Exercise-based cardiac rehabilitation for coronary heart disease

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Abstract

Background—The burden of coronary heart disease (CHD) worldwide is one of great concern to patients and healthcare agencies alike. Exercise-based cardiac rehabilitation aims to restore patients with heart disease to health.

Objectives—To determine the effectiveness of exercise-based cardiac rehabilitation (exercise training alone or in combination with psychosocial or educational interventions) on mortality, morbidity and health-related quality of life of patients with CHD.

Search methods—RCTs have been identified by searching CENTRAL, HTA, and DARE (using *The Cochrane Library* Issue 4, 2009), as well as MEDLINE (1950 to December 2009),

EMBASE (1980 to December 2009), CINAHL (1982 to December 2009), and Science Citation Index Expanded (1900 to December 2009).

Selection criteria—Men and women of all ages who have had myocardial infarction (MI), coronary artery bypass graft (CABG) or percutaneous transluminal coronary angioplasty (PTCA), or who have angina pectoris or coronary artery disease defined by angiography.

Data collection and analysis—Studies were selected and data extracted independently by two reviewers. Authors were contacted where possible to obtain missing information.

Main results—This systematic review has allowed analysis of 47 studies randomising 10,794 patients to exercise-based cardiac rehabilitation or usual care. In medium to longer term (i.e. 12 or more months follow-up) exercise-based cardiac rehabilitation reduced overall and cardiovascular mortality [RR 0.87 (95% CI 0.75, 0.99) and 0.74 (95% CI 0.63, 0.87), respectively], and hospital admissions [RR 0.69 (95% CI 0.51, 0.93)] in the shorter term (< 12 months follow-up) with no evidence of heterogeneity of effect across trials. Cardiac rehabilitation did not reduce the risk of total MI, CABG or PTCA. Given both the heterogeneity in outcome measures and methods of reporting findings, a meta-analysis was not undertaken for health-related quality of life. In seven out of 10 trials reporting health-related quality of life using validated measures was there evidence of a significantly higher level of quality of life with exercise-based cardiac rehabilitation than usual care.

Authors' conclusions—Exercise-based cardiac rehabilitation is effective in reducing total and cardiovascular mortality (in medium to longer term studies) and hospital admissions (in shorter term studies) but not total MI or revascularisation (CABG or PTCA). Despite inclusion of more recent trials, the population studied in this review is still predominantly male, middle aged and low risk. Therefore, well-designed, and adequately reported RCTs in groups of CHD patients more representative of usual clinical practice are still needed. These trials should include validated health-related quality of life outcome measures, need to explicitly report clinical events including hospital admission, and assess costs and cost-effectiveness.

Medical Subject Headings (MeSH)

*Exercise Therapy; Coronary Disease [mortality; *rehabilitation]; Health Status; Myocardial Infarction [mortality; rehabilitation]; Myocardial Revascularization [statistics & numerical data]; Outcome Assessment (Health Care); Quality of Life; Randomized Controlled Trials as Topic

MeSH check words

Female; Humans; Male

BACKGROUND

Description of the condition

Cardiovascular disease accounts for one-third of deaths globally, with 7.22 million deaths from coronary heart disease (CHD) in 2002 (WHO 2004). In Europe, CHD is the most common cause of death and in the UK it accounts for one in five deaths in men and one in six deaths in women (British Heart Foundation 2005; Peterssen 2005). Although the

mortality rate from CHD has been falling in the UK, principally due to a reduction in risk factors, particularly smoking, it has fallen less than in many other developed countries (Peterssen 2005). Treatments to individuals, including secondary prevention, explain about 42% of the decline in CHD mortality in the 1980s and 1990s (Unal 2000).

Description of the intervention

Cardiac rehabilitation has been defined as the "coordinated sum of interventions required to ensure the best physical, psychological and social conditions so that patients with chronic or post-acute cardiovascular disease may, by their own efforts, preserve or resume optimal functioning in society and, through improved health behaviours, slow or reverse progression of disease" (Fletcher 2001). It is a complex intervention that may involve a variety of therapies, including exercise, risk factor education, behaviour change, psychological support, and strategies that are aimed at targeting traditional risk factors for cardiovascular disease. Cardiac rehabilitation is an essential part of contemporary heart disease care and is considered a priority in countries with a high prevalence of CHD. International clinical guidelines consistently identify exercise therapy as a central element of cardiac rehabilitation (Balady 2007; Graham 2007; NICE 2007) i.e. 'exercise-based cardiac rehabilitation'.

Despite the recommendations for exercise-based cardiac rehabilitation as an integral component of comprehensive cardiac care of patients with CHD (particularly those following myocardial infarction, revascularization or with angina pectoris) and heart failure, most patients do not receive it (Bethall 2008). Service provision, though predominantly hospital based, varies markedly, and referral, enrolment and completion are suboptimal, especially among women and older people (Beswick 2004). Costs of cardiac rehabilitation services vary by format of delivery. The UK survey suggests that costs can range of £50 to £712 per patient treated depending on the level of staffing, the equipment used and the intensity of the programme (Evans 2002).

Previous meta-analyses of the effects of exercise-based cardiac rehabilitation for CHD patients reported a statistically significant reduction in total and cardiac mortality, ranging from 20% to 32%, in patients receiving exercise therapy compared with usual medical care (Clark 2005; Jolliffe 2001; Oldridge 1988; O'Connor 1989). However, the evidence for psychological interventions is less convincing. A Cochrane review showed no evidence of an effect on total mortality, cardiac mortality, or revascularisation although there was a significant reduction in the number of non-fatal infarctions in the psychological intervention group (OR 0.78 [95% CI 0.67 to 0.90]) compared to usual care (Rees 2004). A Cochrane review of the effect of educational interventions for CHD is currently being undertaken (Brown 2010).

How the intervention might work

Exercise training has been shown to have direct benefits on the heart and coronary vasculature, including myocardial oxygen demand, endothelial function, autonomic tone, coagulation and clotting factors, inflammatory markers, and the development of coronary collateral vessels (Clausen 1976; Hambrecht 2000). However, findings of the original

Cochrane review of exercisebased cardiac rehabilitation for CHD supported the hypothesis that reductions in mortality may also be mediated via the indirect effects of exercise through improvements in the risk factors for atherosclerotic disease (i.e. lipids, smoking and blood pressure) (Taylor 2006).

Why it is important to do this review

Our original Cochrane review published in 2001 identified a total of 35 RCTs in some 8,440 patients (Jolliffe 2001). This review reported a reduction in total mortality (random effects model, odds ratio: 0.73, 95% confidence interval: 0.54 to 0.98) with exercise intervention compared to usual care. Improvements with exercise were also seen in cardiac death, non-fatal MI, lipid profile and blood pressure. However, the authors identified a number a limitations in the evidence base:

- Trials enrolled almost exclusively low-risk, middle-aged men after myocardial infarction. The exclusion or under representation of women, elderly people, and other cardiac groups (post revascularization and angina pectoris) not only limits the applicability of the evidence to contemporary cardiovascular practice but also fails to consider those who may benefit most from rehabilitation.

- The widespread introduction of a variety of drug therapies as part of the routine management of CHD the cardiac patient that were not available at the time of the earliest trials may offset the magnitude of benefit associated with exercise-based rehabilitation.

- It was unclear whether comprehensive (exercise plus psychosocial and/or educational interventions) cardiac rehabilitation offers incremental outcome benefits compared to exercise only interventions.

- There was a lack of robust evidence for the impact on patient health-related quality of life, costs and cost-effectiveness.

Additionally, recent meta-analyses of the effects of exercise-based cardiac rehabilitation in patients with CHD have indicated an increase in the number of RCTs since the publication of the original Cochrane review (Clark 2005).

The aim of this study is to update the original Cochrane systematic review of the effects of exercise-based rehabilitation for patients with CHD.

Changes in this update review

In addition to updating the searches, this update review has: (1) formally explored the variation in exercise intervention effects using meta-regression and stratified meta-analysis and (2) not updated exercise capacity and cardiac risk outcomes (i.e. serum lipids, blood pressure, and smoking behaviour).

OBJECTIVES

1. To assess the effectiveness of exercise-based cardiac rehabilitation (exercise training alone or in combination with psychosocial or educational interventions)

compared with usual care on mortality, morbidity and health-related quality of life in patients with CHD.

2. To explore the potential study level predictors of exercise-based cardiac rehabilitation in patients with CHD.

METHODS

Criteria for considering studies for this review

Types of studies—Randomised controlled trials (RCTs) of exercise-based cardiac rehabilitation versus usual care with a follow-up period of at least six months have been sought.

Types of participants—Men and women of all ages, in both hospital-based and community-based settings, who have had a myocardial infarction (MI), or who had undergone revascularisation (coronary artery bypass grafting, percutaneous transluminal coronary angioplasty or coronary artery stent), or who have angina pectoris or coronary artery disease defined by angiography have been included.

Studies of participants following heart valve surgery, with heart failure, with heart transplants or implanted with either cardiac-resynchronisation therapy (CRT) or implantable defibrillators (ICD) have been excluded. Studies of participants who completed a cardiac rehabilitation programme prior to randomisation have also been excluded.

Types of interventions—Exercise-based cardiac rehabilitation is defined as a supervised or unsupervised inpatient, outpatient, or community- or home-based intervention including some form of exercise training that is applied to a cardiac patient population. The intervention could be exercise training alone or exercise training in addition to psychosocial and/or educational interventions (i.e. "comprehensive cardiac rehabilitation").

Usual care could include standard medical care, such as drug therapy, but did not receive any form of structured exercise training or advice.

Types of outcome measures—All clinical events or other outcome measures reported post-randomisation were included in this review. No maximum limit was imposed on the length of follow-up.

Primary outcomes

- Total mortality
  - ○ Cardiovascular mortality
  - ○ Non-cardiovascular mortality
- Total MI
  - ○ Fatal MI
  - ○ Non-fatal MI

- Total revascularizations

  - CABG

  - PTCA

  - Restenting

- Total hospitalisations

  - Cardiovascular hospitalisations

  - Other hospitalisations

Secondary outcomes

- Health-related quality of life assessed using validated instruments (e.g. SF-36, EQ5D)

- Costs and cost-effectiveness

Search methods for identification of studies

As this review forms part of a broader review strategy, that includes updates of two other Cochrane systematic reviews addressing cardiac rehabilitation (Davies 2010a; Rees 2004) and two new Cochrane reviews - interventions for enhancing uptake and adherence to cardiac rehabilitation (Davies 2010b) and home versus centre-based cardiac rehabilitation (Taylor 2010), a generic broad search was initially undertaken. This generic search was then further updated for the purposes of this specific review.

Electronic searches—Randomized controlled trials have been identified from the previously published Cochrane review. This list of studies has been updated by the authors searching the Cochrane Central Register of Controlled Trials (CENTRAL) in *The Cochrane Library* Issue 4, 2009, MEDLINE (November 2000 to December 2009), EM-BASE (November 2000 to December 2009), CINAHL (November 2000 to December 2009), and Science Citation Index Expanded (SCI-Expanded, 1900 to December 2009). Health Technology Assessment (HTA) and Database of Abstracts of Reviews of Effects (DARE) databases have been searched via *The Cochrane Library* Issue 4, 2009. The generic (cross review) search was undertaken from 2001 (the search end date of the previous Cochrane review of exercise-based cardiac rehabilitation (Jolliffe 2001)) to January 2008 with a further update search up to December 2009 for this specific review.

Search strategies were designed with reference to those of the previous systematic review (Jolliffe 2001). MEDLINE, EMBASE and CINAHL were searched using a strategy combining selected MeSH terms and free text terms relating to exercise-based rehabilitation and coronary heart disease with RCT filters. The MED-LINE search strategy was translated into the other databases using the appropriate controlled vocabulary as applicable. Due to time and resource constraints, three databases (AMED, BIDS and SPORTSDISCUSS) included the previous review (Jolliffe 2001) were not searched in this case.

Searches have been limited to randomised controlled trials and a filter applied to limit by humans. Consideration was given to variations in terms used and spellings of terms in different countries so that studies were not missed by the search strategy because of such variations.

See Appendix 1 for a list of the search strategies used.

Searching other resources—Reference lists of retrieved articles and systematic reviews and meta-analyses published since the original Cochrane review were checked for any studies not identified by the electronic searches.

Data collection and analysis

Selection of studies—The titles and abstracts of citations identified by the electronic searches prior to 2008 were examined for possible inclusion by two reviewers (RST & Philippa Davies) working independently. The titles and abstracts of citations identified by the electronic searches from 2008 onwards were examined for possible inclusion independently by two reviewers (BSH & LF). Full publications of potentially relevant studies were retrieved (and translated into English where required) and two reviewers (BSH & JMHC) then independently determined study eligibility using a standardized inclusion form. Any disagreements about study eligibility were resolved by discussion and, if necessary, a third reviewer (RST) was asked to arbitrate.

Data extraction and management—Data from included studies were extracted by one reviewer (BSH or JMHC) using standardised data extraction forms and checked by a second reviewer (JMHC or BSH). If data were presented numerically (in tables or text) and graphically (in figures), the numeric data were used because of possible measurement error when estimating from graphs. A second reviewer confirmed all numeric calculations and extractions from graphs or figures. Any discrepancies were resolved by consensus.

Data on patient characteristics (e.g. age, sex, CHD diagnosis) and details of the intervention (including mode of exercise, duration, frequency and intensity), nature of usual care and length of followup were also extracted.

Assessment of risk of bias in included studies—Two reviewers (BSH, JMHC) independently assessed the risk of bias in included studies using the Cochrane Collaboration's recommended tool, which is a domain-based critical evaluation of the following domains: sequence generation; allocation concealment; blinding of outcome assessment; incomplete outcome data; and selective outcome reporting (Higgins 2011). Assessments of risk of bias are provided in the Risk of bias table for each study.

Dealing with missing data—If there were multiple reports of the same study, the duplicate publications were scanned for additional data. Outcome results have been extracted at all follow-up points post-randomisation. Study authors were contacted where necessary to provide additional information.

Assessment of heterogeneity—If there was significant statistical heterogeneity (P-value <0.10) associated with an effect estimate, a random effects model was applied. This model provides a more conservative statistical comparison of the difference between intervention and control because a confidence interval around the effect estimate is wider than a confidence interval around a fixed effect estimate. If a statistically significant difference was still present using the random effects model, the fixed effect pooled estimate and 95% CI have been reported because of the tendency of smaller trials, which are more susceptible to publication bias, to be over weighted with a random effects analysis (Heran 2008a; Heran 2008b).

Assessment of reporting biases—No language restrictions have been applied.

Data synthesis—Data have been processed in accordance with the Cochrane Handbook for Systematic Reviews of Interventions (Higgins 2011). Data synthesis and analyses have been done using Review Manager 5.0 software and STATA version 10 (Stata Corp., College Station, Texas).

