Exercise based rehabilitation for heart failure (Review)

Davies EJ, Moxham T, Rees K, Singh S, Coats AJS, Ebrahim S, Lough F, Taylor RS

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[Intervention Review]

Exercise based rehabilitation for heart failure

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ABSTRACT

Background

From previous systematic reviews and meta-analyses there is consensus about the positive effect of exercise training on exercise capacity; however, the effects on health-related quality of life, mortality and hospital admissions in heart failure remain uncertain.

Objectives

To update the previous systematic review which determined the effectiveness of exercise-based interventions on the mortality, hospitalisation admissions, morbidity and health-related quality of life for patients with systolic heart failure.

Search methods

We searched the Cochrane Central Register of Controlled Trials (CENTRAL) (*The Cochrane Library* 2007, Issue 4). To update searches from the previous review, MEDLINE, EMBASE, CINAHL, and PsycINFO were searched (2001 to January 2008). ISI Proceedings and bibliographies of identified reviews were checked.

Selection criteria

Randomised controlled trials of exercise-based interventions with six months follow up or longer compared to usual medical care or placebo. The study population comprised adults of all ages (> 18 years) with evidence of chronic systolic heart failure.

Data collection and analysis

All identified references were independently screened by two review authors and those that were clearly ineligible were rejected. Full papers of potentially relevant trials were obtained. Data were independantly extracted from the included trials and their risk of bias assessed by a single review author and checked by a second.

Main results

Nineteen trials (3647 participants) met the inclusion criteria. One large trial recuited 2331 of the participants. There was no significant difference in pooled mortality between groups in the 13 trials with < 1 year follow up. There was evidence of a non-significant trend toward a reduction in pooled mortality with exercise in the four trials with > 1 year follow up. A reduction in the hospitalisation rate was demonstrated with exercise training programmes. Hospitalisations due to systolic heart failure were reduced with exercise and there was a significant improvement in health-related quality of life (HRQoL). The effect of cardiac exercise training on total mortality and HRQoL were independent of the degree of left ventricular dysfunction, type of cardiac rehabilitation, dose of exercise intervention, length of follow up, trial quality, and trial publication date.

Authors' conclusions

The previous version of this review showed that exercise training improved exercise capacity in the short term in patients with mild to moderate heart failure when compared to usual care. This updated review provides evidence that in a similar population of patients, exercise does not increase the risk of all-cause mortality and may reduce heart failure-related hospital admissions. Exercise training may offer important improvements in patients' health-related quality of life.

PLAIN LANGUAGE SUMMARY

Exercise based rehabilitation for heart failure

People with heart failure can experience marked reductions in their activities of daily living and health-related quality of life because of their restricted heart capacity. This can reduce their ability to exercise, which can further reduce fitness making their symptoms worse. Chronic heart failure is also associated with a substantially increased risk of death. The review found that for people with mild to moderate systolic heart failure there was neither a reduction or an increase in the risk of death with exercise. However, following exercise training there was a reduction in hospital admissions due to the systolic heart failure. In both the short and longer term, exercise training programmes improved health-related quality of life compared to usual care without the exercise. The kinds of exercise programmes studied varied greatly but were largely aerobic (such as brisk walking). We found no evidence to suggest that exercise training programmes cause harm.

BACKGROUND

Over the past decade chronic heart failure (CHF) has become more prevalent worldwide (AHA 2010). This is mainly due to ageing of the population and the longer survival of people who have suffered a myocardial infarction with associated heart failure. Also, the increasing prevalence of obesity and diabetes is likely to accelerate the incidence of CHF, resulting in high levels of healthcare utilisation and increasing costs (Campbell 2003).

Both the incidence and prevalence of heart failure increase steeply with age, with the average age at first diagnosis being 76 years (Cowie 1999). While around 1 in 35 of people aged 65 to 74 years has heart failure, this increases to about 1 in 15 for those aged 75 to 84 years and just over 1 in 7 for those aged 85 years and above. The risk of heart failure is higher in men than in women, in all age groups, but there are more women than men with heart failure due to population demographics (Campbell 2003).

The prevalence and incidence of CHF is steadily increasing, with approximately 670,000 new cases annually in the United States (AHA 2010). Whilst improved management of hypertension has reduced this condition as an aetiological factor in the development of CHF, the increased survival rate from myocardial infarction has led to a subsequent increase in the number of cases of CHF (Kostis 1997) as has increasing longevity in developed countries. In the developing world the occurrence of heart failure can often be attributed to valvular heart disease and nutritional cardiac disease, such as pellegra, kwashiokor, alcohol induced (Lip 2000). Estimates of the prevalence of heart failure in the United States range from 1.2% to 2.2% in middle-aged adults, ages 40 to 59 years; over 80 years of age the prevalence of CHF is in the region of 12% to 14% (AHA 2009). Heart failure has a poor prognosis as just under 40% of patients diagnosed with heart failure die within a year although thereafter the mortality is less than 10% per year (Cowie 2000). Hospital admission rates for heart failure are ris-

ing in all industrialised countries particularly among the elderly (McMurray 2000). Admissions are projected to rise by 50% over the next 25 years, largely due to the ageing of the population. It is estimated that the total annual cost of heart failure to the UK NHS is around £716 million, or around 1.8% of the total UK NHS budget; approximately 70% of this total is due to the costs of hospitalisation (NCCCC 2003). The costs increase with disease severity and the healthcare costs for patients with the most severe symptoms are between eight and 30 times greater than for those with mild symptoms (Berry 2001).

Patients with CHF present with a variety of symptoms most of which are non-specific (Watson 2000). The most frequently presenting symptom is exertional breathlessness. There is no single diagnostic test for heart failure and diagnosis relies on clinical judgement based on a combination of history, physical examination, and appropriate investigations. Other important symptoms are fatigue and lethargy in addition to swelling of the feet and ankles. The symptoms and functional exercise capacity are used to classify the severity of heart failure, using the New York Heart Association (NYHA) classification (NYHA 1994) and to judge responsiveness to treatment. Whilst disease severity is based upon symptoms diagnosis is achieved using objective measures, for example echocardiographic or magnetic resonance assessment of ejection fraction. The European Task Force report (CHF Taskforce 2001) proposes that the definition of heart failure should rely on two criteria. These are the symptoms of heart failure at rest or during exercise (typically breathlessness and fatigue) and objective evidence of cardiac dysfunction at rest. Where the diagnosis is unclear, a response to treatment directed towards heart failure may be used in addition to the above criteria. However, like many chronic diseases, there is a poor correlation between symptoms and the degree of cardiac impairment and also between symptoms and disease prognosis (Opasich 2001; van den Brock 1992; van Tol 2006).

In the last decade, a number of evidence based guidelines have been developed to help improve diagnosis and treatment for patients with CHF associated with reduced systolic function. These guidelines cover aetiology, prevention, diagnostic modalities, and therapeutic interventions (ESC 1995; Hunt 2001; Remme 2001). Exercise training is now being intensively evaluated for any benefits in the treatment of CHF (Piepoli 1998).

In 2004, the Cochrane systematic review of exercise based interventions for heart failure was published (Rees 2004a). This review concluded that exercise training clearly improved short-term (up to one-year follow up) exercise capacity (see Figure 1; Figure 2; Figure 3; Figure 4). Of the 29 randomised controlled trials that were included, only one trial reported on hospitalisations and mortality in the longer term. The other mainly small-scale trials did not aim to measure clinical events and were of short duration. Furthermore, a number of included trials did not use validated health-related quality of life measures. Also in 2004, an individual patient data meta-analysis by the ExTraMATCH Collaborative Group (ExTraMatch 2004) concluded that there was no evidence that supervised exercise training programmes for CHF patients were dangerous and indeed there was evidence of an overall reduction in mortality (hazard ratio: 0.65, 95% confidence interval 0.46 to 0.92). However, 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. It has, therefore, been difficult to verify the data and the comprehensiveness of the meta-analysis. For example, several of the RCTs included in the Cochrane review were not included in the ExTraMATCH review. In 2006, van Tol and colleagues reported on a meta-analysis confirming the improvements in exercise capacity seen in the Cochrane review and also an improvement in quality of life as assessed by the Minnesota Living with Heart Failure (MLWHF) questionnaire (van Tol 2006). Most recently, a 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). In summary, to date there is a consensus about the positive effect of exercise training on exercise capacity however the effects on mortality, hospital admissions, health-related quality of life and overall healthcare costs remain uncertain.

Figure 1. Forest plot of VO2max (m/kg/min) from previous Cochrane review

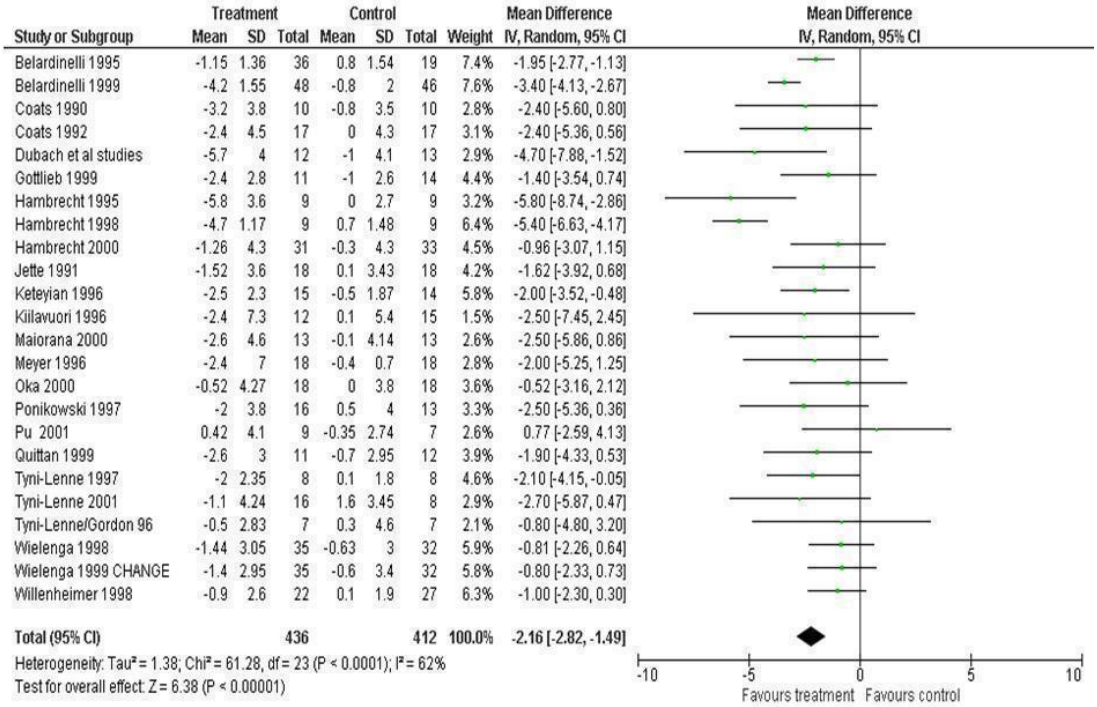


Figure 2. Forest plot of exercise capacity in watts from previous Cochrane review

