle N5 treatment) or (life-style N5 treatment))
38. (MH "Self Care+")
39. TI((self N5 manage*) or (self N5 care) or (self N5 motivat*)) or AB((self N5 manage*) or (self N5 care) or (self N5 motivat*))
40. (MM "Ambulatory Care")
41. TI(aerobic) or AB(aerobic)
42. TI(resistance W1 train*) or AB(resistance W1 train*)
43. TI(muscle W1 strength*) or AB(muscle W1 strength*)
44. TI(resistance W1 train*) or AB(resistance W1 train*)
45. TI(muscle W1 strength*) or AB(muscle W1 strength*)
46. (MH "Psychotherapy+")
47. TI(psychotherap*) or AB(psychotherap*)
48. TI(psycholog* N5 intervent*) or AB(psycholog* N5 intervent*)
49. TI(relax) or AB(relax)
50. (MH "Relaxation Techniques+")
51. TI(counselling or counseling) or AB(counselling or counseling)
52. (MH "Counseling+")
53. TI((behavio?r* N5 modify) or (behavio?r* N5 modificat*) or (behavio?r* N5 therap*) or (behavio?r* N5 change)) or AB((behavio?r* N5 modify) or (behavio?r* N5 modificat*) or (behavio?r* N5 therap*) or (behavio?r* N5 change))
54. (MM "Stress Management")
55. TI(stress N5 manag*) or AB(stress N5 manag*)
56. TI(cognitive N5 therap*) or AB(cognitive N5 therap*)
57. (MM "Meditation")
58. TI(meditat*) or AB(meditat*)
59. (MH "Anxiety+")
60. TI((manage* N5 anxiety) or (manage* N5 depress*)) or AB((manage* N5 anxiety) or (manage* N5 depress*))
61. TI(CBT) or AB(CBT)
62. TI(hypnotherap*) or AB(hypnotherap*)
63. TI(goal* N5 setting) or AB(goal* N5 setting)
64. TI(psycho-educat* or psychoeducat*) or AB(psycho-educat* or psychoeducat*)
65. TI((motivat* N5 interv*) or (motivate* N5 intervent*)) or AB((motivat* N5 interv*) or (motivate* N5 intervent*))
66. TI(psychosocial*) or AB(psychosocial*)
67. (MH "Health Education+")
68. TI(health N5 educat*) or AB(health N5 educat*)
69. TI(heart W1 manual) or AB(heart W1 manual)
70. TI(autogenic*) or AB(autogenic*)
71. S24 OR S25 OR S26 OR S27 OR S28 OR S29 OR S30 OR S31 OR S32 OR S33 OR S34 OR S35 OR S36 OR S37 OR S38 OR S39 OR S40 OR S41 OR S42 OR S43 OR S44 OR S45
72. S46 OR S47 OR S48 OR S49 OR S50 OR S51 OR S52 OR S53 OR S54 OR S55 OR S56 OR S57 OR S58 OR S59 OR S60 OR S61 OR S62 OR S63 OR S64 OR S65 OR S66 OR S67 OR S68 OR S69 OR S70
73. S71 OR S72
74. S23 AND S73
75. PT CLINICAL TRIAL
76. (MH "Clinical Trials+")
77. TI (random* or placebo*) or AB (random* or placebo*)
78. TI(singl* or double* or triple* or treble* and (blind* or mask*)) or AB(singl* or double* or triple* or treble* and (blind* or mask*))
79. TI(controlled w1 clinical w1 trials) or AB(controlled w1 clinical w1 trials)
80. S75 OR S76 OR S77 OR S78 OR S79
81. S74 AND S80 date limit=2008-current

Web of Science, search date 6 February 2013

1. TS=((myocard*) SAME (isch?emia or infarct* or revasculari?*))

2. TS=((coronary* or heart*) SAME (by?pass or disease*))
3. TS=((heart) SAME (infarct* or isch?emia or failure or attack))
4. TS=(angina or cardiac* or PTCA or CABG)
5. TS=(HFNEF or HFPEF or HFREF or "HF NEF" or "HF PEF" or "HF REF")
6. #1 OR #2 OR #3 OR #4 OR #5
7. TS=(rehab* or educat*)
8. #6 AND #7
9. TS=(random* or placebo*)
10. TS=((singl* or doubl* or tripl* or trebl*) SAME (blind* or mask*))
11. TS=("clinic* trial*")
12. #9 OR #10 OR #11
13. #8 AND #12

Databases=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH Timespan=2008-2013

WHAT'S NEW

Last assessed as up-to-date: 30 June 2013.

Date	Event	Description
19 October 2017	Amended	Tables moved to correct section of the review.

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	This update review identified a further 14 trials. Whilst conclusions of the review do not change, this update provides broader body of evidence of the benefit of exercise-based interventions that includes HFPEF patients and delivery in a home-based setting
14 February 2013	New search has been performed	Searches updated
18 May 2004	New citation required and conclusions have changed	Substantive amendment

CONTRIBUTIONS OF AUTHORS

Rod Taylor and Viral Sagar led the design of the update review.

Simon Briscoe developed the updated the searches.

Viral Sagar and Rod Taylor undertook study selection, data extraction, assessment of risk of bias and data analysis.

Viral Sagar and Rod Taylor wrote the first draft of the update review, and 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).

SOURCES OF SUPPORT

Internal sources

- None, Other.

External sources

- None, Other.

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

Compared with previous version of this review, the inclusion criteria extended to include HFPEF.

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