Dichotomous outcomes for each comparison have been expressed as relative risks with 95% confidence intervals (CI). Continuous outcome have been expressed as the mean (±SD) change from baseline to follow-up. Otherwise, continuous outcomes have been pooled as weighted mean difference (WMD). If there was a statistically significant absolute risk difference, the associated number needed to treat/harm was calculated.

Subgroup analysis and investigation of heterogeneity—Where possible, stratified meta-analysis (according to time of follow-up, 6 to12 months versus > 12 months) and meta-regression have been undertaken to explore heterogeneity and examine potential treatment effect modifiers. We tested five a priori hypotheses that there may be differences in the effect of exercise-based cardiac rehabilitation on total mortality, cardiovascular mortality, total MI, and revascularisation (CABG and PTCA) across particular subgroups: (1) CHD case mix (myocardial infarction-only trials versus other trials); (2) type of cardiac rehabilitation (exercise-only cardiac rehabilitation versus comprehensive cardiac rehabilitation); (3) 'dose' of exercise intervention [dose = duration in weeks x number of sessions x number of sessions per week] (dose   1000 units versus dose < 1000 units); (4) follow-up period (12 months versus > 12 months); and (5) year of publication (before 1995 versus 1995 or later).

<u>Year of Publication:</u> We included year of publication as a study level factor (pre versus post-1995) in order to assess the potential effect of a change in the standard of usual care over time, that is to reflect when pharmacologic agents became established therapies for CHD.

<u>Heterogeneity:</u> Heterogeneity amongst included studies was explored qualitatively (by comparing the characteristics of included studies) and quantitatively (using the chi-squared test of heterogeneity and I^2 statistic). Where appropriate, data from each study have been pooled using a fixed effect model, except where substantial heterogeneity exists. We planned to pool the results for health-related quality of life using a standardised mean

difference (SMD) but this was not possible due to the heterogeneity in outcome measures and methods of reporting findings.

The funnel plot and the Egger test have been used to examine small study bias (Egger 1997).

RESULTS

Description of studies

See: Characteristics of included studies; Characteristics of excluded studies; Characteristics of studies awaiting classification; Characteristics of ongoing studies.

Results of the search

Our update cross-cardiac rehabilitation review electronic searches (to January 2008) yielded a total 11,561 titles plus 1802 titles from the update search (to December 2009). After reviewing the titles and abstracts, we retrieved 59 full-text articles for possible inclusion. A total of 30 papers were excluded: two had followup less than six months, 16 reported no useful outcomes, six had inappropriate randomisation, one had an inappropriate control, and five were review articles. In addition, one study was awaiting classification and two were ongoing studies. Seventeen studies (26 publications) met the inclusion criteria and had extractable data to assess the effects of exercise-based cardiac rehabilitation compared with usual care on mortality and morbidity in patients with CHD (Figure 1).

Included studies

The original Cochrane review published in 2001 (Jolliffe 2001) included a total of 35 studies, of which five studies were judged not to meet the revised inclusion criteria of this review update (see Excluded studies).

In addition to the 30 trials (55 publications) from the original Cochrane review that met the inclusion criteria of this update review (Andersen 1981; Bell 1998; Bengtsson 1983; Bertie 1992; Bethell 1990; Carlsson 1998; Carson 1982; DeBusk 1994; Engblom 1996; Erdman 1986; Fletcher 1994; Fridlund 1991; Haskell 1994; Heller 1993; Holmbäck 1994; Kallio 1979; Leizorovicz 1991; Lewin 1992; Miller 1984; Oldridge 1991; Ornish 1990; Schuler 1992; Shaw 1981; Sivarajan 1982; Specchia 1996; Stern 1983; Vecchio 1981; Vermeulen 1983; WHO 1983; Wilhelmsen 1975), an additional 17 studies (26 publications) have been identified by the updated search and have met the revised inclusion criteria (Belardinelli 2001; Bäck 2008; Dugmore 1999; Giallauria 2008; Hofman-Bang 1999; Kovoor 2006; La Rovere 2002; Manchanda 2000; Marchionni 2003; Seki 2003; Seki 2008; Ståhle 1999; Toobert 2000; VHSG 2003; Yu 2003; Yu 2004; Zwisler 2008). Thus, a total of 47 studies reporting data for a total of 10,794 patients have been included in this review update. Details of the studies included in the review are listed in the Characteristics of included studies table. The study selection process is summarised in the PRISMA flow diagram shown in Figure 1.

Although all exercise-based cardiac rehabilitation, 17 studies were judged to be exercise-only intervention trials and 29 were judged to be comprehensive cardiac rehabilitation (exercise plus psychosocial and/or educational interventions); one trial randomly assigned

patients to both exercise-only cardiac rehabilitation and comprehensive cardiac rehabilitation (Sivarajan 1982). The majority of studies were (32 studies, 68%) undertaken in Europe, either as single or multicenter studies. Trial sample sizes varied widely from 28 to 2304, with a median intervention duration of three (range 0.25 to 30) months and a follow-up of 24 (range six to 120) months. Patients with myocardial infarction alone were recruited in 30 trials (64%); the remaining trials recruited either exclusively postrevascularisation patients (i.e., CABG and PTCA) or both groups of patients. The ages of patients in the trials ranged from 46 to 84 years. Although over half of the trials (28 studies, 60%) included women, on average women accounted for only 20% of the patients recruited.

Characteristics of included interventions

Twenty nine studies compared comprehensive programmes (that is, exercise plus education or psychological management, or both), while 17 reported on an exercise only intervention. In addition, one study randomised patients to a comprehensive programme, exercise only intervention or usual care (Sivarajan 1982).

The exercise-based cardiac rehabilitation programmes differed considerably in duration (range 1-12 months), frequency (1-7 sessions/week), and session length (20-90 minutes/ session). Most programmes involved the prescription of individually tailored exercise programmes, which makes it difficult to precisely quantify the amount of exercise undertaken. Most home based programmes included a short initial period of centre based intervention. Centre based programmes typically involved supervised exercise involving cycles, treadmills or weight training, while nearly all home based programmes were based on walking.

Both intervention and control patients received usual care including medication, education and advice about diet and exercise, but control patients received no formal exercise training.

Excluded studies

Five studies that had been included in the original review failed to meet the revised inclusion criteria of this review update. Of these, four studies did not report outcomes relevant to this review (Ballantyne 1982; Carlsson 1997; Krachler 1997; Wosornu 1996) and one study was not randomised (Kentala 1972). For the updated search, 24 studies (25 publications) were excluded for reasons listed in the Characteristics of excluded studies table, with the most common reason being a failure to report any of the pre-specified outcomes of this review update.

Risk of bias in included studies

Limited reporting of the methodology and outcome data in the published papers of the included trials precluded us, in most cases, from adequately performing a critical evaluation of the following domains: sequence generation; allocation concealment; blinding; incomplete outcome data; selective outcome reporting; and other sources of bias. Nevertheless, we attempted to assess the risk of bias for each of the 47 included studies given the available information in the published trial reports.

Allocation

Nearly all the trial publications simply reported that the trial was "randomised" but did not provide any details. A total of 8/47 (17%) studies (Andersen 1981; Bell 1998; Bethell 1990;Erdman 1986; Haskell 1994; Holmbäck 1994; Wilhelmsen 1975;Zwisler 2008) reported details of appropriate generation of the random sequence and 7/47 (15%) studies (Bell 1998; Haskell 1994; Holmbäck 1994; Kovoor 2006; Schuler 1992; VHSG 2003;Zwisler 2008) reported appropriate concealment of allocation.

Blinding

For exercise-based cardiac rehabilitation trials, it is not possible to blind patients and clinicians to the intervention. For the large majority of studies, insufficient information was provided to evaluate the blinding of assessors; only 4 of 47 (9%) studies (Fletcher 1994; Ornish 1990; Wilhelmsen 1975; Zwisler 2008) reported that outcome assessors were blind to group allocation.

Incomplete outcome data

Losses to follow-up and drop out were relatively high, ranging from 21% to 48% in 12 trials. Follow-up of 80% or more was achieved in 33/47 (70%) studies (Andersen 1981; Belardinelli 2001; Bell 1998; Bethell 1990; Bäck 2008; Carlsson 1998; Dugmore 1999;Engblom 1996; Giallauria 2008; Haskell 1994; Heller 1993;Holmbäck 1994; Kallio 1979; Kovoor 2006; La Rovere 2002;Leizorovicz 1991; Lewin 1992; Manchanda 2000; Marchionni 2003; Miller 1984; Oldridge 1991; Schuler 1992; Seki 2003;Shaw 1981; Specchia 1996; Stern 1983; Ståhle 1999; Toobert 2000; Vermeulen 1983; VHSG 2003; Wilhelmsen 1975; Yu 2003;Zwisler 2008). Furthermore, reasons for loss to follow and dropout were often not reported. Two trials (Seki 2008; WHO 1983) did not report information on losses to follow-up. Several trials have excluded significant numbers of patients post-randomisation, and thus in an intention to treat analysis, these then have been regarded as dropouts.

Selective reporting

A number of the included studies were not designed to assess treatment group differences in morbidity and mortality (as these were not the primary outcomes of these trials) and, therefore, may not have fully reported all clinical events that occurred during the follow-up period. All studies collecting validated health-related quality of life outcomes fully reported these outcomes.

Other potential sources of bias

Publication bias—In order to test for the possibility of publication bias, the funnel plots were created for all-cause mortality, cardiovascular mortality, recurrent MI, and revascularisation (CABG and PTCA). There was no evidence of funnel plot asymmetry or significant Egger tests for all-cause mortality, cardiovascular mortality and revascularisation (CABG and PTCA). However, the funnel plot of recurrent MI suggests asymmetry and the Egger test was statistically significant (P = 0.019), which appears to be due to an absence of negative-result trials of small to medium size (Figure 2).

Effects of interventions

Clinical Events

Mortality: Thirty (N = 8971) of the included studies reported total mortality (Analysis 1.1); two trials reported both follow-up to 12 months and longer than 12 months (Wilhelmsen 1975; WHO 1983). In studies reporting follow-up longer than 12 months, compared with control, total mortality was reduced with exercise-based cardiac rehabilitation (RR 0.87 [95% CI 0.75, 0.99]). There was no significant difference in total mortality up to 12 months follow-up.

Nineteen (N = 6583) of included studies reported cardiovascular mortality (Analysis 1.2); one trial reported both follow-up to 12 months and longer than 12 months (WHO 1983). In studies reporting follow-up longer than 12 months, compared to control, cardiovascular mortality was reduced with exercise-based cardiac rehabilitation (RR 0.74 [95% CI 0.63, 0.87]). There was no significant difference in cardiovascular mortality up to 12 months follow-up.

There was no evidence of statistical heterogeneity across trials for either total or cardiovascular mortality.

Morbidity: Twenty-five (N = 7294), 22 (N = 4392), and 11 (N = 2241) of the included studies reported total MI, CABG or PTCA, respectively (Analysis 1.3; Analysis 1.4; Analysis 1.5); follow-up to 12 months and longer than 12 months was reported by two studies for MI (Haskell 1994; WHO 1983), one study for CABG (Ståhle 1999) and two studies for PTCA (Haskell 1994; Ståhle 1999). There was no statistically significant difference between exercise-based cardiac rehabilitation and usual care for these outcome measures. The pooled risk ratios for total MI, CABG and PTCA were 0.92 (95% CI 0.70, 1.22), 0.91 (95% CI 0.67, 1.24) and 1.02 (95% CI 0.69, 1.50), respectively, up to 12 months follow-up. In studies reporting follow-up longer than 12-months, the pooled risk ratios for total MI, CABG and PTCA were 0.97 (95% CI 0.82, 1.15), 0.93 (95% CI 0.68, 1.27) and 0.89 (95% CI 0.66, 1.19) respectively. There was no evidence of statistical heterogeneity across trials for any of the morbidity outcomes.

Hospitalisations: Ten (N = 2379) of the included studies reported hospital admissions; one study reported both follow-up to 12 months and longer than 12 months (Hofman-Bang 1999). In studies reporting up to 12 months follow-up, total readmissions were reduced with exercise-based cardiac rehabilitation compared with usual care (RR 0.69, 95% CI 0.51, 0.93; Analysis 1.6). There was no significant difference in total hospitalisations in studies with follow-up longer than 12 months.

Health-related quality of life—Ten trials assessed health-related quality of life using a range of validated disease-specific (e.g. QLMI) and generic (e.g. Short-form 36) outcome measures (Table 1). Given both the heterogeneity in outcome measures and methods of reporting findings, a meta-analysis was not undertaken.

Although most trials demonstrated an improvement in baseline quality of life following exercise-based cardiac rehabilitation, a within group improvement was also often reported in

control patients. Only in seven out of 10 trials was there evidence of a significantly higher level of quality of life with exercise-based cardiac rehabilitation than control at follow-up (Belardinelli 2001;Dugmore 1999; Sivarajan 1982; Yu 2004).

Costs—Three of the included studies reported limited data on costs per patient (Kovoor 2006; Marchionni 2003; Yu 2004). These results are summarised in Table 2. It was not possible to compare the costs directly across studies due to differences in currencies and the timing of studies.

In two of the three studies the total healthcare costs associated with exercise-based cardiac rehabilitation and usual care were not statistically significantly different. In Marchionni 2003, the total healthcare costs associated with exercise-based cardiac rehabilitation were higher ($4839 more per patient) than usual care.

Only Oldridge 1991 evaluated the cost-effectiveness of exercise-based cardiac rehabilitation in post-MI patients by combining cost information with time trade-off measures of health-related quality of life and data on mortality derived from a 1989 meta-analysis (O'Connor 1989). Based on their analysis, the authors concluded that rehabilitation was "an efficient use of health-care resources and may be economically justified" (Oldridge 1993).

Meta regression—Predictors of all-cause mortality, cardiovascular mortality, recurrent MI, and revascularisation (CABG and PTCA) were examined using univariate meta-regression. Covariates defined *a priori i*ncluded: CHD case mix (myocardial infarction-only trials versus other trials); type of cardiac rehabilitation (exercise-only versus comprehensive cardiac rehabilitation); 'dose' of exercise intervention (calculated as the number of weeks, multiplied by the number of sessions per week, multiplied by the duration of sessions in hours); follow-up period (12 months versus > 12 months); and publication date (before 1995 versus 1995 or later). No statistically significant associations were seen in any of these analyses (Table 3, Table 4, Table 5, Table 6, Table 7).

DISCUSSION

Summary of main results

This updated systematic review of exercise-based cardiac rehabilitation has allowed analysis of an increased number of patients from an additional 17 studies published from 2000 to 2009. A total of 47 RCTs, with 10,794 patients, have now been included. In accord with the original Cochrane review and previous metaanalyses (Clark 2005; Jolliffe 2001; O'Connor 1989; Oldridge 1988) a reduction in both total and cardiac mortality was observed in CHD patients randomised to exercise-based rehabilitation. However, this updated review shows that this mortality benefit is limited to studies with a follow-up of greater than 12 months. We also found that with exercise the rate of hospital readmissions may be reduced in studies up to 12 months follow-up (based on 4 trials with 54/254 versus 73/225 events), but not in longer term follow-up. There was no difference between exercise-based cardiac rehabilitation and usual care groups in the risk of recurrent myocardial infarction or revascularization at any duration of follow-up.