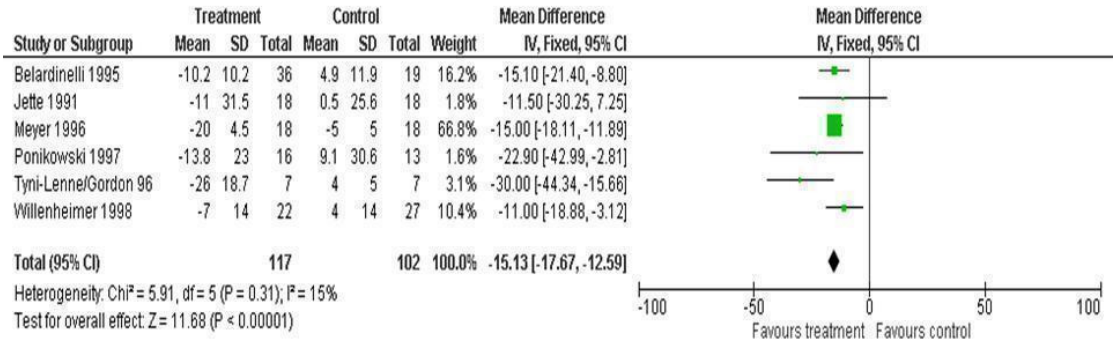


Figure 3. Forest plot of exercise durations (mins) from previous Cochrane review

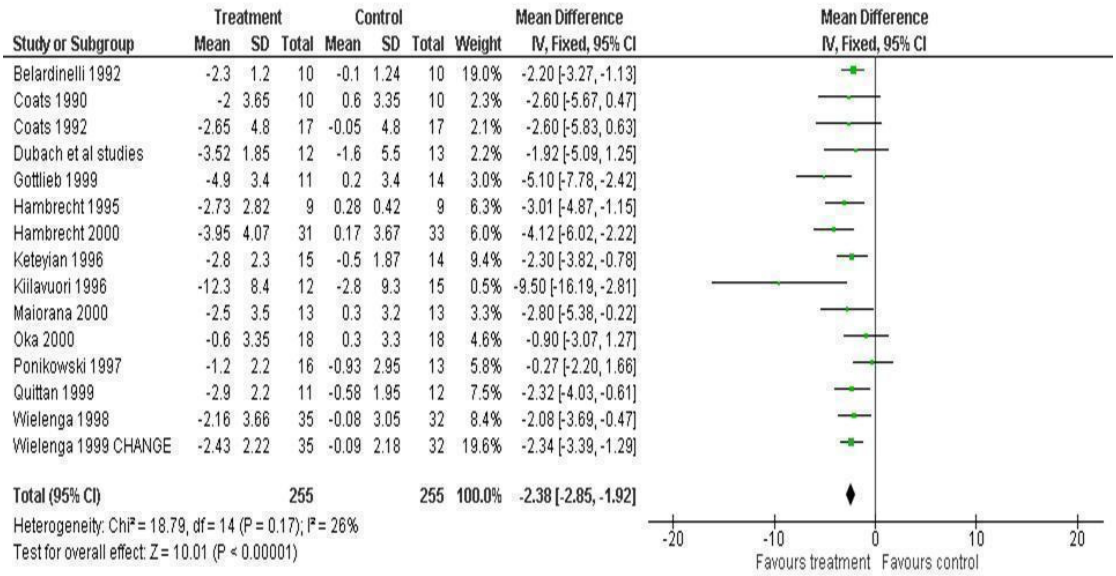
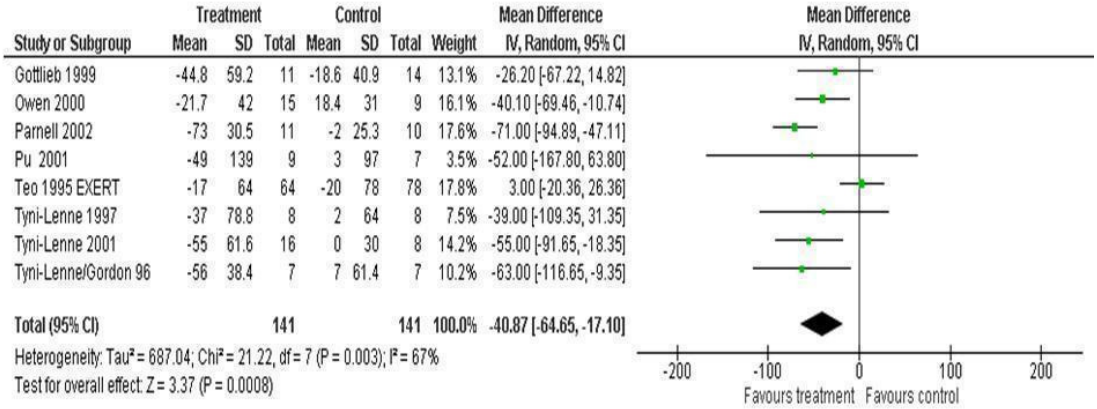


Figure 4. Forest plot of 6 min walk test (metres) from previous Cochrane review



OBJECTIVES

To update the previous sytematic review which determined the effectiveness of exercise based interventions compared with usual medical care by focusing on the mortality, hospital admission rate, morbidity and health-related quality of life in patients with heart failure.

METHODS

Criteria for considering studies for this review

Types of studies

Randomised controlled trials (RCTs) of either a parallel group or cross-over design where the follow up was six months or more after the start of the intervention.

Types of participants

All adults (≥18 years) with CHF due to ischaemic or non-ischaemic cardiomyopathy. Only those studies with criteria for diagnosis of systolic heart failure (based on clinical findings and objective indices such as assessment of ejection fraction) have been included. Studies including patients with normal systolic function (for example restrictive cardiomyopathy or hypertensive disease) were excluded. Where possible, we have distinguished between patients with primary heart failure (for example dilated cardiomyopathy (DCM)) and those with heart failure secondary to coronary heart disease (CHD). Studies that included patients with normal systolic function but poor diastolic function or who had previously been offered cardiac rehabilitation for either myocardial infarction or heart failure were excluded.

Types of interventions

Exercise based interventions either alone or as a component of comprehensive cardiac rehabilitation (defined as programmes including components such as health education and psychological

interventions in addition to exercise interventions). The comparison group was usual medical care (for example monitoring, drug therapy, and advice) as defined by the study.

Types of outcome measures

Primary outcomes

Mortality: all-cause death, deaths due to heart failure and sudden death
Hospital admission or re-hospitalisation, and whether due to CHF

Secondary outcomes

Health-related quality of life (HRQoL) assessed by a validated outcome measure (e.g. Short-form 36 (SF-36), Minnesota Living with Heart Failure (MLWHF) questionnaire)
Healthcare utilisation and costs

Search methods for identification of studies

A generic search strategy was carried out as this review forms one of a series of reviews that includes updates of three Cochrane systematic reviews addressing cardiac rehabilitation (Davies 2008; Jolliffe 2001; Rees 2004a; Rees 2004b; Taylor 2010).

Electronic searches

For the previous review (Rees 2004a) the Cochrane Controlled Trials Register (*The Cochrane Library* 2001, Issue 2), MEDLINE (2000 to March 2001), EMBASE (1998 to March 2001), and CINAHL (1984 to March 2001) were searched (see Appendix 2). This search was updated by searching the Cochrane Central Register of Controlled Trials (CENTRAL) (*The Cochrane Library* 2007, Issue 4), MEDLINE, EMBASE, CINAHL, and PsycINFO (2001 to January 2008).
Conference Proceedings were searched on Web of Science: ISI Proceedings (2001 to April 2008). Additional studies were located in the NHS Centre for Reviews and Dissemination (CRD) databases: Health Technology Assessment (HTA) and Database of Abstracts of Reviews of Effects (DARE).
Searches were limited to RCTs, systematic reviews, and meta-analyses; and a filter was applied to limit to humans. No language or other limitations were imposed. Consideration was given to variations in terms used and the spelling of terms in different countries so that studies were not missed by the search strategy. Search strategies were designed with reference to those of the previous systematic review (Rees 2004a) and in accordance with the Cochrane Handbook of Reviews of Interventions (Higgins 2008), see Appendix 1 for details.

Searching other resources

Reference lists of all eligible trials and identified systematic reviews were searched for additional studies.

Data collection and analysis

Study selection

The references identified by the search strategy were screened by title and abstract and clearly irrelevant studies discarded. For selection, abstracts had to clearly identify the study design, an appropriate population, and relevant components of the intervention as described above. The full-text reports of all potentially relevant trials were obtained and assessed independently by two review authors (EJD and RST) for eligibility based on the defined inclusion criteria. Any disagreements were resolved by discussion.

Data extraction

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 were extracted. Data extraction was undertaken independently by a single review author (EJD) and checked by a second review author (RST). Study authors were contacted 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.

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 2008). The risk of bias in eligible trials was assessed independently by a single review author (EJD) and verified by a second (RST).

Data analysis

Data were processed in accordance with the Cochrane Handbook for Systematic Reviews of Interventions (Higgins 2008). Dichotomous outcomes were expressed as relative risks (RR) and 95% confidence intervals (CI) calculated for each study. For continuous variables net changes were compared (that is exercise group minus control group to give differences) and a weighted mean difference (WMD) or standardised mean difference (SMD) and 95% CI calculated for each study. The Klocek trial had two intervention arms; for the purpose of meta-analysis it was split into two subtrials (sample size assumed to be 50% of the overall control

sample size for each substudy) (Klocek 2005 (Low); Klocek 2005 (High)).

Heterogeneity amongst included studies was explored qualitatively (by comparing the characteristics of included studies) and quantitatively (using the Chi^2 test of heterogeneity and the I^2 statistic). Where appropriate, the results from included studies were combined for each outcome to give an overall estimate of treatment effect. A fixed-effect model meta-analysis was used except where statistical heterogeneity was identified, where a random-effects model was used.

Univariate meta-regression was used to examine the association between the effect of exercise on all-cause mortality and health-related quality of life and specific study covariates: mean left ventricular ejection fraction (%); effect of intensity of the intervention ('dose' calculated as the number of weeks, multiplied by the number of sessions per week, multiplied by the duration of sessions in hours); type of exercise (aerobic training alone or aerobic plus resistance training); age; sex (per cent male); setting (hospital only, home only, both hospital and home); type of rehabilitation (exercise only versus comprehensive); duration of follow up; 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 CHF (Shekelle 2003). These subgroups were defined a priori. Sensitivity analysis was undertaken to examine the effect of omission of the HF-ACTION trial. Funnels plots and Egger tests (Egger 1997) were used to assess potential publication bias.

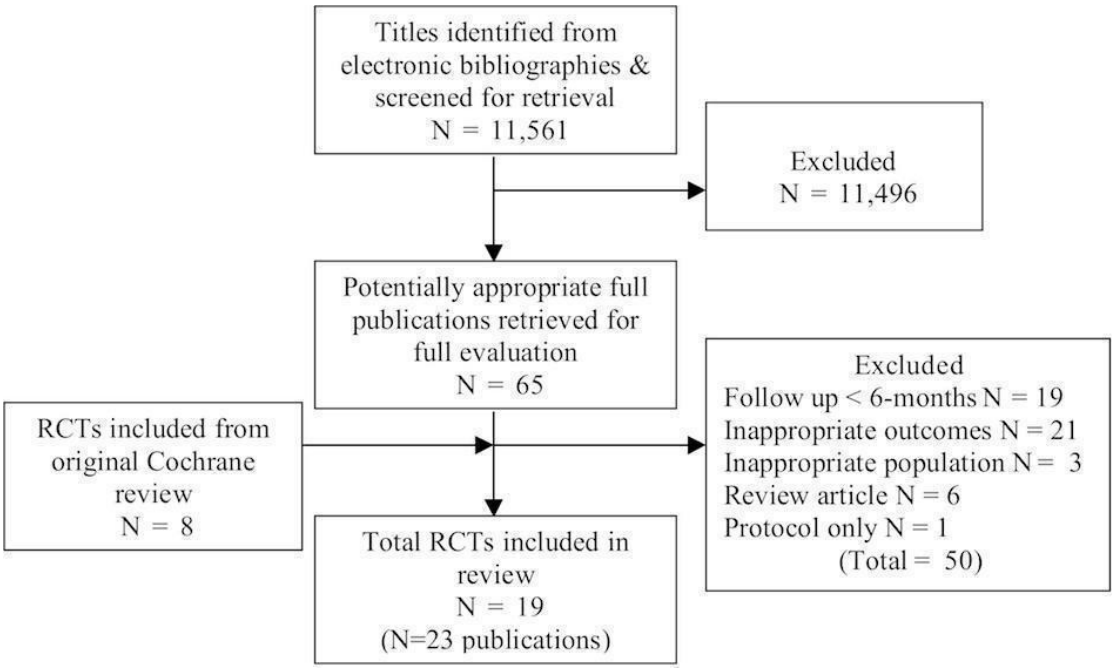
RESULTS

Description of studies

See: Characteristics of included studies; Characteristics of excluded studies.

The original Cochrane review (Rees 2004a) identified eight trials that reported outcomes that met the inclusion criteria of this update review (Belardinelli 1999; Gottlieb 1999; Hambrecht 1995; Hambrecht 1998; Hambrecht 2000; Keteyian 1996; McKelvie 2002; Willenheimer 2000). The remaining trials were excluded as their follow up was less than six months or they reported only exercise capacity outcomes. Our update of the umbrella cardiac rehabilitation electronic search yielded a total 11,561 titles. After reviewing titles and abstracts, an additional 65 full papers were retrieved for possible inclusion. A total of 50 papers were excluded: 19 had follow up less than six months, 21 reported inappropriate outcomes, three were in a non-heart failure population, six were reviews, and one was a study protocol. The total number of included RCTs was therefore 19 trials (23 papers). Although published after completion of the bibliographic searches, the HF-ACTION trial (HF ACTION 2009) was included as the protocol for this study was identified by our searches (Wheelan 2007). The study selection process is summarised in the QUORUM flow diagram shown in Figure 5.

Figure 5. Summary of study selection process



The included 19 trials randomised a total of 3647 heart failure patients with New York Heart Association (NYHA) class I to IV and left ventricular ejection fraction (LVEF) < 40%. The majority of trials were small, ranging from 20 to 200 participants, with only the one large trial, HF-ACTION, which contributed over 60% (2331 participants) of all included patients. The mean age of participants across the included studies ranged from 43 to 72 years. Studies recruited predominantly male patients (43% to 100%). Only four trials reported on ethnicity and 60% to 100% of the study population was white. Four trials reported follow up in excess of 12 months (Austin 2005; Belardinelli 1999; HF ACTION 2009; Mueller 2007). One trial had two treatment arms consisting of high and low intensity exercise. These were treated as two separate trials for the purpose of the analysis (Klocek 2005 (Low), Klocek 2005 (High)).