This reduction in total and cardiovascular mortality with exercise therapy appears consistent across a number of CHD groups (e.g., post-MI, post-revascularisation), as well as a range of strategies for delivery of the exercise-based intervention. We compared trials that assessed exercise therapy alone with exercise in combination with educational and psychological co-interventions and there appears to be no difference in mortality effect. In addition, there was no difference in mortality effect by exercise 'dose' a composite measure based on the overall duration of the exercise program plus the intensity, frequency, and length of exercise sessions.

The mechanism for reduced cardiovascular mortality in patients who have received exercise-based cardiac rehabilitation is not clear, but may be due to improved myocardial revascularisation, protection against fatal dysrhythmias, improved cardiovascular risk factor profile, improved cardiovascular fitness, or increased patient surveillance (Oldridge 1988; Taylor 2006).

There were insufficient data to definitely definitely conclude that exercise-based cardiac rehabilitation improves health-related quality of life compared to control. Only 10 of included trials reported outcomes based on a validated health-related quality of life measure. Furthermore, only three of these 10 trials randomised more than 250 patients; thus, providing relatively adequate power (80% and 5% alpha) to detect a modest difference (standardised effect size of 0.25) between exercise therapy and usual care. Heterogeneity of health-related quality of life outcome measures and their reporting precluded us from quantitatively pooling the available data across trials. Generic health-related quality of life measures that lack sensitivity to change with cardiac treatment, particularly in comparison with disease-specific measures, were used in nearly all the trials (Oldridge 2003; Taylor 1998).

All participants in the included studies had documented CHD, the majority of the participants having suffered an MI. Some participants had documented CHD having suffered angina or undergone coronary angiography, while others had undergone CABG. We have combined these different patient groups as there are insufficient data at present to stratify trials by type of CHD. The number of women participants was low and few studies mentioned the ethnic origin of their participants. The mean age of the participants was 56 years. Although most studies had an upper age limit of at least 65 years of age, this is not reflected in the mean age of the participants. The majority of the studies had exclusion criteria that would have excluded those participants who had co-morbidity, or heart failure. In some studies this may have accounted for up to 60% of the patients considered for the trial, and certainly the older patients would be more likely to be affected.

Quality of the evidence

We found no evidence of publication bias for total mortality, CV mortality, CABG or PTCA. There was evidence of small study bias for total MI.

As with the original Cochrane review, this update review has revealed limitations in the available RCT evidence, most notably the poor reporting of methodology and results in many trial publications (Jolliffe 2001). The method of randomization, allocation

concealment, or blinding of outcomes assessment was rarely described. Although the quality of reporting tends to be poorer for older studies, it does not appear to have appreciably improved over the last decade. Furthermore, incomplete outcome data (primarily due to losses to follow-up or dropouts) were insufficiently addressed in most trials. Losses to follow-up were relatively high across trials (approximately one third of trials reported a greater than 20% loss to follow-up) but reasons for dropout were often not reported. Several trials excluded significant numbers of patients post-randomisation, and thus in an intention-to-treat analysis, these patients have been regarded as dropouts. This may be partly explained by the fact that the majority of trials were not designed to assess treatment group differences in mortality and morbidity but instead surrogate measures of treatment efficacy, such as exercise capacity or lipid levels.

AUTHORS' CONCLUSIONS

Implications for practice

In medium to longer term (i.e. 12 or more months follow-up) exercise-based cardiac rehabilitation is effective in reducing overall and cardiovascular mortality and appears to reduce the risk of hospital admissions in the shorter-term (< 12 months follow-up) in patients with CHD. The available evidence does not demonstrate a reduction in the risk of total MI, CABG or PTCA with exercise-based cardiac rehabilitation as compared to usual care at any duration of follow-up. Exercise-based cardiac rehabilitation should be recommended for patients similar to those included in the randomised controlled trials - predominantly lower risk younger men who had suffered myocardial infarction or are post-revascularisation. It is a question of judgement whether evidence is sufficient to under-represented groups, particularly angina pectoris and higher risk CHD patients and those with major co-morbidities. There appears to be little to choose between exercise only or in combination with psychosocial or educational cardiac rehabilitation interventions. In the absence of definitive cost-effectiveness comparing these two approaches to exercise-based cardiac rehabilitation it would be rational to use cost considerations to determine practise.

Implications for research

In spite of inclusion of recent trial evidence including more post-revascularisation and female patients, the population of CHD patients studied in this review update remains predominately low risk middle-aged males following MI or PTCA. There has been little identification of the ethnic origin of the participants. It is possible that patients who would have benefited most from exercise-based cardiac rehabilitation were excluded from the trials e.g. those of older age or those with co-morbidity. Therefore, well-designed, and adequately reported RCTs in groups of CHD patients more representative of usual clinical practice are still needed. These trials should include validated health-related quality of life outcome measures, need to explicitly report clinical events including hospital admission, and assess costs and cost-effectiveness.

Acknowledgments

CHARACTERISTICS OF STUDIES

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

Andersen 1981

Methods	Post MI randomised four weeks after discharge. 88 participants were randomised, but 13 failed to follow up. Therefore 75 took part in the study
Participants	75 men < 66 yrs with 1st MI. Mean age I = 52.2 (+/−7.5), C= 55.6 (+/−6.3).
Interventions	Aerobic activity e.g. running, cycling, skipping + weights for 1 hour × 2 weekly for 2 months, then × 1 week for 10 months. Then continue at home. F/U @ 1, 13, 25, & 37 months post discharge.
Outcomes	Total & CHD mortality and non fatal MI.
Notes	Several participants in C trained on own initiative, but were analysed as intention to treat. Authors concluded that PT after MI appears to reduce consequences and to improve PWC, but PWC declines once participant on their own. PT had no effect on period of convalescence or return to work, but age and previous occupation were of significance

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	"random numbers"
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding (performance bias and detection bias) All outcomes	Unclear risk	Unclear in terms of assessment of outcomes.
Incomplete outcome data (attrition bias) All outcomes	High risk	15% lost to follow-up, no description of withdrawals or dropouts

Selective reporting (reporting bias)	Unclear risk	No information reported.

Belardinelli 2001

Methods	RCT, single centre in Italy 33 (SD 7) months
Participants	**N Randomised:** Total:118 (99 males, 19 females); EX: 59 (49 males, 10 females) UC: 59 (50 males, 9 females) **Diagnosis (% of pts);** *Myocardial Infarction:* EX 51; UC 47 *Hypercholesterolemia:* EX 61; UC 54 *Diabetes:* EX 17; UC 20 *Hypertension:* EX 42; UC 47 *LVEF (%)*: EX 52 (SD 16); UC 50 (SD 14) **Case mix:** **Age (years):** EX: 53 (SD 11); UC: 59 (SD 10) **Percentage male:** EX 83.1%; UC 84.8% **Percentage white**: Not reported **Inclusion/exclusion criteria:** *Inclusion: successful procedure of coronary angioplasty in 1 or 2 native epicardial coronary arteries and ability to exercise* *Exclusion:* previous coronary artery procedures, cardiogenic shock, unsuccessful angioplasty (defined as residual stenosis>30% of initial value), complex ventricular arrhythmias, uncontrolled hypertension and diabetes mellitus, creatinine ?2.5 mg/dl, orthopedic or neurological limitations to exercise or unstable angina after procedure and before enrolment
Interventions	**Exercise:** *Total duration: six* months *aerobic/resistance/mix: exercise sessions were performedat the hospital gym and were supervised by a cardiologist* *frequency:* 3 sessions/week *duration:* 15 min of stretching and callisthenics; 5 min of loadless warm-up; 30 min of pedaling on electronically braked cycle ergometer at target work rate; 3 min of unloaded cool-down pedaling *intensity:* 60% of peak oxygen uptake (VO_2) *modality:* electronically braked cycle ergometer Usual care: "Control patients were recommended to perform basic daily mild physical activities but to avoid any physical training."
Outcomes	Cardiac mortality; myocardial infarction; coronary angioplasty (percutaneous translu-minal coronary angioplasty, coronary stent); coronary artery bypass graft; health-related quality of life: MOS Short-Form General Health Survey
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not reported.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding (performance bias and detection bias) All outcomes	Unclear risk	"*All studies were performed by experienced operators and evaluated by two independent observers blinded to treatment arm and to each otherls interpretation.*" Comment: This only applied to exercise test & angiography only so assessment of events and health-related quality of life (although patient self complete) not necessarily blinded

Incomplete outcome data (attrition bias) All outcomes	High risk	Cardiac events of 12 patients who were excluded not accounted for
Selective reporting (reporting bias)	Unclear risk	No information reported.

Bell 1998

Methods	Post MI Randomised 4-6 days post event.
Participants	311 men / 89 women < 65 yrs. Mean ages for women 60.7 (+/− 7.2) to 64.3 (+/−7.3), for men 57.8(+/− 8.9) to 59.4 (+/− 9.4). 2 comparisons conventional CR v: the Heart Manual (HM) and HM v: control
Interventions	Conventional CR - 1 to 2 group classes per week, walking etc other days for 8-12 weeks with multidisciplinary team HM - individual - walking programme up to 6 weeks post MI, facilitator and written text. F/U - 1 year.
Outcomes	Total mortality, health-related quality of life: Nottingham Health Profile
Notes	"Heart Manual is a comprehensive home based programme which included an exercise regimen, relaxation and stress management techniques, specific self-help treatments for psychological problems commonly experienced by MI patients and advice on coronary risk-related behaviours." Hospital readmissions significantly reduced in Heart Manual group compared with conventional CR and control in initial 6 month period

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	"Randomisation was achieved by providing each hospital with a series of sealed envelopes containing cards evenly distributed between conditions. The envelopes were taken sequentially and, before opening the envelope, the patient's surname was written diagonally across the sealed flap, in such a way that when the envelope was opened the name was 'torn in two'. Opened envelopes were retained and returned to the trial coordinator. The importance of remaining neutral when advising the patients of the outcome of randomisation was emphasised in the written protocol and was reinforced during the sessions which were held to familiarise facilitators with the protocol.""
Allocation concealment (selection bias)	Low risk	"Randomisation was achieved by providing each hospital with a series of sealed envelopes containing cards evenly distributed between conditions. The envelopes were taken sequentially and, before opening the envelope, the patient's surname was written diagonally across the sealed flap, in such a way that when the envelope was opened the name was 'torn in two'. Opened envelopes were retained and returned to the trial coordinator. The importance of remaining neutral when advising the patients of the outcome ofrandomisation was emphasised in the written protocol and was reinforced during the sessions which were held to familiarise facilitators with the protocol." Comment: Patients were informed of outcome of randomisation.
Blinding (performance bias and detection bias) All outcomes	Unclear risk	Unclear in terms of assessment of outcomes.
Incomplete outcome data (attrition bias) All outcomes	Low risk	1.5% lost to follow up and reported description of withdrawals and/or dropouts

Selective reporting (reporting bias)	Unclear risk	No information reported.

Bengtsson 1983

Methods	RCT; single centre Sweden; F/U 14 months average
Participants	N=87 (EX n= 44; CON n=43) Gender: 74 men / 13 women Mean age: EX = 55.3 +/− 6.6, CON = 57.1 +/− 6.6. Diagnosis: following acute MI. Ethnicity: NR Inclusion: <65 years with MI Exclusion: decisions based on cardiologist: severe cardiac failure, PMI-syndrome, aortic regurgitation, cerebral infarct hemiparesis, disease of hip, status post-poliomyelitis, amputation of lower extremity, Diabetes with retinopathy, hyper/hypo thyroidism, hyper-parathyroidism, mental illness
Interventions	Exercise intervention: Duration: 3 months; Frequency: 30 min twice weekly. Mode: physical training, interval training of large muscle groups, jogging, callisthenics Co-interventions: counselling, social measures, group and individual. Intensity: graded individually
Outcomes	Total mortality, CHD mortality, non-fatal MI up to average 14 months
Notes	Most emphasis on social/ psychological aspects. 171 patients were randomised and at discharge the cardiologist decided whether the patient was fit to take part in the rehab programme - 45 patients were excluded at this point. 7 of intervention group declined to take part, but 6 of these were seen at follow up and included in the analysis because "control group probably had a comparable number who would have declined further treatment."

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	"allocated at random"
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding (performance bias and detection bias) All outcomes	Unclear risk	Unclear in terms of assessment of outcomes.
Incomplete outcome data (attrition bias) All outcomes	High risk	Description of withdrawals & dropouts: 29% I, 33% C lost to follow up from 126 who took part. 171 were randomised and then 45 excluded by cardiologist
Selective reporting (reporting bias)	Unclear risk	No information reported.

Bertie 1992

Methods	Randomised on day of discharge after MI; F/U 12-24 months.
Participants	N = 110 (EX n:57; CON n:53) Gender: NR

Mean age: EX = 52.1 +/− 1.3, CON = 52.7 +/− 1.3
Diagnosis: <65 yrs with acute myocardial infarction confirmed by typical symptoms,
electrocardiographic changes, and a rise in cardiac creatinine kinase isoenzyme
Ethnicity: NR
Inclusion: Men and women with acute myocardial infarction and had been admitted to Plymouth
coronary care unit
Exclusion: uncontrolled heart failure; serious rhythm disturbances which persisted and required
treatment at time of discharge; another disabling disease

Interventions	Exercise group: Duration: 4 weeks; Frequency: 2 × week; Mode: standard pulse-monitored group exercise commonly used in the physiotherapy ofcardiac patients, 12 station circuit started 3 weeks post discharge Control: standard hospital care
Outcomes	Total mortality, non fatal MI, revascularisation; Assessments at day ofdischarge, 3rd week after discharge; after rehabilitation (for intervention group); four months after infarct and 12-24 months after infarct)
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	"randomised"
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding (performance bias and detection bias) All outcomes	Unclear risk	Unclear in terms of assessment of outcomes.
Incomplete outcome data (attrition bias) All outcomes	High risk	24% lost to follow-up, no description of withdrawals or dropouts
Selective reporting (reporting bias)	Unclear risk	No information reported.

Bethell 1990

Methods	Parallel RCT; single centre in Alton, Hampshire
Participants	N: 200 (EX n=99; CON n101=) Gender: 100% men Age: EX = 54.2 (+/−7.2), CON = 53.2 (+/−7.7). Diagnosis: 5 days post MI. Ethnicity:NR Inclusion: <65 yrs post MI; history of chest pain typical of MI, progressive ECG changes, rise and fall in aspartate transaminase concentrations with at least one reading above 40 units/ml Exclusion: medical or orthopaedic problems that precluded their taking part in the exercise course; insulin dependent diabetes mellitus; atrial fibrillation; on investigator's personal general practice list
Interventions	Exercise group: Duration: 3 months; Frequency: 3×/week; Mode: 8 stage circuit aerobic & weight training. Intensity: 70-85% predicted HRmax Control group: given a short talk on the sort of exercise that they might safely take unsupervised
Outcomes	Total mortality, CHD mortality, non fatal MI (11 year follow up published in 1999. 5 year follow up data from unpublished material used for meta analysis.)
Notes	229 patients were randomised; 14 in the intervention group and 15 in control dropped out before the first exercise test due to death, refusal or other problems. Therefore 200 took part in the study

Cardiac mortality of 3% pa, once patients survived to be in the trial. Suggests more severely affected patients were not included.
Significant predictors of cardiac death were pulmonary oedema on admission, complications during admission, one or more previous infarcts, increasing age and low initial fitness

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	random letter sequence
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding (performance bias and detection bias) All outcomes	Unclear risk	Unclear in terms of assessment of outcomes.
Incomplete outcome data (attrition bias) All outcomes	High risk	16% lost to follow up, no description of withdrawals or dropouts
Selective reporting (reporting bias)	Unclear risk	No information reported.

Bäck 2008

Methods	Parallel RCT, single centre in Sweden
Participants	N= 37 randomised (EX n=21; CON n=16) 86.5% male. Age 63.6 years Diagnosis: stable CAD and coronary angiographic changes. Ethnicity: NR Inclusion: coronary artery stenosis documented by angiography or previous coronary artery bypass grafting, classes I-III angina pectoris, classified according to Canadian Cardiovascular Society Exclusion: disabling disease that hindered regular exercise, or if the patient already has engaged in exercise more than 3 days/week
Interventions	Ttraining - high frequency exercise- group: 3 endurance resistance exercises and trained on a bicycle ergometer 30 min, 5 times a week for 8 months at 70% ofV02max. Duration: 8 months
Outcomes	PTCA at 2 months before PCI and 6 months after PCI
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	"randomised"
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding (performance bias and detection bias) All outcomes	Unclear risk	Unclear in terms of assessment of outcomes.

Incomplete outcome data (attrition bias) All outcomes	High risk	8.1% lost to follow-up, no description of withdrawals or dropouts
Selective reporting (reporting bias)	Unclear risk	No information reported.

Carlsson 1998

Methods	RCT; single-centre in Sweden; F/U 1 year
Participants	N= 235 (EX n=118; CON n=117) Diagnosis: AMI or CABG (4 weeks post discharge); CABG (n = 67); AMI (n = 168) Mean age: AMI patients I = 62.2 +/–5.8, C= 61.7 +/–6, CABG patients Mean age I = 62.7 +/– 4.8, C= 59.8 +/– 4.8. Ethnicity: NR Inclusion:Acute MI; coronary artery bypass revascularization surgery less than 2 weeks prior; PTCA less than 2 weeks prior Exclusion: signs of unstable angina; signs of ST-depression at exercise test of more than 3 mm in 2 chest leads or more than 2mm in two limb leads at four weeks post discharge from hospital, signs ofCHF, severe, non-cardiac disease; drinking problems, not Swedish spoken
Interventions	Exercise programme: Duration: 2-3 months; Frequency: 2-3 × weekly Session duration: 60 mins; Mode: walking and jogging followed by relaxation and light stretching exercises; Nurse counselling: 9 hours of counselling in individual & group sessions over 1 year; smoking cessation 1.5, dietary management 5.5 & physical activity 2 hours Control: usual care
Outcomes	Mortality,
Notes	Groups of 20 patients randomly allocated to intervention and control groups (usual care) . Randomised 4 weeks post discharge In first 3 weeks post discharge all participants (I & C) had 2 visits by nurse & 1 by cardiologist + all participants invited to join regular exercise group × 1 per week for 30 mins information & 30 mins easy interval training

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not reported.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding (performance bias and detection bias) All outcomes	Unclear risk	Unclear in terms of assessment of outcomes.
Incomplete outcome data (attrition bias) All outcomes	High risk	<20% lost to follow up, no description of withdrawals or dropouts
Selective reporting (reporting bias)	Unclear risk	No information reported.

Carson 1982

Methods	Randomised 6 weeks post admission
Participants	N: 303 (EX n=151; CON n=152) 100% men Mean age: EX = 50.3 (SE 0.65) years CON =52.8 (SE 0.67) years Diagnosis: MI Ethnicity: NR Inclusion: MI patients admitted to the coronary care unit; diagnosis based on ECG changes and /or elevation of serum glutamic oxaloacetic transaminase or lactic dehydro-genase taken on three consecutive days ExclusIon: >70 years; heart failure at follow-up clinic; cardio-thoracic ratio exceeding 59%; severe chronic obstructive lung disease; hypertension requiring treatment; diabetes requiring insulin; disabling angina during convalescence; orthopaedic or medical disorders likely to impede progress in the gym, personality disorders likely to render patient unsuitable for the course
Interventions	Exercise group: Duration: 12 weeks; Frequency: attended gym 2 × weekly : Mode: Exercises arranged on a circuit basis and pure isometric exercise was avoided. Control group: Did not attend gym
Outcomes	Total mortality, non fatal MI at 5 months, 1 year, 2 year and 3 year after MI (mean F/U 2.1 years)
Notes	There appears to be a reduction in mortality in exercise participants with inferior MI

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	"randomly allocated"
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding (performance bias and detection bias) All outcomes	Unclear risk	Unclear in terms of assessment of outcomes.
Incomplete outcome data (attrition bias) All outcomes	High risk	21% lost to follow up, no description of withdrawals or dropouts
Selective reporting (reporting bias)	Unclear risk	No information reported.

DeBusk 1994

Methods	Randomised 3rd day post MI.
Participants	294 men & 8 women F <70 yrs (mean age 57+/– 8), post MI, in 5 centres
Interventions	Nurse managed, home based, multifactorial risk factor intervention programme with exercise training based on De Busk/Miller. F/U 12 months
Outcomes	Total mortality
Notes	Levels of psychological distress dropped significantly for both groups by 12 months

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	"randomly allocated"
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding (performance bias and detection bias) All outcomes	Unclear risk	Unclear in terms of assessment of outcomes.
Incomplete outcome data (attrition bias) All outcomes	High risk	33% lost to follow up, no description of withdrawals & dropouts
Selective reporting (reporting bias)	Unclear risk	No information reported.

Dugmore 1999

Methods	single-centre RCT in UK; f/u 5 yrs
Participants	N=124 (EX n=62; CON n=62) Gender: 122 men Mean age: EX=54.8 y ;CON = 55.7 y Diagnosis: clinically documented MI between 1984 and 1988 Ethnicity: NR Inclusion: MI according to conventional WHO cardiac enzyme and ECG criteria ofMI Exclusion: NR
Interventions	EX : Duration: 12 months; Frequency: 3 times weekly; Mode: regular aerobic and local muscular endurance training , consisting of warm up and cool down exercises, sit ups, wall bar/bench step ups, cycle ergometry, and major component centered on training of aerobic capacity, using walking and jogging Control: "received no formal exercise training throughout the same 12 month period"
Outcomes	CV mortality; nonfatal MI; QoL at 4, 8, 12 months
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	"randomly allocated"
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding (performance bias and detection bias) All outcomes	Unclear risk	Not reported.
Incomplete outcome data (attrition bias) All outcomes	Low risk	All patients accounted for.
Selective reporting (reporting bias)	Unclear risk	No information reported.

Engblom 1996

Methods	Single-centre open RCT in Finland
Participants	**N Randomised:** Total: 228 (201 males, 27 females); EX: 119 (104 males, 15 females) UC: 109 (97 males, 12 females) **Baseline Characteristics:** *Previous unstable angina (%):* EX: 29; UC: 31 *Previous MI (%):* EX: 42; UC: 46 *Hypertension (%):* EX 31; UC 23 *LVEF (%):* EX: 70.3 (SD 11.5); UC: 71.4 (SD 12.3) **Age (years):** EX: 54.1 (SD 5.9); UC: 54.3 (SD 6.2) **Percentage male:** 88% **Percentage white:** Not reported **Inclusion/exclusion criteria:** *Inclusion: patients who underwent elective CABS* *Exclusion:* any other serious disease; ?65 years of age
Interventions	4 stage rehab over 30 months starting pre CABG with meeting of physician, psychologist and OT/PT. 6-8 weeks post CABG - 3 weeks IP with group sessions with psychologist, aerobic physical activity, relaxation & group discussion. 8 months post CABG - 2 days meeting with OT, nutritionist, physician, physio. 30 months post CABG - one day with nutritionist, physician & exercise.
	F/U I year & 6 years Usual care: no further details
Outcomes	Mortality, CABG, health-related quality of life: Nottingham Health Profile
Notes	5 years after CABG only 20% of participants were working, despite 90% of patients being in functional classes 1-2. Almost half of patients had retired pre CABG. Many other factors affect RTW post CABG - age, education, physical requirements of the job, type of occupation, self employed status, non work income, personality type, self perception of working capacity and mostly length of absence from work pre CABG

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not reported.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding (performance bias and detection bias) All outcomes	High risk	"open randomised trial" Data on deaths &admissions from the hospital records department
Incomplete outcome data (attrition bias) All outcomes	High risk	13% lost to follow up, no description of withdrawals or dropouts
Selective reporting (reporting bias)	Unclear risk	No information reported.

Erdman 1986

Methods	Single centre RCT in Rotterdam; Follow up 5 years.
Participants	N= 80 (EX n=; CON n=)

Gender: 100% male
Mean age: 51years (range 35-60 years)
Diagnosis: within 6 months post MI. Also with CABG/angina.
Ethnicity: NR
Inclusion: First MI within 6 months before the first psychologic investigation; <65 years; meet three psychologic inclusion criteria - one or more symptoms of the anxiety reaction, diminished self-esteem, positive motivation to take part in the programme
Exclusion: severe cardiomyopathy, severe valvular disorders, inadequate performance on exercise, unstable angina pectoris

Interventions	Exercise intervention: duration: 6 months: Frequency: once per week; Session duration and mode: warming up period (15min), gymnastics and jogging (both 15 mins), sports such as volleyball, soccer, and hockey (30min), relaxation exercise (5min) Controls:Usual care plus educational brochure with guidelines about physical fitness training
Outcomes	Mortality, non fatal MI at 5 years
Notes	Complex presentation of results. Authors conclude that patients who will benefit from rehab can be detected on psychological grounds. Those who have engaged in habitual exercise, but feel seriously disabled, yet do not feel inhibited in a group will benefit from rehab

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	"randomly allocated by means of a table for random numbers"
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding (performance bias and detection bias) All outcomes	Unclear risk	Unclear in terms of assessment of outcomes.
Incomplete outcome data (attrition bias) All outcomes	High risk	29 % lost to follow up, no description of withdrawals or dropouts
Selective reporting (reporting bias)	Unclear risk	No information reported.

Fletcher 1994

Methods	Prospecitve, single centre RCT in the US. F/U 6 months.
Participants	N= 88 (EX n=41; CON n=47) 100% male Mean age: EX= 62 +/−8, CON = 63 +/−7; (range 42 - 72) Diagnosis: CAD and a physical disability Ethnicity: NR Inclusion: 73 years; CAD and physical disability. CAD documented by history of MI, coronary artery bypass surgery, percutaneous transluminal coronary angioplasty or angiographically demonstrated CAD; have the functional use ofmore than 2 extremities, 1 being an arm, in order to perform the exercise test and training protocols Exclusion: uncontrolled hypertension or diabetes mellitus, clinically significant cardiac dysrhythmias, unstable angina pectoris, cognitive deficits, or other problems that would interfere with compliance to the prescribed exercise and diet protocol
Interventions	Exercise group (Home exercise training programme): Duration: 6 months; Frequency: 5 days/ week; Session duration: 20mins/day; Intensity: 85% of predicted maximal heart rate Mode: stationary wheelchair ergometer Control group: routine care

Outcomes	Total mortality, non fatal MI at 6 months
Notes	The treatment programme decreased myocardial oxygen demand.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	"randomized"
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding (performance bias and detection bias) All outcomes	Low risk	"The same experienced cardiologist interpreted all echocardiograms and was unaware of randomization procedures"
Incomplete outcome data (attrition bias) All outcomes	High risk	32% lost to follow up, no description of withdrawals or dropouts
Selective reporting (reporting bias)	Unclear risk	No information reported.

Fridlund 1991

Methods	Single centre RCT in Sweden. F/U 1 & 5 years.
Participants	N=178 (EX n=87; CON n=91) randomized N=116 (EX n=53; CON n=63) participated in the 1year F/U Gender: 101 men & 15 women Mean age: EX=55 years CON=57.6 years Ethnicity: NR Inclusion: 65 years or younger at the time of MI; independent living in the Health Care District after discharge from hospital; meaningful communication and rehabilitation that was not hindered by the MI or other serious illness Exclusion:cerebral or cardiac disorders or serious alcohol abuse
Interventions	Exercise group: Duration: 6months; Frequency: 1 weekly; Session duration: 2hrs; Mode: 1 hours exercise + 1 hours group discussion led by nurse Control: routine cardiac follow-up
Outcomes	Total mortality, non fatal MI, revascularisations
Notes	Positive long term effects on physical condition, life habits, cardiac health knowledge. No effects found for cardiac events or psychological condition

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	**"randomly subdivided"**
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding (performance bias and detection bias) All outcomes	Unclear risk	Unclear in terms of assessment of outcomes.

| Incomplete outcome data (attrition bias) All outcomes | High risk | 32% lost to follow up, no description of withdrawals or dropouts |
| Selective reporting (reporting bias) | Unclear risk | No information reported. |

Giallauria 2008

Methods	Parallel single centre RCT in Italy; 6 month F/U
Participants	N=61 (EX n=30; CON n=31) 72.1% male. Mean age: EX=55.9 years; CON=55.1 years Diagnosis: post-infarction Ethnicity: NR Inclusion: acute ST elevation MI Exclusion: residual myocardial ischemia, severe ventricular arrhythmias, AV block, valvular disease requiring surgery, pericarditis, severe renal dysfunction (creatinine >2.5 mg/dL)
Interventions	Exercise group: Duration: 6 month; Frequency: 3×/week; Session duration: 30 min; Mode: bicycle ergometer; Intensity: target of 60-70% of Vo2 peak achieved at the initial symptom-limited cardiopulmonary exercise test Control group: discharged with generic instructions to maintaining physical activity and a correct lifestyle
Outcomes	Fatal/non-fatal MI (6month F/U)
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	"randomized"
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding (performance bias and detection bias) All outcomes	Unclear risk	The physician performing all Doppler-echocardiography and cardiopulmonary exercise tests was unaware of the results of blood sampling and was blinded to the patient allocation into the study protocol Unclear in terms of assessment of outcomes.
Incomplete outcome data (attrition bias) All outcomes	Low risk	All patients were accounted for.
Selective reporting (reporting bias)	Unclear risk	No information reported.