All studies evaluated an aerobic intervention and five also included resistance training. Exercise training was delivered in a centre based setting in 10 studies, in a home based setting in one study, and in a mix of both centre and home in the remaining studies. The dose of exercise training ranged widely across studies with session duration of 15 to 120 mins, two to seven sessions/week, intensity of 40% of maximal heart rate to 85% of maximal oxygen uptake (VO_2 max), over a period of 24 to 52 weeks.

Details of the studies included in the review are shown in the table 'Characteristics of included studies'. Reasons for exclusion are presented in the table 'Characteristics of excluded studies'.

Risk of bias in included studies

The overall quality of trials was poor. A number of studies failed to give sufficient detail to assess their potential risk of bias (Figure 6; Figure 7). Details of generation and concealment of random allocation sequence and if an intention-to-treat analysis was used were particularly poorly reported. Only the studies of Austin 2005, McKelvie 2002 and the HF ACTION 2009 trial provided an adequate description of the randomisation process. Nevertheless, none of the studies had objective evidence of imbalance in baseline characteristics. Austin 2005, Giannuzzi 2003, Keteyian 1996, and HF ACTION 2009 stated that they performed an intention-to-treat analysis. Although often not stated, many studies appeared to compare exercise and control group outcomes according to the initial random allocation. Given the nature of an exercise intervention, is not possible to blind patients and care-givers. Only the studies of McKelvie 2002, Koukouvou 2004 and Willenheimer 2000 reported blinding of outcome assessment. Only the studies of Giannuzzi 2003, HF ACTION 2009, Passino 2006 and McKelvie 2002 were multicentre studies. The majority were in single centres, leading to additional risk of bias.

Figure 6. Methodological quality graph: review authors' judgements about each methodological quality item presented as percentages across all included studies.

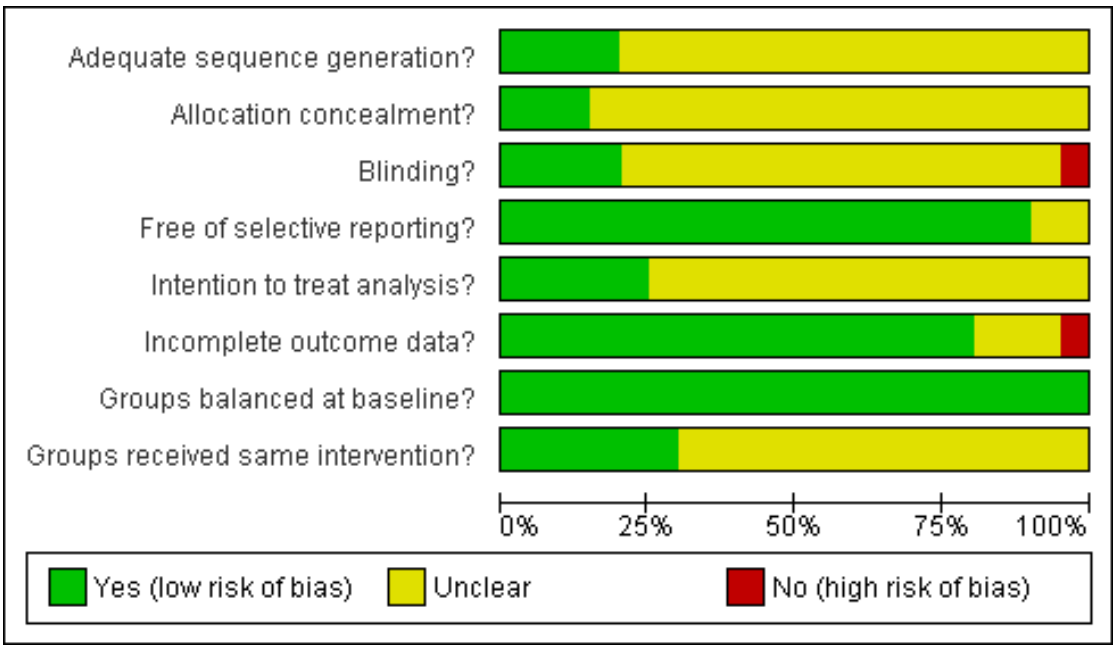
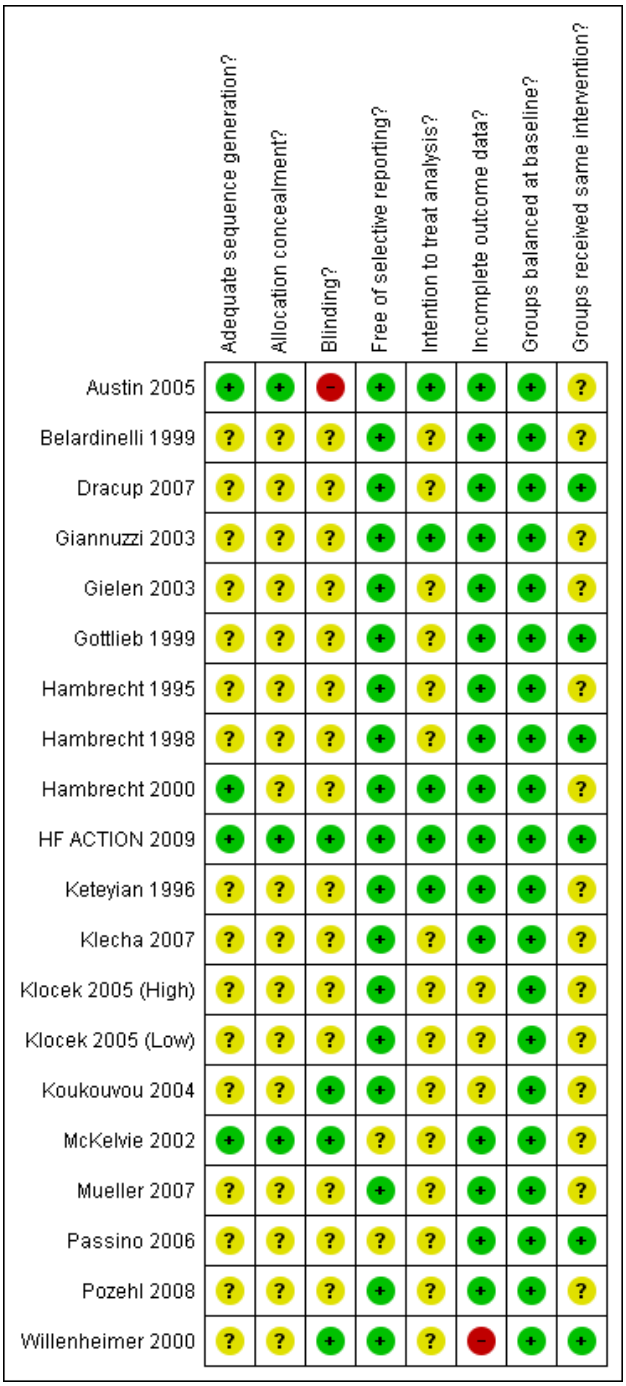


Figure 7. Methodological quality summary: review authors' judgements about each methodological quality item for each included study.



Effects of interventions

Mortality

Thirteen 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 between groups (fixed-effect relative risk (RR) 1.02, 95% CI 0.70 to 1.51; P = 0.90, I^2 = 0%; Chi^2 = 3.89, P = 0.90) (Analysis 1.1). The studies of Austin 2005, Belardinelli 1999, HF ACTION 2009 and Mueller 2007 reported mortality at 26, 60, 75, and 30 months respectively. There was evidence of a non-significant trend towards a reduction in mortality with longer follow up in the three smaller trials and this remained when the four trials were pooled (fixed-effect RR 0.88, 95% CI 0.73 to 1.07; P = 0.21, I^2 = 47%; Chi^2 = 5.69, P = 0.14) (Analysis 1.2). A significant reduction in longer-term mortality was seen with exclusion of the HF-ACTION trial (RR 0.62, 95% CI 0.39 to 0.98). It is important to note that there may be moderate heterogeneity in this observation. Studies did not consistently report deaths due to heart failure or sudden death.

Hospital admissions

Whilst there was a trend towards a reduction in the number of patients experiencing hospital admissions with exercise, none of these reductions achieved statistical significance (at P < 0.05): hospital admissions up to 12-months follow up (fixed-effect RR 0.79, 95% CI 0.58 to 1.07; P = 0.13, I^2 = 0%; Chi^2 = 5.07, P = 0.44) (Analysis 1.3) and hospital admissions > 12-months follow up (fixed-effect RR 0.96, 95% CI 0.90 to 1.02; P = 0.15, I^2 = 37%; Chi^2 = 4.74, P = 0.19) (Analysis 1.4). This longer-term result was consistent when the HF-ACTION trial was excluded (RR 0.75, 95% CI 0.52 to 1.08). Heart failure-specific admissions significantly reduced with exercise (fixed-effect RR 0.72, 95% CI 0.52 to 0.99; P = 0.04, I^2 = 16%; Chi^2 = 7.17, P = 0.31) (Analysis 1.5).

Health-related quality of life

Ten out of the 19 included trials reported a validated health-related quality of life (HRQoL) measure (see Table 1). The majority of studies reported disease-specific quality of life using the Minnesota Living with Heart Failure questionnaire (MLWHF) or the recently developed Kansas City Cardiomyopathy Questionnaire (KCCQ). Generic HRQoL was also assessed using the EuroQoL (EQ-5D), the 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. At follow up there was a consistently higher HRQoL in exercisers versus controls. Across the six studies that reported the total MLWHF score, there was a significant improvement with exercise (random-effects mean difference (MD) -10.3, 95% CI -15.9 to -4.8; P = 0.0003, I^2 = 71%; Chi^2 = 17.15, P < 0.004) (Analysis 1.6). Pooling across all studies, regardless of the HRQoL measure used, there was also evidence of a significant improvement with exercise (using a random-effects model due to significant heterogeneity, SMD -0.56, 95% CI -0.82 to -0.30; P < 0.0001, I^2 = 79%; Chi^2 = 43.25, P < 0.0001) (Analysis 1.7), a finding that remained on exclusion of HF-ACTION (SMD -0.63, 95% CI -0.89 to -0.37). Where studies reported more than one total HRQoL measure score, we randomly selected a single score for meta-analaysis 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 effectiveness

Two studies considered cost effectiveness (Belardinelli 1999; HF ACTION 2009) but only Belardinelli undertook a comprehensive cost-effectiveness analysis, which was reported in a separate publication (Georgiou 2001). The 14-month trial survival and healthcare costs were extrapolated to 15.5 years and the incremental cost per life year gained ratio for exercisers compared to control. The estimated increment cost for the training group, USD 3227/patient, was calculated by subtracting the averted hospitalisation cost, USD 1336/patient, from the cost of exercise training and wage lost due to exercise training, estimated at USD 4563/patient. For patients receiving exercise training, the estimated increment in life expectancy was 1.82 years/person in a time period of 15.5 years compared with patients in the control group. The cost-effectiveness ratio for long-term exercise in patients was thus determined as $1773/life-year saved (at a 3% discount rate, year 1999 costs).

Meta regression

Predictors of all-cause mortality and HRQoL intervention effects were examined using univariate meta-regression. Covariates defined a priori included mean LVEF (%); effect of intensity of the intervention ('dose' calculated as the number of weeks, multiplied by the number of sessions per week, multiplied by the duration of sessions in hours); type of exercise (aerobic training alone or aerobic plus resistance training); age; sex (% male); setting (hospital only, home only, both hospital and home); type of rehabilitation (exercise only versus comprehensive); duration of follow up; and publication date. No significant associations were seen on all-cause mortality and HRQoL at the P < 0.01 level (see Table 2). Sensitivity analysis was undertaken to examine the effect of omission of the HF-ACTION trial.

Small study bias

Although there was no evidence of funnel plot asymmetry for all-cause mortality (Egger test P = 0.874) (Figure 8), the funnel plot for HRQoL did show asymmetry (Egger test P = 0.002) (Figure 9).

Figure 8. Funnel plot of comparison: 1 All exercise interventions versus usual care, outcome: 1.1 All cause mortality <12 month follow up.

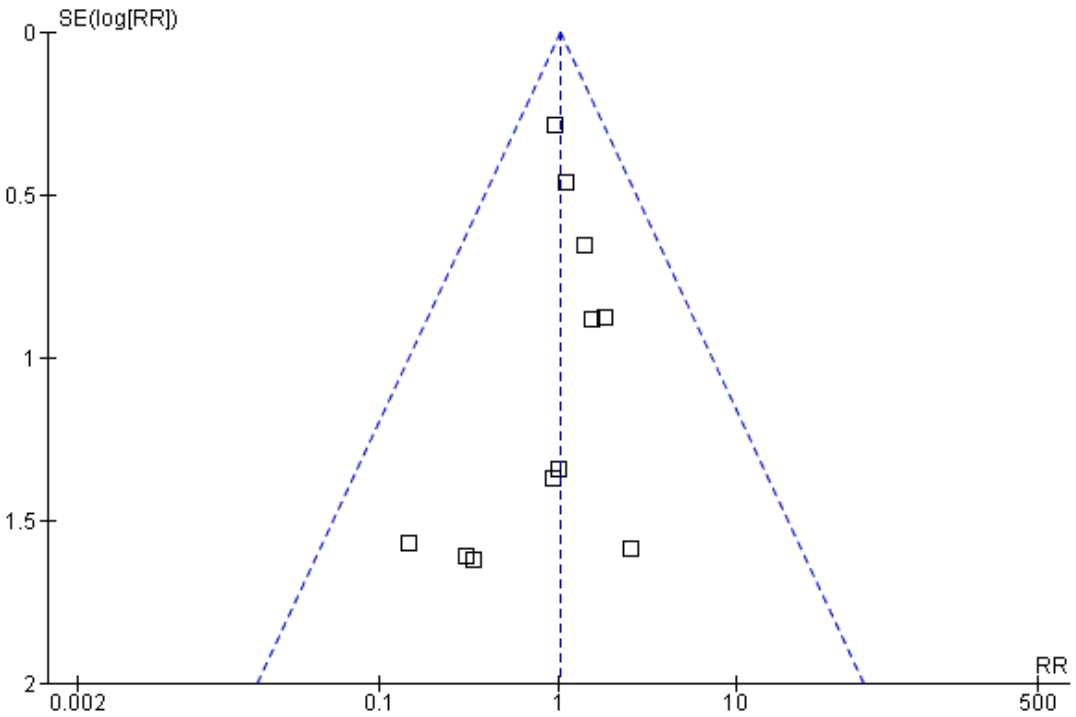
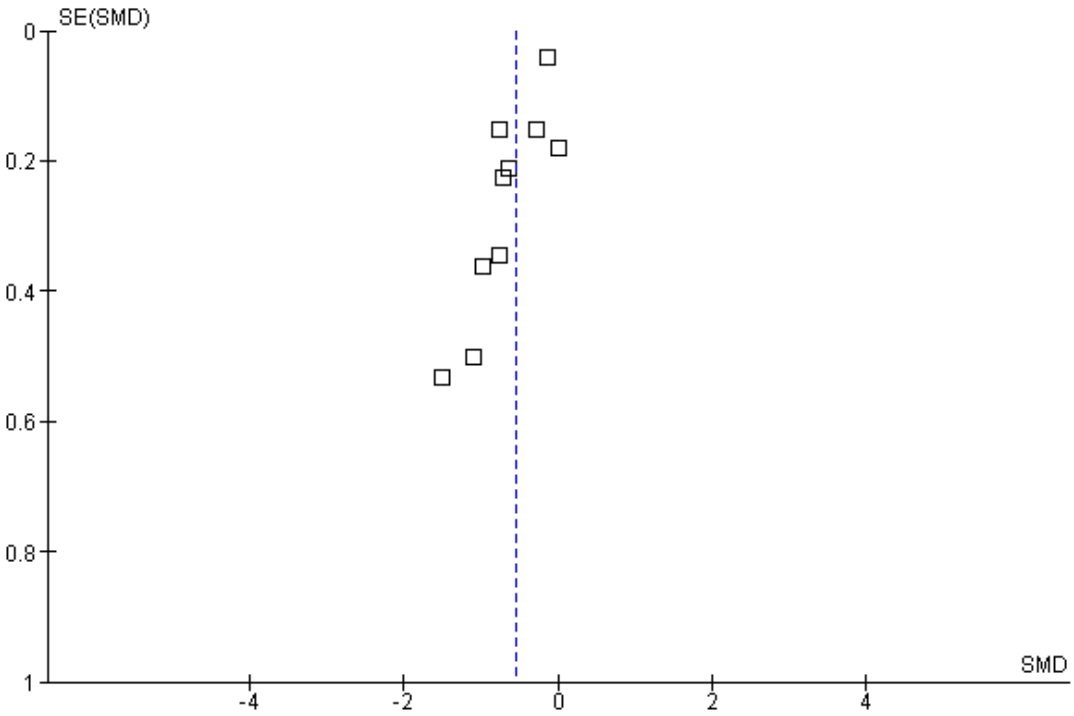


Figure 9. Funnel plot of comparison: 1 All exercise interventions versus usual care, outcome: 1.8 Health related quality of life - all scales.



DISCUSSION

The Cochrane systematic review of exercise based interventions as published in 2004 concluded that exercise training programmes improved exercise capacity and health-related quality of life in the short term (six months or less follow up) (Rees 2004a). However, of the 29 randomised controlled trials (RCTs) included in that review, only one trial reported on hospitalisations and mortality in the longer-term; the remainder were mainly small-scale trials which did not measure clinical events and were of short duration. Furthermore, a number of included trials did not use validated health-related quality of life (HRQoL) measures. Using additional RCT evidence, available since the original Cochrane review, the aim of this update was to reassess the effectiveness of exercise based interventions on mortality, hospitalisation admissions, morbidity, and HRQoL of patients with chronic systolic heart failure when compared with usual medical care. We did not seek to update the evidence on exercise capacity.

Our updated review shows that, when compared to usual care, exercise training programmes did not significantly impact on all-cause mortality. We found a significant reduction in hospitalisations due to systolic heart failure with exercise training programmes and observed consistent significantly higher levels of HRQoL following exercise training programmes compared to control. It is important to note that there was signficant heterogeneity in our observations on HRQoL. On the Minnesota Living with Heart failure (MLWHF) questionnaire, the exercise group was on average 10 points higher than controls. 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). There was no evidence of a difference in the effect of exercise training programmes according to patient characteristics (age, sex, %LVEF), nature of the exercise programme (total dose and inclusion of resistance training), or setting (hospital or home based). The cost-effectiveness ratio for exercise training in heart failure patients, extrapolated to 15.5 years, was USD 1773/per life year saved at 1999 costs.

Previous systematic reviews of exercise training programmes for heart failure, including the 2004 Cochrane review, identified in-

sufficient numbers of deaths and hospital admissions to reliably comment on these outcomes (Lloyd-Williams 2002; Rees 2004a; Smart 2004). Based on an individual patient data pooled analysis, the ExTraMATCH Collaborative Group (ExTraMatch 2004) concluded that exercise significantly reduced overall mortality (hazard ratio 0.65, 95% CI 0.46 to 0.92). However, 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. It has therefore been difficult to verify the data and the comprehensiveness of this meta-analysis; additionally several of the RCTs included in the Cochrane review were not included in the ExTraMATCH review. Re-analysis of the ExTraMatch trial data using meta-analytic methods has shown that the effect of exercise training was not statistically signficant when compared to control (relative risk 0.88, 95% CI 0.70 to 1.10) (Gotzsche 2005), which is consistant with our findings. More recent trials have been conducted in the context of optimal medical therapy. For example, at entry to the HF-ACTION trial 94% of patients were receiving beta-blockers and angiotension-receptor blockers or angiotensin-converting enzyme inhibitors (Wheelan 2007). Forty-five per cent had an implantable cardioverter defibrillator (ICD) 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. Based on the observed levels of mortality seen in four trials with long-term follow up, a total of some 12,000 patients would need to be randomised to exercise based cardiac rehabilitation or usual care to demonstrate a statistically significant benefit of exercise, at 5% alpha and 80% power (Austin 2005; Belardinelli 1999; HF ACTION 2009; Mueller 2007). 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 three-months home based exercise training and concluded that exercise training compared with usual care or activity did not improve the HRQoL of heart failure patients (Chien 2008). Eight of the trials included in our review combined an initial period of supervised hospital exercise training and a following home-based programme (Austin 2005; Gielen 2003; Hambrecht 1995; Hambrecht 1998; Hambrecht 2000; HF ACTION 2009; McKelvie 2002; Passino 2006). Only one included study assessed an entirely home based programme (Gottlieb 1999). We found no difference in the improvement in HRQoL with exercise training in those studies based solely in a hospital setting compared to those that included some level of home based exercise training programme.

The precise mechanism(s) through which exercise training benefits patients with heart failure remains unclear. One explanation, applicable to patients with ischaemic causes of heart failure, 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). Ventricular remodelling has been shown to be attenuated by exercise training (Haykowsky 2007). Regardless of cause, there are important neurohormonal and musculoskeletal abnormalities in heart failure. 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).

Although we believe this is the most comprehensive systematic review to date of RCT based evidence for the impact of exercise training programmes on patients with heart failure, our review has a number of limitations. Funnel plot asymmetry for HRQoL is indicative of small study bias and possible publication bias. However, when regression based adjustment was applied, it was found that improvement in HRQoL with exercise training remained (SMD -0.16, 95% CI -0.02 to -0.29) (Moreno 2009). 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 and potential to overestimate the effect of exercise training programmes. However, they do not appear to be sensitive to risk of bias criteria such as intention-to-treat analysis and outcome 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 the majority of 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. The majority of studies were in low to moderate risk males, included predominantly patients (43% to 100%) with NYHA class II to III and LVEF < 40%, with a mean age of participants across studies ranging from 43 to 72 years. The generalisability of our findings may, therefore, be limited. Although the majority of evidence in this review comes from the recently reported HF-ACTION study, the findings of previous trials appear consistent with this important trial. Given the time limits for this update, we did not contact authors for further details.

AUTHORS' CONCLUSIONS

Implications for practice

This review shows that exercise training programmes may provide some important improvements in HRQoL in patients with NYHA class II or III systolic heart failure and LVEF < 40%, and may also reduce heart failure-related hospitalisations. There is no evidence to support that exercise training programmes increase the risk of death. The effect of exercise training programmes on total mortality and HRQoL were independent of the degree of left ventricular dysfunction, type of cardiac rehabilitation, dose of

exercise intervention, length of follow up, trial quality, and trial publication date. Aerobic exercise training with or without a resistance exercise element is recommended in a supervised hospital or home based setting. Given the variation in exercise training programmes across studies, it was not possibe to provide a definitive recommendation on the minimum dose of exercise.

Implications for research

To improve generalisability, future trials should include patients with more severe heart failure, the elderly, people from different ethic backgrounds, and women; and report the outcomes by key patient subgroups (for example with atrial fibrillation or diabetes mellitus). Furthermore, there is a need to examine more home based exercise rehabilitation programmes and how such programmes can be most effectively integrated alongside current models of service delivery in terms of clinical effectiveness and cost, such as utilising specialist heart failure nurses. Few of the included studies reported the actual level of exercise training undertaken by the participants. Notably, in the HF-ACTION study only 30% of patients randomised to exercise training exercised at or above their prescribed level. Future studies need to consider interventions to enhance the long-term maintenance of exercise training.

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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 pts):** *aetiology:* ischaemic 77%, hypertension 15.5%, DCM 5.5%, other 2% *NYHA*: II: 51.5% ; III: 48.5% *LVEF:* 40-35% : 16.5% <35-30%: 45% <30%: 38.5% **Case mix:** 100% as above **Age:** 71.8 (SD 6.8) Control, 71.9 (SD 6.3) Exercise **Percentage male:** 43% **Percentage white:** Unclear I**nclusion/exclusion criteria:** *Inclusion:* >60 years, NYHA II or III, & 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 musculo-skeletal disorder, unstable IHD, advanced valvular disease), resident outside the catchment area or in a long-term care establishment
Interventions	**Exercise:** *Total duration:* 24 weeks *aerobic/resistance/mix:* aerobic endurance training and low resistance training/high repetitive muscular strength work *frequency*: two sessions/week (for 8 weeks) one session/week (16 weeks) plus 3 sessions/week at home *duration:* 2.5 hr class (8 weeks) & 1 hour class (next 16 weeks) *intensity:* Not reported *modality*: Not reported Exercise component was based on Eur Cardiac Society & Chartered Society of Physiotherapy
Outcomes	Health-related quality of life (Minnesota Living with Heart Failure questionnaire & EuroQol/ EQ-5D); health care utilisation (length of stay of hospital admissions arising from heart disease, prescribed heart failure medication); mortality
Comparison	Standard care group (including monitoring of clinical status, explanation of heart failure & its treatment self monitoring; dietary advice & contact details of clinical nurse specialist)
Country and Setting	UK Single centre
Follow Up	6 months and 5 years (after randomisation).
Notes	
Risk of bias	

Austin 2005 (*Continued*)

Bias	Authors' judgement	Support for judgement
Adequate sequence generation?	Low risk	*"A computer was used to generate a list of random numbers"*
Allocation concealment?	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? All outcomes	High risk	No, for HRQoL. Data on deaths, admissions from the hospital records department
Free of selective reporting?	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 patient 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?	Unclear risk	Not reported