Haskell 1994

| Methods | Multicentre parallel RCT (4 centres in US) ; F/U 4 years |
| Participants | N=300 (EX n=145; CON n=155)
Gender: 259 men & 41 women
Mean age: EX = 58.3 =/− 9.2, CON = 56.2 +/− 8.2.
Diagnosis: CAD
Ethnicity: NR |

Inclusion: < 75 years; clinically indicated coronary arteriography. After arteriography, patients received PTCA or CABG and remained eligible if at least one major coronary artery had a segment with lumen narrowing between 5% and 69% that was unaffected by revascularization procedures
Exclusion: severe congestive heart failure, pulmonary disease, intermittent claudication, or noncardiac life-threatening illnesses; no qualifying segments, medical complication occurred during angiography, left ventricular ejection fraction of less than 20%, or patient was in another research study

Interventions	Exercise group (risk reduction group): Intructed by dietitian in a low-fat, low-cholesterol, and high-carbohydrate diet with a goal of <20% of energy intake from fat, <6% from saturated fat, and <75mg of cholesterol per day. Physical activity program : increase in daily activities such as walking, climbing stairs, and household chores and a specific endurance exercise training program with the exercise intensity based on the subject's treadmill exercise test performance. (Nurse managed, home based programme based on Miller, with specific goals to be attained) Control group: usual care F/U 4 years.
Outcomes	Total & CHD mortality, non fatal MI, revascularisation at yr 1, 2, 3 and 4
Notes	The rate of change in the minimal coronary artery diameter was 47% less in I than C. This was still significant when adjusted for age and baseline segment diameter (p=0.03)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	"stratified random numbers in sealed envelopes"
Allocation concealment (selection bias)	Low risk	"stratified random numbers in sealed envelopes"
Blinding (performance bias and detection bias) All outcomes	Unclear risk	Unclear in terms of assessment of outcomes.
Incomplete outcome data (attrition bias) All outcomes	High risk	18% lost to follow up, no description of withdrawals or dropouts
Selective reporting (reporting bias)	Unclear risk	No information reported.

Heller 1993

Methods	Cluster randomised multi-centre study (hospitals in and around Newcatle, Australia); F/U of 6 months
Participants	N=450 (EX n=213; CON n=237) 71% male Mean age: EX = 59 +/− 8, CON = 58 +/− 8 years Diagnosis: Ethnicity: NR Inclusion: <70 years with a suspected heart attack registered by the Newcastle collaborating centre of the WHO MONICA Project and discharged alive from hospital Exclusion: renal failure or other special dietary requirements and those considered by their physicians to have 'endstage' heart disease
Interventions	Exercise group: 3 packages to participant - 1st package: Step 1"Facts on fat" kit, together with walking programmme information (also (encouragement to walk in the form of a magnetic reminder sticker), and "Quit for Life" program for smokers. 2nd package: Step 2-3 "Facts on fat" kit; exercise log. 3rd package: Step 4-5 "Facts on fat" kit, together with information regarding local "Walking for Pleasure" groups Control group: usual care

Outcomes	Total mortality, health-related quality of life: QLMI Study outcomes assessed at 6 months	
Notes	Low use of preventative services (dietary, anti smoking) by both groups. 10% of patients received rehab - mostly having had CABG.	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Cluster randomisation by GP.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding (performance bias and detection bias) All outcomes	Unclear risk	Unclear in terms of assessment of outcomes.
Incomplete outcome data (attrition bias) All outcomes	High risk	17% lost to follow up, no description of withdrawals or dropouts
Selective reporting (reporting bias)	Unclear risk	No information reported.

Hofman-Bang 1999

Methods	Single-center, RCT in Sweden; F/U 2 years
Participants	N=87 (EX n=46; CON=41) Gender 83.9% male Mean age: EX=53 years; CON=53 years Diagnosis: treated with percutaneous transluminal angioplasty Ethnicity: NR Inclusion: at least one significant coronary stenosis suitable for PTCA and at least one additional clinically insignificant coronary atherosclerotic lesion that could be evaluated by quantitative computerized angiography; <65 years; employed; able to perform a bicycle ergometer test with a minimum capacity of 70 W following the PTCA; absence of other disease of importance for completion of the programme
Interventions	Exercise group: 12 month rehabilitation programme (intense health education and activities promoting behavioural changes - stress management, diet, exercise and smoking habits). Each subject was assigned a daily individual task including self-observation, Type A behavioural drills, relaxation training and exercise. This programme is followed by 11-month step-down period, leaving the patients on their own during the second year of follow up Control group: standard care
Outcomes	Cardiovascular mortality, MI, CABG, PTCA, health-related quality of life: AP-QLQ recorded during the 2 years F/U
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	"randomly assigned"

Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding (performance bias and detection bias) All outcomes	Unclear risk	Unclear in terms of assessment of outcomes.
Incomplete outcome data (attrition bias) All outcomes	High risk	21.8 % lost to follow up, no description of withdrawals or dropouts
Selective reporting (reporting bias)	Unclear risk	No information reported.

Holmbäck 1994

Methods	Single centre RCT in Sweden; F/U 1 yr
Participants	N= 69 (EX n=34; CON n=35) Gender: 67 men & 2 women Mean age 55, range 38 - 63 years Diagnosis: Post-MI Inclusion: Acute MI patients under 65 years of age Exclusion: Not stated by patients have been excluded for being incapable of performing strenuous training due to poor left ventricular function or arrhythmias, orthopaedic disorders, other incapacitating somatic diseases or mental disorders
Interventions	Exercise group: Duration: 12 weeks starting 8 weeks post MI.; Frequency: 2× per week; Session duration and mode: at least 45 mins (bicycling 10 mins, callisthenics 10min, jogging 15 min, relaxation 10min); Intensity: 70% to 85% of peak heart rate at the bicycle test for initial session and workload individually adjusted to obtain the desired maximum heart rate if possible Control group: not enrolled in the training programme
Outcomes	Total mortality, non-fatal MI & revascularisation. health-related quality of life: Self report questionnaire. Evaluations at 6 weeks and 1 year post MI
Notes	Authors found no benefit from exercise training. Outcomes were related to self-rated levels of physical and psychological well being

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	"Randomization was performed according to random numbers in sealed envelopes"
Allocation concealment (selection bias)	Low risk	"Randomization was performed according to random numbers in sealed envelopes"
Blinding (performance bias and detection bias) All outcomes	Unclear risk	Unclear in terms of assessment of outcomes.
Incomplete outcome data (attrition bias) All outcomes	High risk	14.5% lost to follow up, no description of withdrawals or dropouts

Selective reporting (reporting bias)	Unclear risk	No information reported.

Kallio 1979

Methods	RCT in 2 Finnish centres; F/U 3 years.
Participants	N= 375 (EX n=188; CON n=187) Gender: 80.3% male Mean age: EX=54.4 years; CON=54.1 years Diagnosis; acute myocardial infarction. Ethnicity: NR Inclusion: AMI based on WHO criteria
Interventions	Exercise group (Intervention group) consisted of anti-smoking and dietary advice, and discussions on psychosocial problems as well as a physical exercise programme, tailored to the individual's working capacity determined in a bicycle ergometer test Control group: usual care
Outcomes	Total mortality; Cardiovascular mortality (F/U 3 years)
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	"randomly allocated"
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding (performance bias and detection bias) All outcomes	Unclear risk	Unclear in terms of assessment of outcomes.
Incomplete outcome data (attrition bias) All outcomes	Low risk	1% lost to follow up.
Selective reporting (reporting bias)	Unclear risk	No information reported.

Kovoor 2006

Methods	RCT in Australia (2 centres); F/U 6 months
Participants	N=142 (EX n=70; CON n=72) Mean age: EX=56.2; CON=55.8 years Male: EX=89% vs CON=86% Diagnosis: had an AMI Ethnicity: NR Inclusion: AMI; <75 years of age; no angina; <2mm ST-segment depression with exercise and if they attained >7-METS workload; left ventricular ejection fraction >40% or no inducible ventricular tachycardia
Interventions	Exercise (conventional treatment group): 5 week rehabilitation program consisted of exercise, education, and counseling sessions that were held 2 to 4 times per week, including work at 6 weeks after AMI Control group (ERNA - early return to normal activities group): work at 2 weeks after AMI without a formal rehab program

Outcomes	Total mortality; fatal/non-fatal mortality; CABG; PTCA; HRQL Assessment at 6 weeks and at 6 months
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	"randomisation schedules were generated by an independent investigator" Comment: no description of randomisation methods.
Allocation concealment (selection bias)	Low risk	"…opaque sealed envelopes. These envelopes were opened by the nurse coordinator only at randomization of a patient"
Blinding (performance bias and detection bias) All outcomes	Unclear risk	"GHPS..analysed in a blinded fashion by an independent nuclear medicine specialist" Comment: Unclear in terms of other relevant outcomes.
Incomplete outcome data (attrition bias) All outcomes	High risk	20.4% lost to follow-up, no description of withdrawals or dropouts
Selective reporting (reporting bias)	Unclear risk	No information reported.

La Rovere 2002

Methods	Parallel RCT; single-centre f/u 10 yrs
Participants	N=95 (EX: n=49; CON: n=46) Age: EX: 51 years; CON: 52 years 100% males Diagnosis: surviving first uncomplicated MI Ethnicity: NR Inclusion: post MI patients admitted at Centro Medico di Montescano in 1984 and 1985 Exclusion: atrial fibrillation or abnormal sinus node function, insuline-dependent diabetes, exercise-induced myocardial ischemia, and arterial BP > 160/90
Interventions	EX: Duration: 4-week endurance training; session duration: 30 minutes, 5 times a week; mode: callisthenics and stationary bicycle ergometry. All patients attended sessions, held by cardiologist and psychologist, dealing with secondary prevention of cardiovascular disease and stressing dietary changes and smoking cessation UC: "no training"
Outcomes	Cardiac mortality; nonfatal MI; CABG at 3 to 4 month intervals from the time of entry into the study for the first 3 years and contacted periodically by telephone thereafter
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	"randomized"
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding (performance bias and detection bias) All outcomes	Unclear risk	Unclear in terms of assessment of outcomes.

Incomplete outcome data (attrition bias)bias) All outcomes	Low risk	All patients accounted for.
Selective reporting (reporting bias)	Unclear risk	No information reported.

Leizorovicz 1991

Methods	RCT in 4 participating hospitals in France F/U 2 years
Participants	N=182 (EX n=61; CON n=60) n=60 for counselling group 100% male Mean age: EX = 51, CON = 49 yrs. Diagnosis: MI Ethnicity: NR Inclusion: admitted to participating CCUs with suspected MI; under 65 years old with typical MI, no major irreversible complication or disability Exclusion: contraindication to exercise testing i.e., recent stroke, disability of lower limbs, uncontrolled heart failure, severe rhythm disturbances, SBP> 180 mmHg, severe angina pectoris, or abnormalities triggered by baseline exercise test
Interventions	Exercise group (rehab programme): Duration: 6 week; Frequency 3×/week; Session duration and mode: 25min cycloergometer Intensity: 80% of maximal heart rate. Also included walking, gymnastic and respiratory physiotherapy, relaxation, recommendations on control ofcardiovascular risk factors; recommendations to continue regular physical training at the end of the 6 week programme Control: usual care
Outcomes	Non fatal MI, angina, surgery, smoking
Notes	Only 14% of all MI patients admitted to the participating hospitals were randomised to the trial. Exclusion of women and patients >65 accounted for 60% of exclusions

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not reported.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding (performance bias and detection bias) All outcomes	Unclear risk	Unclear in terms of assessment of outcomes.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No losses to follow up.
Selective reporting (reporting bias)	Unclear risk	No information reported.

Lewin 1992

Methods	F/U 1 year
Participants	126 men & 50 women, mean age 55.8 yrs, post MI.
Interventions	Heart manual: home based facilitated programme with manual and tapes, 3 stage exercise plan - home, walking and life long, graded according to patient's ability. Control had placebo facilitator's time. F/U 1 year
Outcomes	HRQL: HAD; GHQ
Notes	Study terminated (due to expiry of funding) before all pts reached 6 or 12-month stage. Anxiety scores showed significant treatment effect @ 6 weeks and 1 year, depression @ 6 weeks. Pre hospital discharge 52% of all pts had HAD scores indicating clinically significant anxiety or depression (8+). C were significantly more anxious and depressed at all follow ups

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	"allocated to the experimental or control group by use of a written pre-determined randomisation protocol" Methods not described.
Allocation concealment (selection bias)	Unclear risk	Not described.
Blinding (performance bias and detection bias) All outcomes	Unclear risk	"The medical secretary who held the list was blind to the purpose of the study and to the patients taking part, and the cardiologist and nursing staff were blind to which study group the patients were in" Unclear in terms of assessment of outcomes.
Incomplete outcome data (attrition bias) All outcomes	High risk	17% lost to follow up, no description of withdrawals or dropouts
Selective reporting (reporting bias)	Unclear risk	No information reported.

Manchanda 2000

Methods	Single-centre RCT in India; f/u 1 yr
Participants	N=42 (EX n=21; CON n=21) 100% male Mean age: EX = 51 years; CON=52 years Diagnosis: chronic stable angina and angiographically proven CAD Ethnicity: NR Inclusion: chronic stable angina and angiographically proven CAD
	Exclusion: recent (within last six months) MI or unstable angina
Interventions	Exercise group: program consisting of yoga at home for average of 90 min daily, control of risk factors, diet control and moderate aerobic exercise Control: usual care = àCmanaged by conventional methods i.e. risk factor control and American Heart Association step I diet"
Outcomes	total mortality; CABG; PTCA Assessments are baseline and 1 yr.
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement

Random sequence generation (selection bias)	Unclear risk	"randomized"
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding (performance bias and detection bias) All outcomes	Unclear risk	"Two independent observers who were blinded to group allocation analysed all arteriograms" Blinding of other outcome assessments were not mentioned.
Incomplete outcome data (attrition bias) All outcomes	Low risk	All patients accounted for.
Selective reporting (reporting bias)	Unclear risk	No information reported.

Marchionni 2003

Methods	Single-centre RCT in Italy; f/u 14 mos
Participants	N= 270 (EX n=90; Home n=90; CON n=90) Gender: 67.8% males Mean age: 69 years Diagnosis: post-MI Ethnicity: NR Inclusion: >56 years; referred to unit for functional evaluation 4 to 6 weeks after MI Exclusion: severe cognitive impairment or physical disability, left ventricular EF <35%, contraindications to vigorous physical exercise, eligibility for myocardial revascularization because of low-effort myocardial ischemia, refusal, or living too far from the unit
Interventions	EX: Hospital-CR: program consisted of 40 exercise sessions: 24 sessions (3/wk) of endurance training on cycle ergometer (5-min warm-up, 20-min training at constant workload, 5-min cool down, 5-min post-exercise monitoring) plus 16 (2/wk) 1-hr sessions of stretching and flexibility exercises Home-CR: 4-8 supervised instruction sessions in CR unit, where taught how to perform training at home; then patients received exercise prescription similar to Hosp-CR group CON: no CR, attended single structured session on CV risk factor management with no exercise prescription and were referred back to their family physicians
Outcomes	mortality, MI, CABG, PTCA, HRQL at month 2, 8 and 14 costs over study duration
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not reported.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding (performance bias and detection bias) All outcomes	Unclear risk	Unclear in terms of assessment of outcomes.
Incomplete outcome data (attrition bias) All outcomes	High risk	38 (14.1%) dropped out; clinical event data for these patients not reported per treatment group

Selective reporting (reporting bias)	Unclear risk	No information reported.