Belardinelli 1999

Methods	Parallel group RCT
Participants	**N Randomised:** 99 (50 exercise; 49 control) **Diagnosis (% of pts):** *Aetiology:* ischaemic cardiomyopathy (85%) or idiopathic dilated cardiomyopathy (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:** Exercise 56 (SD 7) Control 53 (SD 9) **Percentage male:** 89% **Percentage white:** Not reported I**nclusion/exclusion criteria:** *Inclusion*: heart failure, LVEF <40%, and sinus rhythm, diagnosis of chronic heart failure based on clinical symptoms & signs and/or radiological evidence of pulmonary congestion *Exclusion:* unstable angina, recent acute myocardial infarction, decompensated congestive heart failure, hemodynamically significant valvular heart disease, significant chronic pulmonary illness, uncontrolled hypertension, renal insufficiency (serum creatinine >2.5 mg/dl), and orthopedic or neurological limitations)

Belardinelli 1999 (*Continued*)

Interventions	**Exercise:** *Total duration:* 14 month; eight weeks supervised then 12 months maintenance *aerobic/resistance/mix:* aerobic *frequency:* 2-3 sessions/wk*; duration:* 40mins/session; 60% max VO_2 *modality*: cycling **Other:** All sessions were held at the hospital gymnasium under the supervision of a cardiologist
Outcomes	Health-related quality of life (Minnesota Living With Heart Failure questionnaire); 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**
Adequate sequence generation?	Unclear risk	Not reported
Allocation concealment?	Unclear risk	Not reported
Blinding? All outcomes	Unclear risk	Not reported
Free of selective reporting?	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."*
Groups received same intervention?	Unclear risk	Not reported

Dracup 2007

Methods	Parallel group RCT
Participants	**N Randomised:** 173 (Exercise 86, Control 87) **Diagnosis (% of pts):** *aetiology:* ischaemic, idiopathic, valvular, DCM, other *NYHA*: 2-4 *LVEF:* 26.4 (SD6.8) **Case mix:** 100% as above **Age:** 54 (SD12.5) **Percentage male:** 71.7 **Percentage white:** 60.1 I**nclusion/exclusion criteria:** *Inclusion*: English-speaking, aged between 18 to 80 years, NYHA II to IV & LVSD with LVEF <40% as documented by echocardiogram or radionuclide ventriculography within <6 months, and sinus rhythm *Exclusion:* myocardial infarction or recurrent angina within <3 months, orthopedic impediments to exercise, severe obstructive pulmonary disease with a forced expiratory volume <1 L in one second as measured by spirometry, stenotic valvular disease as measured by echocardiogram, history of uncontrolled ventricular tachyarrhythmias (documented by electrophysiology study or 24-hour Holter monitor), or absence of an implantable cardioverter-defibrillator despite a history of sudden cardiac death
Interventions	**Exercise:** *Total duration: one* year *aerobic/resistance/mix:* Mix *frequency:* four sessions/week *duration:* 10 to 45 mins *intensity:* 40 to 60% max HR *modality*: walking **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."*
Outcomes	Health-related quality of life (Minnesota Living with Heart Failure questionnaire), mortality, morbidity
Comparison	Maintained usual level of daily activities. No exercise component
Country and Setting	USA. Single centre. Home based exercise program.
Follow Up	Six and 12 months (after randomisation).
Notes	

Risk of bias

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

Dracup 2007 (*Continued*)

Adequate sequence generation?	Unclear risk	Not reported
Allocation concealment?	Unclear risk	Not reported
Blinding? All outcomes	Unclear risk	Blinding reported for physical activity (accelerometer) outcopme but not reported for other outcomes
Free of selective reporting?	Low risk	All outcomes described in methods reported.
Intention to treat analysis?	Unclear risk	Although not reported as ITT analysis, groups did appear to be analysed according to original randomised allocation
Incomplete outcome data?	Low risk	*"Two patients (one from the experimental and one from the control group) were lost to follow-up within the first three months of enrollment. One was incarcerated and the second left the geographic area with no forwarding information. The remaining 173 patients compose the final study."*
Groups balanced at baseline?	Low risk	*"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."*
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."*

Giannuzzi 2003

Methods	Parallel group RCT
Participants	**N Randomised: 90,** 45 each group **Diagnosis (% of pts):** *Aetiology:* heart failure secondary to idiopathic dilated cardiomyopathy, ischemic heart disease, or valvular disease *NYHA*: 2-3 *LVEF:* <35% **Case mix:** 100% **Age:** Exercise 60 (SD 7), Control 61 (SD 7) **Percentage male:** Not stated **Percentage white:** Not stated I**nclusion/exclusion criteria:** *Inclusion*: (1) heart failure secondary to idiopathic dilated cardiomyopathy, ischemic heart disease, or valvular disease; (2) echocardiographic ejection fraction <35%; (3) clinical stability for at least 3 months under optimized therapy; (4) New York Heart Association 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:* six months *frequency:* three-five sessions/week *duration:* 30mins *intensity:* 60% peak VO_2 *modality*: Exercise cycle, daily brisk walk, callisthenic. Also, requested to take brisk daily walk of >30mins **Other:** not stated
Outcomes	Mortality and morbidity.
Comparison	Educational support but no formal exercise protocol.
Country and Setting	Italy Multicentre (15 Cardiac rehabilitation units)
Follow Up	six months (after randomisation)
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Adequate sequence generation?	Unclear risk	Not reported
Allocation concealment?	Unclear risk	Not reported
Blinding? All outcomes	Unclear risk	Not reported
Free of selective reporting?	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 two 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*

Giannuzzi 2003 (*Continued*)

		failure, or New York Heart Association functional class. Furthermore, there was no difference between the 2 groups in the medications received during the 6-month period of the study."
Groups received same intervention?	Unclear risk	Not clearly stated if co-treatments (i.e. cardiovascular medication) in two groups were the same

Gielen 2003

Methods	Parallel group RCT
Participants	**N Randomised:** 20 (Exercise 10, Control 10) **Diagnosis (% of pts):** *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:** Exercise: 55 (SD 6) Control 53 (SD 9), **Percentage male:** 100% **Percentage white:** Not reported I**nclusion/exclusion criteria:** *Inclusion:* <70 years with CHF (NYHA II to III) as result of dilated cardiomyopathy or IHD as assessed by cardiac catheterization. All had clinical, radiologic, and echocardiographic signs of CHF and a 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:* two weeks inpatient followed by six months outpatient. *aerobic/resistance/mix:* aerobic *frequency:* seven sessions/wk *duration:* 20 mins/session *intensity:* 70% symptom limited VO_2 max *modality*: cycle ergometers. **Other:** Expected to participate in one group training session (walking, callisthenics, and non-competitive ball games) of 60 min each week
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 weeks (after randomisation)

Gielen 2003 (*Continued*)

Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Adequate sequence generation?	Unclear risk	Not reported
Allocation concealment?	Unclear risk	Not reported
Blinding? All outcomes	Unclear risk	Not reported
Free of selective reporting?	Low risk	All outcomes described in methods are reported in results.
Intention to treat analysis?	Unclear risk	Although ITT analysis not reported, groups do appear to 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) 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 pts):** *aetiology:* ischaemic or primary *NYHA*: 2-3 *LVEF:* <40% **Case mix:** 100% as above **Age:** Control 64 (SD 10), Exercise 67 (SD 7) **Percentage male:** Control 11/14 (79%), Exercise 15/16 (94%) **Percentage white:** Not reported I**nclusion/exclusion criteria:** *Inclusion:* NYHA 2-3 for at least three months and were on stable meds for the past one month. All patients were on maximal medical therapy with ACEi, diuretic and digoxin. All patients had EF<40% by nuclear ventriculography. No patient had obstructive valvular disease, myocardial infarction within three months, or limitation of exercise secondary to angina or new arrhythmias

Gottlieb 1999 (*Continued*)

	Exclusion: Not reported.
Interventions	**Exercise:** *Total duration:* three months *aerobic/resistance/mix:* aerobic *frequency:* three session/week; *duration:* not reported *intensity:* Borg 12-13 *modality*: bike and treadmill **Other:** Care provided by specialist heart failure physician.
Outcomes	Health-related quality of life (Minnesota Living with Heart Failure & MOS Short-Form 36 questionnaires), mortality, morbidity
Comparison	Usual medical care **Other:** Care provided by specialist heart failure physician
Country and Setting	USA Single centre
Follow Up	six months (after randomisation)
Notes	MLWHF, MOS SF-36 results not reported for the control group.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Adequate sequence generation?	Unclear risk	Not reported
Allocation concealment?	Unclear risk	Not reported
Blinding? All outcomes	Unclear risk	Not reported
Free of selective reporting?	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.*
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 (12 exercise & 10 control) **Diagnosis (% of pts):** *aetiology:* DCM (86%) or 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:** Exercise 50 (SD 12); Control 52 (SD 8) **Percentage male:** 100% **Percentage white:** Not reported I**nclusion/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 25km of the training facility. Physical work capacity at baseline >25Watts 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:* six months *aerobic/resistance/mix:* aerobic *frequency:* four-six sessions/wk *duration:* 10-60 mins/session, one hour at home *intensity:* 70% VO_2max *modality*: cycling, walking, ball games and callisthenics **Other:** First three weeks supervised hospital based training; thereafter home-based.
Outcomes	Morbidity and mortality.
Comparison	After discharge medical therapy continued and patients supervised by private physician
Country and Setting	Germany Single centre
Follow Up	Six months (after randomisation)
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Adequate sequence generation?	Unclear risk	Not reported
Allocation concealment?	Unclear risk	Not reported

Hambrecht 1995 (*Continued*)

Blinding? All outcomes	Unclear risk	Not reported
Free of selective reporting?	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 three weeks of hospital stay, the control only three. 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 (10 exercise, 10 control) **Diagnosis (% of pts):** *aetiology:* IHD 35%, DCM 65% *NYHA*: class II - 65% & class III: 35% *LVEF:* <40%; Exercise; mean 24% (SD 13), Control 23% (SD 10%) **Case mix:** as above **Age:** Exercise 54 (SD 9), Control 56 (8) **Percentage male:** 100% **Percentage white:** not reported I**nclusion/exclusion criteria:** *Inclusion:* <70 years old, with CHF as a result of DCM or IHD. *Exclusion:* DM, hypertension, overt atherosclerotic peripheral vascular disease, hypercholesterolaemia, ventricular tachycardia, COPD and primary valvular disease
Interventions	**Exercise:** *Total duration:* six months *aerobic/resistance/mix:* Aerobic *frequency:* two-six sessions/day *duration:* 10-20 mins/session *intensity:* 70% VO_2 max *modality*: Bike ergogometer. **Other:** plus one group session/week.
Outcomes	Mortality
Comparison	**Description:** Stayed on previous medication, continued sedentary lifestyle, and supervised by their private physicians

Hambrecht 1998 (*Continued*)

Country and Setting	Germany Single centre
Follow Up	Six months (after randomisation)
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Adequate sequence generation?	Unclear risk	Not reported
Allocation concealment?	Unclear risk	Not reported
Blinding? All outcomes	Unclear risk	Not reported
Free of selective reporting?	Low risk	All outcomes described in methods reported in results.
Intention to treat analysis?	Unclear risk	It appears that groups are analysed according to original randomised allocation
Incomplete outcome data?	Low risk	Detailed description of losses to follow 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, LVEFEF or LVEDD."*
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 pts):** *Aetiology:* IHD 16%; DCM 84% *NYHA*: Class I & II: 74% Class III: 26% *LVEF:* 29% (SD 9) **Case mix:** 100% as above. **Age:** Exercise 54 (SD 9), Control 54 (SD 8) **Percentage male:** 100

	Percentage white: Not reported I**nclusion/exclusion criteria:** *Inclusion:* documented heart failure by signs, symptoms and angiographic evidence of reduced LV function (LVEF<40%) as a result of DCM or IHD; physical work capacity at baseline >25W, 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:* Six-months *aerobic/resistance/mix:* Aerobic *frequency:* six-seven sessions/wk *duration:* 10-20/session *intensity:* 70% of peak VO_2 *modality*: Cycle ergometer **Other:** Plus group sessions one hour twice weekly, walking, ball games and callisthenics. First two weeks in hospital, remainder home based
Outcomes	Mortality
Comparison	Continued individually tailored cardiac medications, supervised by their physicians
Country and Setting	Germany Single centre
Follow Up	Six months (after randomisation)
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Adequate sequence generation?	Low risk	*"Patients were randomly assigned to either a training group or an inactive group sing a list of random numbers."*
Allocation concealment?	Unclear risk	Not reported
Blinding? All outcomes	Unclear risk	Not reported
Free of selective reporting?	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,*

Hambrecht 2000 (*Continued*)

		LVEDD, 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 RCT
Participants	**N Randomised:** 2331 (exercise 1159; control 1172) **Diagnosis (% of pts):** *Aetiology:* IHD 51% *NYHA*: Class II: 63% Class III: 35% Class IV: 1% *LVEF: 25*% (SD not reported) **Case mix:** 100% as above. **Age:** Exercise 59 (SD not reported), Control 59 (SD not reported) **Percentage male:** 72% **Percentage white:** 62% I**nclusion/exclusion criteria:** *Inclusion:* LVEF <35%, NYHA class II-IV heart failure for the previous three months despite a six week period of treatment, optimal heart failure therapy at stable doses for six weeks before, enrollment or documented rationale for variation, including intolerance, contraindication, patient preference, and personal physicians judgment, sufficient stability, by investigator judgment, to begin an exercise program *Exclusion:* (selected) Age <18 yr, comorbid disease or behavioral or other limitations that interfere with performing exercise training or prevent the completion of one yr of exercise training, major cardiovascular event or cardiovascular procedure, including implantable cardioverter defibrillator (ICD) use and cardiac resynchronization, within the previous six wks
Interventions	**Exercise:** *Total duration:* period of study (three months supervised, remainder home based) *aerobic/resistance/mix:* Aerobic *frequency:* three-five sessions/wk *duration:* 15-35 mins/session *intensity:* 60-70% of heart rate reserve *modality*: Cycling or walking **Other:** First 36 sessions were supervised then advised to follow home based exercise programme
Outcomes	Mortality, hospitalisation, and health-related quality of life (Kansas City Cardiomyopathy Questionnaire - KCCQ)
Comparison	Usual care: all patients, regardless of group allocation, received self-mamagement educational materials consistent with guidelines of American College of Cardiology and American Heart Association
Country and Setting	USA Multicentre

HF ACTION 2009 (*Continued*)

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**
Adequate sequence generation?	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?	Low risk	"patients are randomized at the enrolling centers using an interactive voice response"
Blinding? All outcomes	Low risk	Event outcomes were blinded.
Free of selective reporting?	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 shows two groups are well balanced.
Groups received same intervention?	Low risk	"All patients, regardless of group allocation, received self-mamagement educational materials...consistent with guidelines of American College of Cardiology and American Heart Association"

Keteyian 1996

Methods	Parallel group RCT
Participants	**N Randomised:** 40 (exercise 21; control 19) **Diagnosis (% of pts):** *aetiology:* DCM 40% , IHD 60% *NYHA*: Class II 67.5% Class III 32.5% *LVEF:* 21% (SD 7) **Case mix:** 100% as above **Age:** 56 (SD 11) **Percentage male:** 100% **Percentage white:** 62.5% (remainder black) I**nclusion/exclusion criteria:** *Inclusion:* NYHA class II or III, a resting EF ?35% measured by echocardiography or gated equilibrium radionuclide angiography, and no change in medical therapy ?30 days before

Keteyian 1996 (*Continued*)

	randomisation *Exclusion:* atrial fibrillation, acute myocardial infarction ?3 months, angina pectoris at rest or induced by exercise, current enrolment in another clinical trial, and current participation in a regular exercise program (at least twice weekly).'
Interventions	**Exercise:** *Total duration:* 24 weeks *aerobic/resistance/mix:* aerobic *frequency:* three sessions/wk (RPE 12-14) *duration:* 33mins*; intensity:* 60-80% peak HR *modality*: treadmills, stationary cycles, rowing machines, and arm ergometers.
Outcomes	Morality and hospital admissions
Comparison	Not reported
Country and Setting	North America Single centre
Follow Up	Six 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**
Adequate sequence generation?	Unclear risk	*"patients were randomly assigned to the exercise group or the control group. "*
Allocation concealment?	Unclear risk	"*Each patient's assignment was sealed in an envelope until completion of the second exercise test."*
Blinding? All outcomes	Unclear risk	Not reported
Free of selective reporting?	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-*

Keteyian 1996 (*Continued*)

		up testing, one developed atrial fibrillation between week 12 and week 24, one was hospitalized at week 22 for an acute myocardial infarction, and one died suddenly."
Groups balanced at baseline?	Low risk	"*Among patients who completed the study, no differences in demographic characteristics were seen between the two study groups after randomization.* "
Groups received same intervention?	Unclear risk	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 pts):** *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:** Exercise 59.6 (SD 10.2), Control 61.2 (SD 9.5) **Percentage male:** exercise 80%, Control 72% **Percentage white:** Not reported I**nclusion/exclusion criteria:** *Inclusion:* Ischaemic heart failure in NYHA groups II-III of > six months, clinically stable > six weeks & LVEF <35% *Exclusion:* Uncontrolled arterial hypertension, history of major ventricular arrhythmias, ACS, PCI 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, diabetes mellitus, COPD and anaemia
Interventions	**Exercise:** *Total duration :* six months *aerobic/resistance/mix:* aerobic *frequency:* three sessions/week *duration: 25* mins/session *intensity:* 80% predicted HR at VO_2 max *modality*: Cycling.
Outcomes	Mortality
Comparison	Standard medical care only.
Country and Setting	Poland Single centre
Follow Up	26 weeks (after randomisation).

Klecha 2007 (*Continued*)

Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Adequate sequence generation?	Unclear risk	Not reported
Allocation concealment?	Unclear risk	Not reported
Blinding? All outcomes	Unclear risk	Not reported
Free of selective reporting?	Low risk	All outcomes described in methods reported in results.
Intention to treat analysis?	Unclear risk	Not implicit but numbers used suggest that groups analysed according to randomised allocation
Incomplete outcome data?	Low risk	No patients 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 (High)

Methods	Parallel randomised controlled trial
Participants	**N Randomised:** 42 (14 Exercise group B, 14 control) **Diagnosis (% of pts):** *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:** Exercise group B: 57 (SD 8), Control 55 (SD 9) **Percentage male:** 100% **Percentage white:** Not reported I**nclusion/exclusion criteria:** *Inclusion: Stable chromic heart failure, LVEF < 40% on echocardiography ? one month before inclusion, age <65 years."* *Exclusion: Moderate or severe pulmonary disease, orthostatic blood pressure fall (>20mmHg), or with myocardial infarction, unstable angina, heart surgery or coronary angioplasty within 3 months prior to inclusion as well as inability to perform bicycle training.*

Klocek 2005 (High) (*Continued*)

Interventions	**Exercise:** *Total duration:* six months *aerobic/resistance/mix:* aerobic *frequency:* three sessions/week *duration:* Group B - 25 mins/session (exercise workload gradually increased after each five minute training period to a total of 25 minutes*); intensity:* Group B: up to 75% max HR*; modality*: Cycle ergometer.
Outcomes	HRQoL (Psychological general Wellbeing index, PGWB).
Comparison	Controls were asked not to change their degree of physical activity during the study
Country and Setting	Poland Single centre
Follow Up	26 weeks (after randomisation)
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Adequate sequence generation?	Unclear risk	Not reported
Allocation concealment?	Unclear risk	Not reported
Blinding? 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".*
Free of selective reporting?	Low risk	All outcomes described in methods are reported in results.
Intention to treat analysis?	Unclear 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 total index was similar in groups A and B. Controls had lower total index than patients in group B".*

Klocek 2005 (High) (*Continued*)

Groups received same intervention?	Unclear risk	Details of co-interventions not reported although degree of follow up was stated to equivalent

Klocek 2005 (Low)

Methods	Parallel group RCT
Participants	**N Randomised:** 42 (14 Exercise group A 14 control) **Diagnosis (% of pts):** *aetiology:* Ischaemic 100% *NYHA*: Class II/III Exercise group A 55%; Control 100% *LVEF:* Exercise Group A: mean 33.6% (SD 3.6); Control 33.2% (SD 3.8) **Case mix:** 100% as above **Age:** Exercise group A 54 (SD 7), Control 55 (SD 9) **Percentage male:** 100% **Percentage white:** Not reported I**nclusion/exclusion criteria:** *Inclusion: Stable chromic heart failure, LVEF < 40% on echocardiography ? one month before inclusion, age <65 years."* *Exclusion: Moderate or severe pulmonary disease, orthostatic blood pressure fall (>20mmHg), or with myocardial infarction, 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:* six months *aerobic/resistance/mix:* aerobic *frequency:* three sessions/week *duration:* Group A - 20 minutes/session (four minute constant workload with one minute rest repeated five times). *intensity: Group A* - 60% max HR; *; modality*: Cycle ergometer.
Outcomes	HRQoL (Psychological general Wellbeing index PGWB).
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 weeks (after randomisation)
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Adequate sequence generation?	Unclear risk	Not reported

Klocek 2005 (Low) (*Continued*)

Allocation concealment?	Unclear risk	Not reported
Blinding? 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".*
Free of selective reporting?	Low risk	All outcomes described in methods are reported in results.
Intention to treat analysis?	Unclear 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 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 be equivalent

Koukouvou 2004

Methods	Parallel randomised controlled trial
Participants	**N Randomised: 26** (16 Exercise group, 10 control) **Diagnosis (% of pts):** *aetiology:* DCM 7%/Ischaemic 100% *NYHA*: Class II: 58%; Class III: 42% *LVEF: < 40%* **Case mix:** 100% as above **Age:** Exercise group: 52 (SD 9), Control 53 (SD 11) **Percentage male:** 100% **Percentage white:** Not reported I**nclusion/exclusion criteria:** ***Inclusion:*** Aetiology of CHF was either ischaemic heart disease or dilated cardiomyopathy. Diagnosis of CHF was mainly based on clinical signs (NYHA II and III), radiological findings, and echocardiographically determined ejection fraction < 40% and shortening fraction < 30% ***Exclusion:*** recent myocardial infarction or unstable angina, aortic stenosis, diabetes mellitus, uncontrolled hypertension, musculoskeletal limitations or other contraindications for participating in an exercise training program, documented exercise-induced severe ischaemia and/or serious arrhythmias
Interventions	**Exercise:** *Total duration:* six months *aerobic/resistance/mix: mix* *frequency:* three-four sessions/week *duration: 60* mins/session*; intensity*: 50-75% peak VO_2*; modality*: Cycle ergometer, walking or jogging, stair climber and step-aerobics

Koukouvou 2004 (*Continued*)

	Plus "light" resistance exercise (not defined).	
Outcomes	HRQoL (Minnesota Living with Heart Failure and Spritzer Quality of Life Index)	
Comparison	No stated	
Country and Setting	Greece Single centre	
Follow Up	Six months (after randomisation)	
Notes		
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Adequate sequence generation?	Unclear risk	Not reported
Allocation concealment?	Unclear risk	Not reported
Blinding? 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."*
Free of selective reporting?	Low risk	All outcomes outlined in methods are reported.
Intention to treat analysis?	Unclear risk	Not stated explictly but appear to analysed according to initial group allocation
Incomplete outcome data?	Unclear risk	Losses to follow up, drop-outs not reported.
Groups balanced at baseline?	Low risk	*"The two groups of patients participating in the study were similar as regards their clinical data".*
Groups received same intervention?	Unclear risk	Not reported

McKelvie 2002

Methods	Parallel grout RCT
Participants	**N Randomised:** 181 (Exercise: 90 & Control: 91) **Diagnosis (% of pts):** *aetiology:* Ischaemic (76%), hypertensive (7%), valvular (5%), other (12%) *NYHA*: one-three *LVEF:* <40%

	Case mix: 100% as above **Age:** Control: 66.1 (SD 9.4), Exercise: 64.8±1.1 (SD 10.5) **Percentage male:** Control 80, Exercise 82 **Percentage white:** Unclear **Inclusion/exclusion criteria:** *Inclusion*: documented clinical signs and symptoms of heart failure; left ventricular ejection fraction <40%; New York Heart Association Functional class I to III; and 6-minute walk test distance < 500 metres *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 one second and/or vital capacity <60% of predicted); poorly controlled cardiac arrhythmias; and any noncardiac condition affecting regular exercise training or decreasing survival
Interventions	**Exercise:** *Total duration:* nine months (three supervised, six home based) *aerobic/resistance/mix:* Mix *frequency:* two sessions/week *duration:* Aerobic; 30 mins/session *intensity:* Aerobic; 60-70% max heart rate. Resistance; 40% of 1-repetition maximum, with 10 repetitions for the arm exercises and 15 repetitions for the leg exercises, with an increase over five weeks to an intensity of 60% of 1-repetition maximum and a total of three 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 **Other:** After three months of supervised training, patients in the exercise group were provided an exercise cycle and set of free weights with instructions to continue training at home three times per week for the remainder of the study
Outcomes	Health-related quality of life (Minnesota Living with Heart Failure Questionnaire), mortality, Composite of mortality & hospital admission for heart failure
Comparison	Usual medical care. Control patients 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**

McKelvie 2002 (*Continued*)

Adequate sequence generation?	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?	Low risk	*"Eligible patients were registered in a log and treatment group determined by opening the next sequential study allocation envelope."*
Blinding? 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."*
Free of selective reporting?	Unclear risk	All outcomes described in methods are reported in results.
Intention to treat analysis?	Unclear 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."*
Groups received same intervention?	Unclear risk	*"All patients were reviewed monthly throughout the study".*