Miller 1984

Methods	Randomised 3 weeks post MI
Participants	198 men < 70 yrs with MI. Mean age 52 +/−9.
Interventions	Patients divided into 5 interventions; 1a-extended home 1b-brief home 2a-extended group 2b-brief group 3-ETT but no further training 4-no ETT or training.
	Home; detailed instructions + HR monitors. If free of ETT induced angina @3 weeks pts used stationary bikes for 30 mins/day, 5 days/week. If had ETT induced angina @ 3 weeks, brisk walking programme for 100 mins/week. 2× weekly telemetry to base from HR monitors. Brief intervention trained for 8 weeks, extended intervention for 23 weeks. Group intervention trained in a group with clinical supervision for 8 or 23 weeks for 3 × 1 hour/week with 100 mins/week at training rate All pts in 1a & b, 2 a & b and 3 received counselling from a physician (30-45 mins) and nurse (30-45 mins). F/U 23 weeks.
Outcomes	CHD mortality, non fatal MI and revascularisation
Notes	Low rate of cardiac events reflects identification of low risk population. Group 3 were unexpectedly active, th authors concluding that ETT + good explanation may enhance physical activity in the early stages

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not reported.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding (performance bias and detection bias) All outcomes	Unclear risk	Unclear in terms of assessment of outcomes.
Incomplete outcome data (attrition bias) All outcomes	High risk	5% lost to follow up, no description of withdrawals or dropouts
Selective reporting (reporting bias)	Unclear risk	No information reported.

Oldridge 1991

Methods	Stratified by status (work type and employed or not) and randomised at time of MI. All participants were depressed and/or anxious (Beck Depression Inventory <5, < 43 on Spielberger State Anxiety Inventory, or <42 on Spielberger Trait Anxiety Inventory.)
Participants	177 men & 24 women with MI. Mean age I =52.9+/− 9.5 yrs, C = 52.7 +/− 9.5 yrs.
Interventions	ET for participant & spouse. 50 minutes 2 × weekly for 8 weeks at 65% of HRmax during ETT. Plus cognitive behavioural group intervention of 8 sessions of 1.5 hours + relaxation.
	CPR training offered to spouse. F/U 1 year.
Outcomes	Mortality health-related quality of life: QOLMI time trade-off.
Notes	Both groups improved over 12 months, with the biggest changes occurring in the first 8 weeks

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	"randomized"
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding (performance bias and detection bias) All outcomes	Unclear risk	Unclear in terms of assessment of outcomes.
Incomplete outcome data (attrition bias) All outcomes	High risk	For the primary outcome -HRQL- 9% lost to follow up, no description of withdrawals or dropouts
Selective reporting (reporting bias)	Unclear risk	No information reported.

Ornish 1990

Methods	Prospective RCT in US (patients recruited from 2 sites) F/U 5 years
Participants	N= 48 (EX n=28; CON n=20) Gender: NR for all 48 patients Mean age: EX = 56.1 +/− 7.5; CON=59.8 +/− 9.1 years Diagnosis: moderate to severe CAD (MI, PTCA, CABG, angina) Ethnicity: NR Inclusion: 35-75 years, male or female; residence in the greater San Francisco area; no other life-threatening illnesses; no MI during the preceding 6 weeks, no history of receiving streptokinase or alteplase; not currently receiving lipid-lowering drugs; 1, 2, 3 vessel coronary artery disease (defined as any measurable coronary atherosclerosis in a non-dilated or non-bypass grafting; permission granted by patient's cardiologist and primary care physician
Interventions	Exercise intervention: exercise (typically walking) for a minimum of 3 hours per week and 30 min per session; target training heart rate of 50-80%. Co-interventions: stress management, low fat vegetarian diet, group psychosocial support . 1 year duration Control group: usual care.
Outcomes	CHD mortality, non-fatal MI, revascularisation, Assessment at baseline and after 1 year and 5 year
Notes	I had 91% reduction in reported frequency of angina after 1 year and 72% after 5, C had 186% increase in reported frequency of angina after 1 year and 36% decrease after 5. I had 7.9% relative improvement in coronary artery diameter at 5 years, C had 27.7% relative worsening at 5 years

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	"randomly assigned"
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding (performance bias and detection bias) All outcomes	Low risk	"…investigators carrying out all medical tests remained unaware of both patient group assignment and the order of the tests. Different people provided the lifestyle intervention, carried out the tests, analysed the results, and carried out statistical analyses. Coronary arteriograms were analysed without knowledge of sequence or of group assignment."
Incomplete outcome data (attrition bias) All outcomes	High risk	45/93 (48%) of randomised patients did not participate, no description of withdrawals or dropouts
Selective reporting (reporting bias)	Unclear risk	No information reported.

Schuler 1992

Methods	Participants randomised after routine angiography for angina. 66% study population had previous MI. All participants spent one week as inpatient on a metabolic ward receiving instruction on exercise and diet
Participants	113 men with CAD, aged 35 - 68 yrs (mean 53.5)
Interventions	2 further weeks as IP, then daily exercise at home on cycle (30 mins at 75% HR max) + 2 group training sessions of 60 mins/week. Informative session held 5 times/year for participants and spouses. F/U yearly for 6 years.
Outcomes	Total and CHD mortality, non fatal MI, revascularisation,
Notes	Exercise adherence in the first year was 68% (39-92%, over the next 5 years 33% (389%). Pts with regression of coronary atheroma attended exercise sessions significantly more often (54+/− 24%) than patients with no change (20+/− 24%) or progression 31+/− 20%)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not reported.
Allocation concealment (selection bias)	Low risk	"sealed envelopes"
Blinding (performance bias and detection bias) All outcomes	Unclear risk	Unclear in terms of assessment of outcomes.
Incomplete outcome data (attrition bias) All outcomes	High risk	20% lost to follow up, no description of withdrawals or dropouts

Selective reporting (reporting bias)	Unclear risk	No information reported.

Seki 2003

Methods	Single centre RCT in Japan; F/U 6 months.
Participants	N= 38 (EX n=20; CON n=18) 100% male Mean age: 70 years Ethnicity: Japanese patients Diagnosis: Chronic CAD Inclusion: referred at least 6 months after a major coronary event, including acute MI, coronary artery bypass grafting or percutaneous balloon angioplasty for acute coronary syndrome
Interventions	Exercise: Duration 6 months; Frequency: weekly; Session duration and mode: 20-30min upright aerobic and dynamic exercise (walking, bicycling, jogging etc) and light isometric exercise (hand weights) and 20 min cool-down stretching and callisthenics. Intensity: prescribed individually at the anaerobic threshold level at baseline. Patients also encouraged to exercise twice a week outside the clinicCo intervention: dietary and educational program Control group: standard care
Outcomes	health-related quality of life at 6 months
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	"randomly assigned..by envelope method"
Allocation concealment (selection bias)	Unclear risk	"randomly assigned..by envelope method"
Blinding (performance bias and detection bias) All outcomes	Unclear risk	Unclear in terms of assessment of outcomes.
Incomplete outcome data (attrition bias) All outcomes	Low risk	All 38 patients accounted for.
Selective reporting (reporting bias)	Unclear risk	No information reported.

Seki 2008

Methods	Single centre RCT in Japan; F/U months
Participants	N= 39 (EX n=20; CON n=19) 100% male Mean age: 69.5 years Diagnosis: stable CAD Ethnicity: Japanese patients Inclusion: <65 years old with stable CAD Exclusion:ongoing congestive heart failure, liver dysfunction, renal dysfunction, or systemic diseases, including malignancy and collagen disease
Interventions	EX:exercise training Duration 6 months; Frequency: weekly; Session duration and mode: 20-60min upright aerobic and dynamic exercise (walking, bicycling, jogging etc) and light

isometric exercise (hand weights) and 15 min cool-down stretching and callisthenics. Intensity: prescribed individually at the anaerobic threshold level as measured by a treadmill exercise test. Patients also encouraged to perform aerobic exercise twice weekly (30 min) at home. Co-intervention: diet therapy, and weekly counselling
Control: usual outpatient care

Outcomes	Total mortality; non-fatal/fatal mortality. See notes below.
Notes	"No subject in either group showed any worsening of symptoms or had clinical events during this study."

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	"randomly assigned"
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding (performance bias and detection bias) All outcomes	Unclear risk	Unclear in terms of assessment of outcomes.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	No information reported.
Selective reporting (reporting bias)	Unclear risk	No information reported.

Shaw 1981

Methods	Participants treated at one of 5 participating centres. Participants randomised after participating in low level exercise course for 6 weeks
Participants	651 men aged 30 - 64 yrs with MI between 8 weeks and 3 years prior to start of study (mean 14 months). Mean age I = 51.5+/− 7.4, C= 52.1 +/− 7.2
Interventions	ET- 1 hour/day, 3 days/week for 8 weeks. 6 station circuit + gym exercises or swimming and games. F/U 3 years. Long term follow up to 19 years published in 1999, but not used for meta analysis
Outcomes	Total & CHD mortality, non fatal MI
Notes	90% of ET attended 90% of 24 scheduled sessions post randomisation, only 48% attending > 50% of sessions at 18 months. 30% of control alleged exercising regularly, on own initiative. At 19 years any protective effect form the programme had decreased over time, but an increase with PWC from the beginning to the end of the trial was associates with a consistent reduction in mortality throughout the 19 years of follow up

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	"randomized"

Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding (performance bias and detection bias) All outcomes	Unclear risk	Unclear in terms of assessment of outcomes.
Incomplete outcome data (attrition bias) All outcomes	High risk	6.5% lost to follow up, no description of withdrawals or dropouts
Selective reporting (reporting bias)	Unclear risk	No information reported.

Sivarajan 1982

Methods	Multicentre study. Random allocation of individuals to two intervention groups (exercise only or exercise plus teaching and counselling) and a control group (usual care)
Participants	258 patients (>80% men) aged <71 yrs. Mean age I = 55.6+/− 9.3, 56.3 +/− 8.3, C = 57.1 +/− 7.3. Following acute MI.
Interventions	All patients exercise whilst in hospital. Ex only: Weekly clinic appointments 3 months post discharge for progressive callisthenics and walking. Exercise 2 × daily until RTW and then × 1 daily. Ex + T&C: Same exercise programme + 8 × 1 hour teaching/ counselling sessions with family & friends F/U 6 months.
Outcomes	Total mortality; health-related quality of life: Sickness Impact Profile
Notes	Several reports of the same trial all with various bits of information. Authors conclude that multiple intervention trial ofthis short duration did not change patient's behaviour. MI itself acts as a strong stimulus to alter behaviour with respect to risk factors

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not reported.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding (performance bias and detection bias) All outcomes	Unclear risk	Unclear in terms of assessment of outcomes.
Incomplete outcome data (attrition bias) All outcomes	High risk	24% lost to follow up, no description of withdrawals or dropouts
Selective reporting (reporting bias)	Unclear risk	No information reported.

Specchia 1996

Methods	Randomised at hospital discharge. All participants went to a rehab centre for 3 weeks for ETT, 24 hour tape. All participants had sessions with cardiologist & psychologist for secondary prevention advice
Participants	182 men & 18 women < 65 yrs with MI. Mean age I = 51.5 +/−7, C= 54.3+/−8.
Interventions	4 weeks supervised cycling for 30 mins 5 days/week + callisthenics @ 75% max work capacity. After discharge to walk for 30 minutes every 2 days. F/U 34 months.
Outcomes	CHD mortality, revascularisations
Notes	Ejection fraction was the only prognostic factor. Among 51 patients with EF <41%, relative risk for the 27 untrained participants was 8. 63 times higher than for 24 trained ones. (p=0.04) If EF > 40%, estimated risk for untrained participant was 1.07 times higher than for trained

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	"randomized"
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding (performance bias and detection bias) All outcomes	Unclear risk	Unclear in terms of assessment of outcomes.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No losses to follow up.
Selective reporting (reporting bias)	Unclear risk	No information reported.

Stern 1983

Methods	Randomized by blocks of 6 into one of three groups: exercise, group counselling & control. Eligibility - work capacity <7 METs (men), <6 METs (women), Taylor Manifest Anxiety Scale raw score of 19+ and/or Zung self rating Depression Scale raw score of 40+
Participants	91 men & 15 women aged 30-60 yrs with MI between 6 weeks and 1 year prior to entry to study
Interventions	3×1 hour sessions/week over 12 week period for 36 sessions. All exercises dynamic against resistance, exercising upper limb and lower limb alternately for 4 minutes with 2 mins rest in between. Target HR 85% of HRmax at ETT. F/U 1 year.
Outcomes	Mortality, non fatal MII
Notes	Minimal differences between groups at one year.

Risk of bias

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

Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding (performance bias and detection bias) All outcomes	Unclear risk	Unclear in terms of assessment of outcomes.
Incomplete outcome data (attrition bias) All outcomes	High risk	7.7% lost to follow up, no description of withdrawals or dropouts
Selective reporting (reporting bias)	Unclear risk	No information reported.

Ståhle 1999

Methods	Single-centre RCT in Sweden; f/u 1 y
Participants	109 patients ?65 years (80% males) admitted to hospital because of acute coronary event (defined as either acute MI, n=64; or episode of unstable angina, n=45) EX: n=56 (mean age = 71 y, range 64-84; 41 men) UC : n=53 (mean age = 68 y, 65-83; 40 men)
Interventions	EX : 50 min aerobic outpatient group-training programme (including warm-up and cool-down) 3 times a week for 3 mos. Complete programme was supervised by specialized physiotherapist and supported by music which guided intensity of performance during session). Training followed by 10 min of music-supported relaxation. After 3 mos, patients had possibility of participating in programme once a week for another 3 mos UC: encouraged to re-start usual/prior physical activity as soon as they felt fit
Outcomes	total mortality, CABG, PTCA, health-related quality of life; Karolinska Questionnaire at 12-months
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not reported.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding (performance bias and detection bias) All outcomes	Unclear risk	Unclear in terms of assessment of outcomes.
Incomplete outcome data (attrition bias) All outcomes	High risk	Clinical event data for 8 (7%) who withdrew before 3 months were not accounted for at 1 yr
Selective reporting (reporting bias)	Unclear risk	No information reported.