Mueller 2007

Methods	Parallel group RCT
Participants	**N Randomised:** 50 (25 exercise, 25 control) **Diagnosis (% of pts):** *aetiology:* ischaemic and DCM (%s nor reported) *NYHA*: Not reported *LVEF:* <40% (%s not reported) **Case mix:** 100% as above **Age:** 55 (SD 10) **Percentage male:** 100%

	Percentage white: Not reported I**nclusion/exclusion criteria:** *Inclusion:* Chronic heart failure was documented by clinical, angiographic or echocardiographic criteria, and a resting ejection fraction <40% *Exclusion:* Not reported.
Interventions	**Exercise:** *Total duration:* one month *aerobic/resistance/mix:* aerobic *frequency:* five sessions/wk*; duration:* 30 min/session cycling, 90 min walking each day; *intensity:* Borg 12-14 (60-80% max HR); *modality*: cycling and walking. **Other:** Resided at the rehabilitation centre for one month.
Outcomes	Morbidity and mortality
Comparison	Usual medical care
Country and Setting	Switzerland Single centre
Follow Up	6.2 years (after randomisation).
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Adequate sequence generation?	Unclear risk	Not reported
Allocation concealment?	Unclear risk	Not reported
Blinding? All outcomes	Unclear risk	Not reported
Free of selective reporting?	Low risk	Outcomes described in the methods are reported in the results
Intention to treat analysis?	Unclear 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."*

Passino 2006

Methods	Parallel group RCT
Participants	**N Randomised:** 95 (Training: 47; Control: 48) **Diagnosis (% of pts):** * *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:** Exercise 60 (SD 13), Control 61 (SD 13) **Percentage male:** 87% **Percentage white:** not reported I**nclusion/exclusion criteria:** *Inclusion:* impaired left ventricular systolic function (EF<45%) and exercise capacity (peak VO_2<25 ml/min/kg). *Exclusion* NYHA class IV, myocardial infarction or unstable angina <6 months before the examination, exercise-limiting diseases, and severe pulmonary or renal disease * baseline data only available in 85 patients.
Interventions	**Exercise:** *Total duration:* nine months *aerobic/resistance/mix:* aerobic*; frequency:* >3 sessions/week *duration:* 30 mins/session *intensity:* 65% max VO_2 *modality*: Cycle **Other:** Not reported.
Outcomes	Health-related quality of life (Minnesota Living with Heart Failure Questionnaire) Morbidity
Comparison	Not reported
Country and Setting	Italy Multicentre
Follow Up	Nine months (after randomisation).
Notes	

Passino 2006 (*Continued*)

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Adequate sequence generation?	Unclear risk	Not reported
Allocation concealment?	Unclear risk	Not reported
Blinding? All outcomes	Unclear risk	Exercise test assessor blinded.
Free of selective reporting?	Unclear risk	Not reported
Intention to treat analysis?	Unclear 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 six) **Diagnosis (% of pts):** *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:** Exercise 66.3 (SD 9.6), Control 66 (SD 12.6) **Percentage male**: 90% **Percentage white:** 100% I**nclusion/exclusion criteria:** *Inclusion:* able to speak and read English; stable NYHA class II-IV no change in medical therapy ?30 days; resting LVEF <40% measured by echocardiography or gated equilibrium radionuclide angiography; medical diagnosis of heart failure either ischemic or non-ischaemic; and standard pharmacologic therapy for heart failure (diuretics, ACE inhibitors, and beta-blockers)

	Exclusion: participation in a formal exercise program <30 days prior to this study; clinical evidence decompensated heart failure; and any of the following medical conditions: atrial fibrillation, acute myocardial infarction <3 months, unstable angina pectoris, end-stage renal disease, or orthopedic impediments to exercise
Interventions	**Exercise:** *Total duration :* 24 weeks *aerobic/resistance/mix:* mix *frequency:* three sessions/week*; duration:* 30 mins aerobic, 20 mins 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, and/or pelvic tilts **Other:** Strategies from social learning theory (goal-setting, feedback and problem-solving guidance) utilised to facilitate, improve adherence to the training program
Outcomes	Mortality
Comparison	Usual medical care
Country and Setting	USA Single centre
Follow Up	Six months (after randomisation)
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Adequate sequence generation?	Unclear risk	Not reported
Allocation concealment?	Unclear risk	Not reported
Blinding? All outcomes	Unclear risk	Not reported
Free of selective reporting?	Low risk	Outcomes described in methods are reported in results.
Intention to treat analysis?	Unclear 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.*

Pozehl 2008 (*Continued*)

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

Willenheimer 2000

Methods	Parallel group RCT
Participants	**N Randomised:** 54, (27 exercise & 27 control) **Diagnosis (% of pts):*** *aetiology:* 75% ischaemic, 25% non-ischaemic *NYHA*: 2.2 (SD 0.7) & 2.5 (0.7) *LVEF:* 55% (SD 11) & 36% (SD 11) **Case mix:** 100% as above **Age:** 64 (SD 5) Training and 64 (SD 9) Control **Percentage male:** 73% Training and 70% Control **Percentage white:** Unknown I**nclusion/exclusion criteria:** *Inclusion*: 1) Eight points on Boston heart failure criteria; 2) left ventricular ejection fraction 0.45 at the most recent radionuclide or echocardiographic examination (not older than one year at inclusion); and 3) 75 years of age *Exclusion*: 1) change of clinical status and / or medication within four weeks prior to inclusion; 2) myocardial infarction, heart surgery, or coronary angioplasty within three 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 beats / min) at the most recent maximal exercise test (including the baseline test); 5) pulmonary disease judged to be the main exercise-limiting factor and/or peak expiratory flow rate <50% of the age- and sex-adjusted reference value; 6) New York Heart Association class IV; and 7) clinically significant aortic stenosis.
Interventions	**Exercise:** *Total duration:* four months *aerobic/resistance/mix:* aerobic/interval *frequency:* two-three sessions per week *duration:* 15 mins/session increasing to 45 mins/session *intensity:* 80% peak VO_2, or 15 on Borg score *modality*: cycle ergometry.
Outcomes	HRQoL (Patient's Global Assessment of Quality of Life, PGACQoL), mortality
Comparison	Control patients were asked not to change their degree of physical activity during the active study period. Neither training patients nor controls were instructed regarding physical activity during the six-month extended follow up
Country and Setting	Sweden Single centre

Willenheimer 2000 (*Continued*)

Follow Up	10 months (after randomisation)	
Notes		
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Adequate sequence generation?	Unclear risk	Not reported
Allocation concealment?	Unclear risk	Not reported
Blinding? All outcomes	Low risk	Outcome assessors blinded. Patients, clinical care-givers not blinded
Free of selective reporting?	Low risk	All outcomes described in methods reported in results.
Intention to treat analysis?	Unclear 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%) patients randomised at 10-months follow up. No imputation or sensitivity analysis undertaken to assess effect of loss to follow up. Authors state that patients available at 10-month 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".*

AF: atrial fibrillation
CHF: chronic heart failure
CHD: coronary heart disease
DCM : dilated cardiomyopathy
HR: heart rate
HRQoL: health related quality of life
ITT: intention-to-treat analysis
LVEF: left ventricular ejection fraction
NYHA: New York Heart Association classification
RCT : randomised controlled trial

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

Study	Reason for exclusion
Adamopoulos 2001	Relevant outcomes not reported
Barrow 2008	<6 months follow up
Belardinelli 2005	<6 months follow up
Berg-Emons 2004	<6 months follow up
Briffa 2005	Not heart failure
Chang 2004	Relevant outcomes not reported
Coats 1992	<6 months follow up
Collins 2004	<6 months follow up
Corvera-Tindel 2004	<6 months follow up
Deng 2003	Relevant outcomes not reported
Dingli 2002	Relevant outcomes not reported
Erbs 2003	Relevant outcomes not reported
ExTraMATCH 2004	Meta-analysis
Franco 2006	<6 months follow up
Gary 2004	Relevant outcomes not reported
Haykowsky 2007	Meta-analysis
Inglis 2006	Exercise advice only
Jolly 2007	Protocol only
Jónsdóttir 2004	<6 months follow up
Kilavouri 1999	Relevant outcomes not reported
Kobayashi 2003	Relevant outcomes not reported
Lloyd-Williams 2002	Meta-analysis

(*Continued*)

Meyer 2005	Relevant outcomes not reported
Molloy 2006	Relevant outcomes not reported
Myers 2001	Relevant outcomes not reported
Myers 2002	Relevant outcomes not reported
Myers 2007	Relevant outcomes not reported
Niebauer 2005	Relevant outcomes not reported
Niebauer 2005 (2)	Relevant outcomes not reported
Oka 2000	Relevant outcomes not reported
Owen 2000	<6 months follow up
Parnell 2002	<6 months follow up
Ponikowski 2007	<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
Stewart 1998	Exercise advice only
Taylor-Piliae 2004	Meta-analysis
Tyni-Lenne 2001	<6 months follow up
van Tol 2006	Meta-analysis
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

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 month follow up	13	962	Risk Ratio (M-H, Fixed, 95% CI)	1.02 [0.70, 1.51]
2 All cause mortality more than 12 months follow up	4	2658	Odds Ratio (M-H, Fixed, 95% CI)	0.88 [0.73, 1.07]
3 Hospital admission up to 12 month follow up	8	659	Risk Ratio (M-H, Fixed, 95% CI)	0.79 [0.58, 1.07]
4 Hospital admission more than 12 months follow up	4	2658	Risk Ratio (M-H, Fixed, 95% CI)	0.96 [0.90, 1.02]
5 Hospital admission heart failure only	7	569	Risk Ratio (M-H, Fixed, 95% CI)	0.72 [0.52, 0.99]
6 Health related quality of life - MLWHF	6	700	Mean Difference (IV, Random, 95% CI)	-10.33 [-15.89, -4.77]
7 Health related quality of life - all scales	10	3109	Std. Mean Difference (IV, Random, 95% CI)	-0.56 [-0.82, -0.30]

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

Review: Exercise based rehabilitation for heart failure

Comparison: 1 All exercise interventions versus usual care

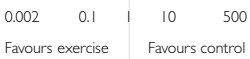
Outcome: 1 All cause mortality up to12 month follow up

Study or subgroup	Treatment n/N	Control n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Austin 2005	5/85	4/94		8.8 %	1.38 [0.38, 4.98]
Dracup 2007	9/87	8/86		18.6 %	1.11 [0.45, 2.75]
Giannuzzi 2003	0/45	1/45		3.5 %	0.33 [0.01, 7.97]
Gielen 2003	0/10	0/10			Not estimable
Gottlieb 1999	1/17	1/16		2.4 %	0.94 [0.06, 13.82]
Hambrecht 1995	1/12	0/10		1.3 %	2.54 [0.11, 56.25]
Hambrecht 1998	1/10	1/10		2.3 %	1.00 [0.07, 13.87]
Hambrecht 2000	3/36	2/37		4.6 %	1.54 [0.27, 8.69]
Keteyian 1996	0/21	1/19		3.6 %	0.30 [0.01, 7.02]
Klecha 2007	0/25	0/25			Not estimable
McKelvie 2002	19/90	20/91		46.0 %	0.96 [0.55, 1.68]
Pozehl 2008	0/15	1/6		4.8 %	0.15 [0.01, 3.16]
Willenheimer 2000	3/27	2/33		4.2 %	1.83 [0.33, 10.19]
Total (95% CI)	**480**	**482**		**100.0 %**	**1.02 [0.70, 1.51]**

Total events: 42 (Treatment), 41 (Control)

Heterogeneity: Chi^2 = 3.89, df = 10 (P = 0.95); I^2 =0.0%

Test for overall effect: Z = 0.12 (P = 0.90)



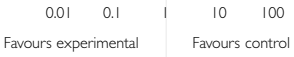
Analysis 1.2. Comparison 1 All exercise interventions versus usual care, Outcome 2 All cause mortality more than 12 months follow up.

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	Experimental n/N	Control n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
Austin 2005	31/85	38/94		10.8 %	0.85 [0.46, 1.55]
Belardinelli 1999	9/50	20/49		7.8 %	0.32 [0.13, 0.80]
HF ACTION 2009	189/1159	198/1171		77.8 %	0.96 [0.77, 1.19]
Mueller 2007	9/25	12/25		3.6 %	0.61 [0.20, 1.89]
Total (95% CI)	**1319**	**1339**		**100.0 %**	**0.88 [0.73, 1.07]**
Total events: 238 (Experimental), 268 (Control)					
Heterogeneity: Chi^2 = 5.69, df = 3 (P = 0.13); I^2 =47%					
Test for overall effect: Z = 1.24 (P = 0.21)					



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

Review: Exercise based rehabilitation for heart failure

Comparison: 1 All exercise interventions versus usual care

Outcome: 3 Hospital admission up to 12 month follow up

Study or subgroup	Experimental n/N	Control n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Austin 2005	9/85	19/94		28.9 %	0.52 [0.25, 1.09]
Dracup 2007	35/87	37/86		59.5 %	0.94 [0.66, 1.33]
Giannuzzi 2003	2/45	1/45		1.6 %	2.00 [0.19, 21.28]
Gielen 2003	1/10	0/10		0.8 %	3.00 [0.14, 65.90]
Hambrecht 1995	0/12	1/10		2.6 %	0.28 [0.01, 6.25]
Keteyian 1996	0/21	1/19		2.5 %	0.30 [0.01, 7.02]
Klecha 2007	0/25	0/25			Not estimable
Passino 2006	0/44	2/41		4.1 %	0.19 [0.01, 3.78]
Total (95% CI)	**329**	**330**		**100.0 %**	**0.79 [0.58, 1.07]**

Total events: 47 (Experimental), 61 (Control)

Heterogeneity: Chi^2 = 5.07, df = 6 (P = 0.54); I^2 =0.0%

Test for overall effect: Z = 1.51 (P = 0.13)

Analysis 1.4. Comparison 1 All exercise interventions versus usual care, Outcome 4 Hospital admission more than 12 months follow up.