Toobert 2000

Methods	Randomised controlled trial with follow-up of 24 months.
Participants	28 postmenopausal women with coronary heart disease, defined as atherosclerosis, MI, percutaneous transluminal coronary angioplasty, and/or coronary bypass graft surgery. Mean age: 64 years
Interventions	Randomised to PrimeTime program (very low-fat vegetarian diet, stress-management training, exercise, group support, and smoking cessation) or to usual care n=17 for PrimeTime program and n=11 for usual care
Outcomes	health-related quality of life: SF-36 at 24 months
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	"randomized"
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding (performance bias and detection bias) All outcomes	Unclear risk	Unclear in terms of assessment of outcomes.
Incomplete outcome data (attrition bias) All outcomes	High risk	3/28 (10.7%) patients lost to follow-up, no description of withdrawals or dropouts
Selective reporting (reporting bias)	Unclear risk	No information reported.

Vecchio 1981

Methods	Randomised after ETT, 30 days after MI.
Participants	50 patients aged 40 to 60 yrs with MI (mean 50.1).
Interventions	6 weeks physical training programme. F/U 1 year.
Outcomes	CV mortality
Notes	Trained patients showed a better mid term prognosis than controls, but this could not be explained by the physical training procedure

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not reported.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding (performance bias and detection bias) All outcomes	Unclear risk	Unclear in terms of assessment of outcomes.
Incomplete outcome data (attrition bias) All outcomes	High risk	24% lost to follow up, no description of withdrawals or dropouts

| Selective reporting (reporting bias) | Unclear risk | No information reported. |

Vermeulen 1983

Methods	Randomised 4-6 weeks post MI after ETT.
Participants	98 men aged 40- 55 yrs with MI. Mean age I = 49.4 +/− 3.7, C = 49.1 +/− 4.5.
Interventions	Rehabilitation programme. F/U 5 years
Outcomes	Mortality, non fatal MI,
Notes	Authors conclude that cardiac rehab benefits patients after MI due to direct effect on myocardial perfusion and to lowering of cholesterol levels

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	"randomized"
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding (performance bias and detection bias) All outcomes	Unclear risk	Unclear in terms of assessment of outcomes.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No losses to follow up.
Selective reporting (reporting bias)	Unclear risk	No information reported.

VHSG 2003

Methods	RCT of 2 years duration
Participants	197 patients admitted to hospital for acute MI, unstable angina pectoris or after coronary artery bypass grafting. 82.2% male. Mean age: 55 years n=98 for intervention group and n=99 for usual care group.
Interventions	EX: lifestyles intervention program (low fat diet, regular exercise, smoking cessation, psychosocial support and education, delivered by nurses on the rationale for pharmacological and lifestyle measures) Usual care
Outcomes	Total mortality
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	'randomised'

Allocation concealment (selection bias)	Low risk	'[Randomization] was performed with pre-prepared sealed opaque envelopes containing details on group allocation. The patients opened the envelopes themselves so that their allocation to IP or UC was revealed to them without the prior knowledge of the study investigators'
Blinding (performance bias and detection bias) All outcomes	Unclear risk	Unclear in terms of assessment of outcomes.
Incomplete outcome data (attrition bias) All outcomes	High risk	17.8 % lost to follow up, no description of withdrawals or dropouts
Selective reporting (reporting bias)	Unclear risk	No information reported.

WHO 1983

Methods	24 centre, pan European study conducted between 1973 and 1978. Randomised on discharge from hospital. 12 centres accepted for meta analysis
Participants	160 Men < 65 yrs with first or consecutive MI. Mean age for all participants I = 52.3, C= 53.5.
Interventions	Comprehensive programme dependent on local provision. Physical training was not compulsory but was strongly recommended. F/U 3 years Local training for 6 weeks
Outcomes	Total mortality, CVD, CHD & sudden death. Fatal & non fatal re-infarction.
Notes	Methodological problems with the execution of the study allowed only death and rein-farction to be successfully used as endpoints

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Individually randomised, but method unclear.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding (performance bias and detection bias) All outcomes	Unclear risk	Unclear in terms of assessment of outcomes.
Incomplete outcome data (attrition bias) All outcomes	High risk	No description of withdrawals or dropouts. Varied greatly from site to site
Selective reporting (reporting bias)	Unclear risk	No information reported.

Wilhelmsen 1975

Methods	Randomised on discharge. All patients received information on increasing physical activity during convalescence

Participants	280 men & 35 women < 55 yrs with MI. Mean age 50.6.
Interventions	Training programme 3 months after MI, 3 × half hour sessions per week based in hospital, at home or in workplace. F/U 5 years
Outcomes	Mortality, re-infarction.
Notes	1 year post MI, 39% of those who started training were training at the hospital. A further 21% trained at home or at work

Risk of bias

Bias	Authors judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	"By the use of a random number table the patients were allocated…"
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding (performance bias and detection bias) All outcomes	Low risk	"The exercise test 1 yr after the MI followed the same protocol but was conducted by another physician, who did not know if the patients belonged to the experimental or the control group."
Incomplete outcome data (attrition bias) All outcomes	Low risk	No losses to follow up for clinical events.
Selective reporting (reporting bias)	Unclear risk	No information reported.

Yu 2003

Methods	Unblinded, single-centre RCT in China; f/u 2 y
Participants	112 obese patients with CHD who had either recent AMI (n=72) or had undergone elective PCI (n=40) within 6 wks EX: n=72 (mean age = 62.3 y; 59 men, 13 women) UC : n=40 (mean age = 61.2 y; 30 men, 10 women)
Interventions	EX : Phase 1 was impatient ambulatory program that lasted 7-14 d; phase 2 was 16-session, twice weekly, outpatient exercise and education program lasting for 8 weeks, each session included 1 hr of education class followed by 2 hrs of exercise training, 1st hour oftraining was conducted by physiotherapist; phase 3 was community-based home exercise program for another 6 mos; phase 4 was long-term follow-up program until end of 2 years which stressed importance of regular exercise and risk factor modification UC: attended 2-hr talk that explained CHD, importance of risk factor modification, and potential benefits of physical activity, but without undergoing outpatient exercise training program
Outcomes	health-related quality of life: 3F-36 at 8 & 24 months
Notes	

Risk of bias

Bias	Authors judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not reported.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding (performance bias and detection bias) All outcomes	Unclear risk	Unclear in terms ofassessment ofother outcomes.

Incomplete outcome data (attrition bias) All outcomes	Low risk	All patients accounted for.
Selective reporting (reporting bias)	Unclear risk	No information reported.

Yu 2004

Methods	Single-center, unblinded, single-centre RCT in China; f/u 2 y
Participants	269 patients (76% men; mean age 64 y) with recent AMI (n=193) or after elective percutaneous coronary intervention (n=76) EX: n=181 (mean age, 64 SD 11 y; 138 males, 43 females) UC: n=88 (mean age, 64 SD 11 y; 66 males, 22 females)
Interventions	EX : Phase 1 was impatient ambulatory program that lasted 7-14 d; phase 2 was 16-session, twice weekly, outpatient exercise and education program lasting for 8 weeks, each session included 1 hr of education class followed by 2 hrs of exercise training, 1st hour oftraining was conducted by physiotherapist; phase 3 was community-based home exercise program for another 6 mos; phase 4 was long-term follow-up program until end of 2 years which stressed importance of regular exercise and risk factor modification UC: attended 2-hr talk that explained CHD, importance of risk factor modification, and potential benefits of physical activity, but without undergoing outpatient exercise training program
Outcomes	Total mortality
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	"randomized"
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding (performance bias and detection bias) All outcomes	Unclear risk	"The QOL assessments were performed on all patients in all 4 phases by a trained social worker who was unaware of the randomization" Unclear in terms ofassessment ofother outcomes.
Incomplete outcome data (attrition bias) All outcomes	High risk	24 % lost to follow up, no description of withdrawals or dropouts
Selective reporting (reporting bias)	Unclear risk	No information reported.

Zwisler 2008

Methods	Pragmatic, open-label, single-centre RCT in Denmark; f/u 1 y
Participants	446 patients having IHD (MI or angina pectoris in accordance with European guidelines) EX: n=227 (mean age 67 y) UC: n=219 (mean age 67 y)

Interventions	EX : 6-week intensive rehabilitation program including patient education, 12 exercise training sessions, dietary counseling, smoking cessation, psychosocial support, risk factor management and clinical assessment UC: attended 2-hr talk that explained CHD, importance of risk factor modification, and potential benefits of physical activity, but without undergoing outpatient exercise training program
Outcomes	Total mortality, MI, CABG, PTCA, health-related quality of life: SF-36 at 1-yr follow up
Notes	

Risk of bias

Bias	Authors judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	"The Copenhagen Trial Unit computer generated the allocation sequence and provided central secretary-staffed telephone randomization"
Allocation concealment (selection bias)	Low risk	"The essential patient data were registered, and the result of the randomization as delivered to the research nurse, who informed the CCR team and the patient about the allocation"
Blinding (performance bias and detection bias) All outcomes	Low risk	"The interventions were open to the patients and investigators. Investigator-independent outcome data from registries were chosen to ensure blinded outcome assessment. The scientific team and CCR team collected secondary outcome measures blinded to intervention at baseline and without blinding at 12 months"
Incomplete outcome data (attrition bias) All outcomes	Low risk	All IHD patients accounted for.
Selective reporting (reporting bias)	Unclear risk	No information reported.

EX: exercise based cardiac rehabilitation

UC: usual care

MI: Myocardial infarction

CHD: Coronary heart disease

SBP: Systolic blood pressure

DBP: Diastolic blood pressure

HDL: High density lipoprotein

LDL: Low density lipoprotein

QoL: Quality of life

V02max: Maximum oxygen uptake

CV: Cardiovascular

PWC: physical work capacity.

ET: exercise training

RTW: return to work

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

Study	Reason for exclusion
Agren 1989	Improper method of randomisation (based on date of birth).
Aronov 2006	No useful outcome data reported.
Ballantyne 1982	No useful outcome data reported.
Belardinelli 2007	Abstract only with incomplete reporting of study characteristics and outcome data. Full trial report not published

Bettencourt 2005	Only a small subset of randomised patients responded via questionnaire. Incomplete outcome data
Björntorp 1972	Not a randomised study. Participants divided alternately after admission
Blumenthal 1997	Control group was not randomised, but selected on geographical basis
Bär 1992	Method of randomisation was inadequate; of a study population of 265 across 5 centres only one centre randomised their patients, leaving a control group of 50 and an intervention group of 215
Carlsson 1997	No useful outcome data reported.
Gao 2007	No useful outcome data reported. Duration of follow-up not reported
Giannuzzi 2008	All patients (treatment and control) participated in 3-6 week cardiac rehabilitation programme (including supervised exercise sessions) prior to randomization. Control group was not "usual care"
Gielen 2003	No useful outcome data reported.
Heldal 2000	No useful outcome data reported.
Higgins 2001	No useful outcome data reported.
Jiang 2007	No useful outcome data reported.
Kentala 1972	Quote: "On admission the patients were divided up according to their year of birth into a control group and a training group…" Not a randomised study.
Krachler 1997	No useful outcome data reported.
Li 2004	Follow-up <6 months.
Liao 2003	Follow-up too short (3-4 weeks) and no useful outcome data reported
Mezey 2008	Not a randomised study.
Peschel 2007	No useful outcome data reported.
Piestrzeniewicz 2004	No useful outcome data reported.
Roviaro 1984	Not a randomised study. Assigned to treatment group according to geographic location
Schumacher 2006	No useful outcome data reported.
Stenlund 2005	No useful outcome data reported.
Takeyama 2000	No useful outcome data reported.
Tokmakidis 2003	No useful outcome data reported.
Wosornu 1996	No useful outcome data reported.
Zheng 2008	No useful outcome data reported.

Characteristics of studies awaiting assessment [ordered by study ID]

Son 2008

Methods	Unclear if randomized study.
Participants	Subjects consisted of 58 CAD patients who underwent PCI (experimental group: 30, control group: 28)
Interventions	The experimental group participated in an integrated symptom management program for 6 months which was composed of tailored education, stress management, exercise, diet, deep breathing, music therapy, periodical telephone monitoring and a daily log The control group received usual care.
Outcomes	Recurrent cardiac events, self care activity, quality of life

Notes	Article in Korean. Unable to find translator to answer following questions to determine study inclusion:
	• Was this study randomized?
	• How do the authors define "recurrent cardiac events"?
	• Any other pre-specified outcomes measured reported?
	• What scale did the authors use to assess self care activity and quality of life

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

Blumenthal 2007

Trial name or title	The Understanding Prognostic Benefits of Exercise and Antidepressant Therapy for Persons with Depression and Heart Disease (UPBEAT) Study
Methods	5-year, single-site randomised clinical trial sponsored by the National Heart, Lung, and Blood Institute
Participants	200 clinically depressed patients (with scores of Beck Depression Inventory 9) with stable CHD, including a previous (>60 days) myocardial infarction, revascularisation procedure, such as a PTCA or CABG, or a cardiac catheterization demonstrating significant coronary artery stenosis
Interventions	4 months of treatment with supervised aerobic exercise, sertraline, or placebo
Outcomes	Depressive symptoms, heart rate variability, baroreflex control, vascular function (i.e., flow-mediated dilation), measures of inflammation and platelet aggregation
Starting date	Not reported.
Contact information	Blume003@mc.duke.edu
Notes	"This study is not powered to assess treatment group differences in CHD morbidity and mortality."