Review: Exercise based rehabilitation for heart failure

Comparison: 1 All exercise interventions versus usual care

Outcome: 4 Hospital admission more than 12 months follow up

Study or subgroup	Treatment n/N	Control n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Austin 2005	28/85	33/94		3.9 %	0.94 [0.62, 1.41]
Belardinelli 1999	5/50	14/49		1.8 %	0.35 [0.14, 0.90]
HF ACTION 2009	729/1159	760/1171		94.0 %	0.97 [0.91, 1.03]
Mueller 2007	2/25	3/25		0.4 %	0.67 [0.12, 3.65]
Total (95% CI)	**1319**	**1339**		**100.0 %**	**0.96 [0.90, 1.02]**
Total events: 764 (Treatment), 810 (Control)					
Heterogeneity: Chi^2 = 4.74, df = 3 (P = 0.19); I^2 =37%					
Test for overall effect: Z = 1.45 (P = 0.15)					

Analysis 1.5. Comparison 1 All exercise interventions versus usual care, Outcome 5 Hospital admission heart failure only.

Review: Exercise based rehabilitation for heart failure

Comparison: 1 All exercise interventions versus usual care

Outcome: 5 Hospital admission heart failure only

Study or subgroup	Treatment 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		22.5 %	0.35 [0.14, 0.90]
Dracup 2007	35/87	37/86		59.3 %	0.94 [0.66, 1.33]
Giannuzzi 2003	2/45	1/45		1.6 %	2.00 [0.19, 21.28]
Hambrecht 1995	0/12	1/10		2.6 %	0.28 [0.01, 6.25]
Mueller 2007	2/25	3/25		4.8 %	0.67 [0.12, 3.65]
Passino 2006	0/44	2/41		4.1 %	0.19 [0.01, 3.78]
Willenheimer 2000	0/23	3/27		5.1 %	0.17 [0.01, 3.07]
Total (95% CI)	**286**	**283**		**100.0 %**	**0.72 [0.52, 0.99]**

Total events: 44 (Treatment), 61 (Control)

Heterogeneity: Chi^2 = 7.17, df = 6 (P = 0.31); I^2 =16%

Test for overall effect: Z = 2.03 (P = 0.042)

Analysis 1.6. Comparison 1 All exercise interventions versus usual care, Outcome 6 Health related quality of life - MLWHF.

Review: Exercise based rehabilitation for heart failure

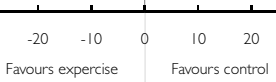
Comparison: 1 All exercise interventions versus usual care

Outcome: 6 Health related quality of life - MLWHF

Study or subgroup	Treatment N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
Austin 2005	95	22.9 (14.7)	94	36.9 (21.3)		20.0 %	-14.00 [-19.22, -8.78]
Belardinelli 1999	48	39 (20)	46	52 (20)		16.1 %	-13.00 [-21.09, -4.91]
Dracup 2007	87	35.7 (23.7)	86	43.2 (26.5)		16.9 %	-7.50 [-14.99, -0.01]
Koukouvou 2004	16	34.1 (13)	19	45.2 (9)		16.8 %	-11.10 [-18.65, -3.55]
McKelvie 2002	57	-3.4 (18.1)	67	-3.3 (13.9)		19.3 %	-0.10 [-5.86, 5.66]
Passino 2006	44	32 (26.5)	41	53 (32)		10.9 %	-21.00 [-33.54, -8.46]
Total (95% CI)	**347**		**353**			**100.0 %**	**-10.33 [-15.89, -4.77]**

Heterogeneity: Tau^2 = 33.04; Chi^2 = 17.49, df = 5 (P = 0.004); I^2 =71%

Test for overall effect: Z = 3.64 (P = 0.00027)



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

Review: Exercise based rehabilitation for heart failure

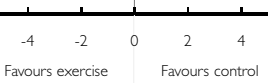
Comparison: 1 All exercise interventions versus usual care

Outcome: 7 Health related quality of life - all scales

Study or subgroup	Treatment 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)		13.1 %	-0.76 [-1.06, -0.47]
Belardinelli 1999	48	39 (20)	46	52 (20)		11.2 %	-0.64 [-1.06, -0.23]
Dracup 2007	87	35.7 (23.7)	86	43.2 (26.5)		13.0 %	-0.30 [-0.60, 0.00]
HF ACTION 2009	1159	-5.21 (13.72)	1171	-3.28 (13.97)		15.6 %	-0.14 [-0.22, -0.06]
Klocek 2005 (High)	14	-109 (23.5)	7	-71.7 (23.5)		4.4 %	-1.52 [-2.57, -0.48]
Klocek 2005 (Low)	14	-99 (23.5)	7	-71.7 (23.5)		4.8 %	-1.12 [-2.10, -0.13]
Koukouvou 2004	16	34.1 (13)	19	45.2 (9)		7.2 %	-0.99 [-1.69, -0.28]
McKelvie 2002	57	-3.4 (18.1)	67	-3.3 (13.9)		12.2 %	-0.01 [-0.36, 0.35]
Passino 2006	44	32 (26.5)	41	53 (32)		10.8 %	-0.71 [-1.15, -0.27]
Willenheimer 2000	20	-0.7 (0.8)	17	0 (1)		7.6 %	-0.76 [-1.44, -0.09]
Total (95% CI)	**1554**		**1555**			**100.0 %**	**-0.56 [-0.82, -0.30]**

Heterogeneity: $Tau^2 = 0.11$; $Chi^2 = 43.25$, df = 9 ($P<0.00001$); $I^2 = 79\%$

Test for overall effect: Z = 4.27 (P = 0.000020)



ADDITIONAL TABLES

Table 1. Health-related quality of life

Trial First author (year)	Follow up	HRQoL measure	Outcome values at follow up Mean (SD) Control versus Exercise, between-group P value	Between-group difference
Austin (2005)	6 months	MLWHF Physical Emotional	 20.4 (12.2) vs 12.6 (9.7) P < 0.0001*	 Exercise > Control Exercise > Control

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

	5 years	Total EQ-5D MLWHF Physical Emotional Total EQ-5D	8.0 (7.1) vs 4.4 (10.4) P < 0.01* 36.9 (24.0) vs 22.9 (17.8) P < 0.001* 0.58 (0.19) vs 0.70 (0.16) P < 0.0001* 19.3 (23.5) vs 18.3 (11.2) P = 0.66* 7.6 (7.1) vs 7.4 (6.5) P = 0.88* 37.1 (24.9) vs 35.5 (21.7) P = 0.72* 0.58 (0.22) vs 0.64 (0.19) P = 0.12*	Exercise > Control Exercise > Control Exercise = Control Exercise = Control Exercise = Control Exercise = Control
Bellardinelli (1999)	15 months 29 months	MLWHF Total	52 (20) vs 39 (20) P < 0.001 54 (22) vs 44 (21) P < 0.001	Exercise > Control Exercise > Control
Dracup (2007)	6 months	MLWHF Physical Emotional Total	19.4 (11.5) vs 16.1 (10.0) P = 0.04* 10.5 (7.4) vs 7.8 (6.6) P = 0.01* 43.2 (26.5) vs 35.7 (23.7) P = 0.05	Exercise > Control Exercise > Control Exercise > Control
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)	30 months	KCCQ	5.21 (95%CI 4.42 to 6.00) vs 3.28 (2.48 to 4.09) P < 0.001	Exercise > control
Klocek (2005)	6.5 months	PGWB Total	99.0 vs 109.0 (training grp A) vs 71.7 (training grp B) P < 0.01	Exercise > Control

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

Koukouvou 2004	6 months	MLWHF Total Spritzer QLI Total	34.1 (13.0) vs 45.1 (9.9) P = 0.05* 7.1 (1.1) vs 9.1 (1.1) P < 0.0001*	Exercise > Control Exercise > Control
McKelvie (2002)	12 months	MLWHF Total	-3.3 (13.9) vs -3.4 (18.1) P = 0.98	Exercise = Control
Passino (2006)	9.75 months	MLWHF	53 (32) vs 32 (26.5) P < 0.0001*	Exercise > Control
Willenheimer (2001)	10 months	PGAQoL	0 (1) 0.7 (0.9) P = 0.023	Exercise > Control

*calculated by Cochrane authors
QLI: quality of life index; MLWHF: Minnesota Living with Heart Failure questionnaire; PGAQoL: Patient's Global Assessment of Quality of life; PGWB: Psychological general Wellbeing index; KCCQ: Kansas City Cardiomyopathy Questionnaire
Exercise = Control: no statistically significant difference (P > 0.05) in HRQoL between exercise and control groups at follow up
Exercise > Control: statistically significant (P $\leqq$ 0.05) higher HRQoL in exercise compared to control group at follow up
Exercise < Control: statistically significant (P $\leqq$ 0.05) lower HRQoL in exercise versus control group at follow up
Exercise/control =: no statistically significant difference (P > 0.05) in HRQoL in exercise/control group compared to baseline
Exercise/control =+: statistically significant (P $\leqq$ 0.05) higher HRQoL in exercise/control group compared to baseline
Exercise/control =-: statistically significant (P $\leqq$ 0.05) lower HRQoL in exercise/control group compared to baseline

Table 2. Univariate meta-regression: all-cause mortality and HRQoL

	All-Cause Mortality *P* value	**HRQoL *P* value**
Mean left ventricular ejection fraction (%)	0.54	0.19
Mean age (years)	0.76	0.62
Sex (% male)	0.56	0.40
Type of rehabilitation (exercise only versus comprehensive)	0.65	0.59
Type of exercise (aerobic training alone or aerobic plus resistance training)	0.75	0.50

Table 2. Univariate meta-regression: all-cause mortality and HRQoL (*Continued*)

Exercise dose (no. of weeks X no. number of sessions/ week X duration of sessions in hours)	0.66	0.14
Exercise setting (hospital only, home only, both hospital and home)	0.65	0.04
Duration of follow up (months)	0.93	0.060.11
Publication date (pre 2000 versus 2000 and later)	0.89	0.47
Risk of bias Random code generation Random code concealment Outcome blinding Intention-to-treat analysis	0.90 0.93 0.96 0.88	0.11 0.27 0.74 0.53

APPENDICES

Appendix 1. 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: 01/04/2008

# 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 2. Search Strategy 2001

Cochrane Controlled Trials Regiser (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)

WHAT'S NEW

Last assessed as up-to-date: 30 June 2008.

Date	Event	Description
4 March 2010	New citation required and conclusions have changed	The original review identified eight trials that reported outcomes which met the inclusion criteria of this review update. The remaining were excluded as their follow-up was less than 6 months or reported only exercise capacity outcomes The conclusions have focussed more on the impact of exercise-based cardiac rehabilitation in terms of clinical event and HRQoL outcomes
4 March 2010	New search has been performed	The search was updated to January 2008. Nineteen trials have been included

HISTORY

Protocol first published: Issue 4, 2001

Review first published: Issue 3, 2004

Date	Event	Description
18 May 2004	New citation required and conclusions have changed	Substantive amendment

CONTRIBUTIONS OF AUTHORS

Edward Davies, Tiffany Moxham, Shah Ebrahim, and Rod Taylor were involved in the design of the update review. Tiffany Moxham developed the search strategy. Study selection, data extraction, assessment of risk of bias and data analysis were undertaken by Edward Davies and Rod Taylor. Edward Davies and Rod Taylor wrote the first draft of the review, and all co-authors contributed the various drafts of the report.

DECLARATIONS OF INTEREST

None

SOURCES OF SUPPORT

Internal sources

- No sources of support supplied

External sources

- NIHR Cochrane Heart Programme Grant, UK.

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

Review updated with the following changes: (1) limited to RCTs of six months or more follow up, (2) excluded RCTs reporting only exercise capacity (e.g. VO_2 max), (3) limited inclusion of HRQoL to studies using validated HRQoL outcomes, and (4) included cost-effectiveness outcomes.

NOTES

None

INDEX TERMS

Medical Subject Headings (MeSH)

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

MeSH check words

Adult; Aged; Humans; Middle Aged; Young Adult