Pater 2000

Trial name or title	Akershus Comprehensive Cardiac Rehabilitation Trial (the CORE Study)
Methods	Randomized, controlled, parallel-group design, single centre trial, driven by the Medical Department of the Akershus Central Hospital in Oslo, Norway
Participants	500 patients, men and women, aged 40-85 years, who have sustained at least one of the following: myocardial infarction, acute coronary syndrome, percutaneous transluminal coronary angioplasty and coronary artery bypass grafting
Interventions	Intervention: 8 weeks of supervised, structured physical training of three periods of 20 min per week, targeting a heart rate of 60-70% of the individual's maximum; home-based physical exercise training with the same basic schedule as in the supervised period; quantification of patients' compliance with the exercise programme by the use of wristwatches, information stored in the watch memory being retrieved once a month during the 3-year follow-up period; and life-style modification with an emphasis on the cessation of smoking and on healthy nutrition and weight control Control: Conventional care.
Outcomes	Primary: Quality of life. Secondary: total mortality, cardiovascular mortality, morbidity and recurrence rates of coronary events throughout a 3-year follow-up period
Starting date	Originally states as April 2000 with follow up complete by April 2004. No sign of publication to date. Contacted author with no reply
Contact information	drcornelpater@aol.com

Notes	Study design described at http://cvm.controlled-trials.com/content/1/3/177

DATA AND ANALYSES

Comparison 1
Exercise-based rehabilitation versus usual care

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Total mortality	33		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
1.1 Follow-up of 6 to 12 months	19	6000	Risk Ratio (M-H, Fixed, 95% CI)	0.82 [0.67, 1.01]
1.2 Follow-up longer than 12 months	16	5790	Risk Ratio (M-H, Fixed, 95% CI)	0.87 [0.75, 0.99]
2 Cardiovascular mortality	19		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
2.1 Follow-up of 6 to 12 months	9	4130	Risk Ratio (M-H, Fixed, 95% CI)	0.93 [0.71, 1.21]
2.2 Follow-up longer than 12 months	12	4757	Risk Ratio (M-H, Fixed, 95% CI)	0.74 [0.63, 0.87]
3 Fatal and/or nonfatal MI	26		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
3.1 Follow-up of 6 to 12 months	12	4216	Risk Ratio (M-H, Fixed, 95% CI)	0.92 [0.70, 1.22]
3.2 Follow-up longer than 12 months	16	5682	Risk Ratio (M-H, Fixed, 95% CI)	0.97 [0.82, 1.15]
4 CABG	21		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
4.1 Follow-up of 6 to 12 months	14	2312	Risk Ratio (M-H, Fixed, 95% CI)	0.91 [0.67, 1.24]
4.2 Follow-up longer than 12 months	9	2189	Risk Ratio (M-H, Fixed, 95% CI)	0.93 [0.68, 1.27]
5 PTCA	11		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
5.1 Follow-up of 6 to 12 months	7	1328	Risk Ratio (M-H, Fixed, 95% CI)	1.02 [0.69, 1.50]
5.2 Follow-up longer than 12 months	6	1322	Risk Ratio (M-H, Fixed, 95% CI)	0.89 [0.66, 1.19]
6 Hospital Admissions	10		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
6.1 Follow-up of 6 to 12 months	4	463	Risk Ratio (M-H, Fixed, 95% CI)	0.69 [0.51, 0.93]
6.2 Follow-up longer than 12 months	7	2009	Risk Ratio (M-H, Fixed, 95% CI)	0.98 [0.87, 1.11]

ADDITIONAL TABLES

Table 1
Summary of health related quality of life (HRQL)
scores at follow-up

Measure of HRQL	Mean (SD) outcome values at follow-up		P value	Difference between groups
	Exercise	**Usual Care**		
Bell 1998				
Nottingham health profile at 10.5 months follow-up:				
Energy	17.6 (27.1)	18.3 (29.8)	0.87[**]	Exercise = Usual care
Pain	2.8 (8.8)	4.82 (11.9)	<0.05	Exercise > Usual care
Emotional reactions	6.4 (17.0)	12.2 (19.9)	<0.001	Exercise > Usual care
Sleep	7.5 (18.4)	20.5 (27.8)	<0.001	Exercise > Usual care
Social isolation	2.3 (10.6)	4.0 (13.3)	0.37[*]	Exercise = Usual care
Physical mobility	8.4 (11.1)	8.9 (14.5)	0.82[**]	Exercise = Usual care
Belardinelli 2001				
MOS at 6 months follow-up:				
PF	78 (19)	55 (20)	0.001	Exercise > Usual care
RP	75 (13)	65 (14)	0.01	Exercise > Usual care
BP	4(9)	22 (10)	0.001	Exercise > Usual care
GH	68 (14)	50 (19)	0.001	Exercise > Usual care
VT	NR	NR		
SF	66 (10)	69 (12)	0.14[*]	Exercise = Usual care
RE	NR	NR		
MH	65 (12)	48 (15)	0.01	Exercise > Usual care
MOS at 12 months follow-up:				
PF	82 (18)	54 (20)	0.001	Exercise > Usual care
RP	76 (9)	58 (14)	0.01	Exercise > Usual care
BP	4(9)	32 (12)	0.001	Exercise > Usual care
GH	70 (14)	50 (18)	0.001	Exercise > Usual care
VT	NR	NR		
SF	68 (11)	68 (12)	1.00[*]	Exercise = Usual care
RE	NR	NR		
MH	70 (14)	45 (15)	0.001	Exercise > Usual care
Engblom 1992				
Nottingham health profile at 5 years follow-up:				
Energy	18	25	0.08	Exercise = Usual care
Pain	12	18	0.07	Exercise = Usual care
Emotional reactions	14	21	0.27	Exercise = Usual care
Sleep	24	29	0.42	Exercise = Usual care
Social isolation	7	9	0.42	Exercise = Usual care

Measure of HRQL	Mean (SD) outcome values at follow-up		P value	Difference between groups
Physical mobility	6	14	0.005	Exercise > Usual care
Heller 1993				
QLMI at 6 months follow-up:				
Emotional	5.4 (1.1)	5.2 (1.2)	0.04	Exercise > Usual care
Physical	5.4 (1.2)	5.2 (1.3)	0.17[*]	Exercise = Usual care
Social	5.9 (1.1)	5.8 (1.1)	0.35[*]	Exercise = Usual care
Hofman-Bang 1999				
AP-QLQat 12 months follow-up:				
Physical activity	4.9	4.3	<0.05	Exercise > Usual care
Somatic symptoms	NR	NR	NS	Exercise = Usual care
Emotional distress	NR	NR	NS	Exercise = Usual care
Life satisfaction	NR	NR	NS	Exercise = Usual care
Oldridge 1991				
QLMI at 4 months follow-up:				
Limitations	54	54	NS	Exercise = Usual care
Emotions	103	101	NS	Exercise = Usual care
QLMI at 8 months follow-up:				
Limitations	54	54	NS	Exercise = Usual care
Emotions	103	103	NS	Exercise = Usual care
QLMI at 12 months follow-up:				
Limitations	54	55	NS	Exercise = Usual care
Emotions	105	102	NS	Exercise = Usual care
Stahle 1999				
Karolinska Questionnaire at 12 months follow-up:				
Chest pain	0.6 (1.2)	0.4 (1.3)	NS	Exercise = Usual care
Shortness of breath	0.4 (1.1)	0.2 (1.0)	NS	Exercise = Usual care
Dizziness	−0.1 (1.1)	0.2 (0.9)	NS	Exercise = Usual care
Palpitation	−0.1 (1.0)	0.1 (0.9)	NS	Exercise = Usual care
Cognitive ability	−0.1 (0.6)	0.0 (0.7)	NS	Exercise = Usual care
Alertness	0.0 (0.9)	0.1 (0.8)	NS	Exercise = Usual care
Quality of sleep	0.0 (0.5)	0.1 (0.5)	NS	Exercise = Usual care
Physical ability	0.2 (0.7)	0.1 (0.4)	NS	Exercise = Usual care
Daily activity	0.3 (0.5)	0.1 (0.5)	NS	Exercise = Usual care
Depression	0.1 (0.3)	0.1 (0.2)	NS	Exercise = Usual care
Self perceived health	0.5 (1.3)	0.3 (1.0)	NS	Exercise = Usual care
"Ladder of Life" present	1.2 (1.2)	0.9 (1.8)	NS	Exercise = Usual care
"Ladder of Life future"	0.8 (2.7)	0.4 (2.3)	NS	Exercise = Usual care
Fitness	0.6 (1.4)	0.4 (1.0)	NS	Exercise = Usual care
Physical ability	0.7 (1.0)	0.4 (1.1)	NS	Exercise = Usual care

Measure of HRQL	Mean (SD) outcome values at follow-up		P value	Difference between groups
Toobert 2000				
SF-36 at 24 months follow-up:				
PF	NR	NR	NS	Exercise = Usual care
RP	NR	NR	NS	Exercise = Usual care
BP	NR	NR	NS	Exercise = Usual care
GH	NR	NR	<0.05	Exercise > Usual care
VT	NR	NR	NS	Exercise = Usual care
SF	NR	NR	<0.05	Exercise > Usual care
RE	NR	NR	NS	Exercise = Usual care
MH	NR	NR	NS	Exercise = Usual care
Yu 2003				
SF-36 at 8 months follow-up:				
PF	88 (12)	82 (17)	0.03[*]	Exercise > Usual care
RP	75 (33)	66 (35)	0.18[*]	Exercise = Usual care
BP	80 (25)	80 (25)	1.00[*]	Exercise = Usual care
GH	64 (26)	60 (28)	0.45[*]	Exercise = Usual care
VT	79 (18)	65 (17)	0.0001	Exercise > Usual care
SF	89 (27)	82 (28)	0.15	Exercise = Usual care
RE	93 (18)	83 (35)	0.05	Exercise = Usual care
MH	84 (16)	80 (15)	0.20	Exercise = Usual care
SF-36 at 24 months follow-up:				
PF	88 (13)	87 (9)	0.67[*]	Exercise = Usual care
RP	80 (32)	79 (30)	0.87[*]	Exercise = Usual care
BP	81 (21)	85 (20)	0.33[*]	Exercise = Usual care
GH	64 (20)	61 (18)	0.43[*]	Exercise = Usual care
VT	73 (21)	73 (17)	1.00[*]	Exercise = Usual care
SF	79 (30)	90 (18)	0.04[*]	Exercise > Usual care
RE	89 (25)	93 (25)	0.42[*]	Exercise = Usual care
MH	85 (14)	85 (12)	1.00[*]	Exercise = Usual care
Zwisler 2008				
SF-36 at 12 months follow-up:				
PCS	45.2 (9.8)	46.4 (9.8)	0.39[*]	Exercise = Usual care
MCS	50.6 (10.8)	48.4 (11.5)	0.16[*]	Exercise = Usual care

MOS=Medical Outcomes Study (MOS); Short Form-36 (SF-36); QLMI=Quality of Life After Myocardial Infarction questionnaire;

AP-QLQ=Angina Pectoris-Quality of Life questionnaire; PF=physical problems; RP=role limitations because of physical problems;

RE=role limitations because of emotional problems; VT=vitality; BP=bodily pain; SF=social functioning; MH=mental health; GH=general health perceptions; PCS=physical component summary; MCS=mental component summary; NR=not reported; NS=not significant

Exercise = Usual care: no statistically significant difference (P>0.05) between exercise and usual care groups at follow up

Exercise > Usual care: statistically significant difference (P=<0.05) between exercise and usual care groups at follow up

[*]
Calculated by authors of this report based on independent two group t test.

[**]
Adjusted for baseline difference between groups.

Table 2
Summary of costs of exercise-based rehabilitation and usual care

Variable	Kovoor 2006	Marchionni 2003	Yu 2004
Follow-up (months)	12	14	24
Year of costs	1999 ($AUD)	2000 ($USD)	2003 ($USD)
Mean cost of exercise-based rehabilitation (per patient):			
Exercise	$394	$5246	NR
Usual Care	$0	$0	$0
Mean difference (95% CI)	$394	$5246	NR
P value	NR	NR	NR
Costs considered	assessments, counseling, education	NR	staff salary, equipment, investigations
Mean total healthcare costs (per patient):			
Exercise	NR	$17 272	$15 292
Usual Care	NR	$12 433	$15 707
Mean difference (95% CI)	NR	$4839	−$415
P value	NS, see below for details	NR	NS
Additional healthcare costs considered	phone calls (p=0.10); hospital admissions (p=0.11); gated heart pool scan (p=0.50); exercise stress test (p=0.72); other diagnostics (p=0.37); visits to general practitioner (p=0.61), specialist doctor (p=0.35), or health-care professional (p=0.31)	NR	hospitalisations; revascularisations; private clinic visit; cardiac clinic visits; public non-cardiac visits; casualty visits; drugs

NR=not reported

Table 3
Results of univariate meta-regression analysis for total mortality

Explanatory variable	Exp(slope)*	95% Confidence interval*	Proportion of variation explained	Interpretation
Case mix (% MI patients)	RR=0.99	0.99 to 1.00	0%	No evidence that relative risk is associated with case mix
Dose of exercise (dose=duration in weeks × number of sessions × number of sessions per week)	RR=1.00	1.00 to 1.00	0%	No evidence that relative risk is associated with case mix
Type of rehabilitation (exercise only vs comprehensive rehab)	RR=0.92	0.66 to 1.28	0%	No evidence that relative risk differs between types of rehabilitation

Explanatory variable	Exp(slope)*	95% Confidence interval*	Proportion of variation explained	Interpretation
Follow up (months)	RR=0.99	0.98 to 1.01	0%	No evidence that relative risk is associated with case mix
Publication year (pre 1995 vs post 1995)	RR=0.80	0.54 to 1.20	0%	No evidence that relative risk is associated with publication year

Table 4
Results of univariate meta-regression analysis for cardiovascular mortality

Explanatory variable	Exp(slope)*	95% Confidence interval*	Proportion of variation explained	Interpretation
Case mix (% MI patients)	RR=1.01	0.98 to 1.04	0%	No evidence that relative risk is associated with case mix
Dose of exercise (dose=duration in weeks × number of sessions × number of sessions per week)	RR=1.00	1.00 to 1.00	0%	No evidence that relative risk is associated with case mix
Type of rehabilitation (exercise only vs comprehensive rehab)	RR=0.84	0.57 to 1.23	0%	No evidence that relative risk differs between types of rehabilitation
Follow up (months)	RR=0.99	0.98 to 1.00	0%	No evidence that relative risk is associated with case mix
Publication year (pre 1995 vs post 1995)	RR=1.37	0.73 to 2.22	0%	No evidence that relative risk is associated with publication year

Table 5
Results of univariate meta-regression analysis for total MI

Explanatory variable	Exp(slope)*	95% Confidence interval*	Proportion of variation explained	Interpretation
Case mix (% MI patients)	RR=1.00	0.99 to 1.02	3.5%	No evidence that relative risk is associated with case mix
Dose of exercise (dose=duration in weeks × number of sessions × number of sessions per week)	RR=1,00	1.00 to 1.00	0%	No evidence that relative risk is associated with case mix

Explanatory variable	Exp(slope)*	95% Confidence interval*	Proportion of variation explained	Interpretation
Type of rehabilitation (exercise only vs comprehensive rehab)	RR=0.87	0.55 to 1.36	0.4%	No evidence that relative risk differs between types of rehabilitation
Follow up (months)	RR=0.99	0.98 to 1.01	6.3%	No evidence that relative risk is associated with case mix
Publication year (pre 1995 vs post 1995)	RR=1.38	0.82 to 2.33	0%	No evidence that relative risk is associated with publication year

Table 6

Results of univariate meta-regression analysis for CABG

Explanatory variable	Exp(slope)*	95% Confidence interval*	Proportion of variation explained	Interpretation
Case mix (% MI patients)	RR=1.01	1.00 to 1.02	3.5%	No evidence that relative risk is associated with case mix
Dose of exercise (dose=duration in weeks × number of sessions × number of sessions per week)	RR=1.00	1.00 to 1.00	0%	No evidence that relative risk is associated with case mix
Type of rehabilitation (exercise only vs comprehensive rehab)	RR=1.13	0.67 to 1.93	0%	No evidence that relative risk differs between types of rehabilitation
Follow up (months)	RR=0.99	0.99 to 1.00	0%	No evidence that relative risk is associated with case mix
Publication year (pre 1995 vs post 1995)	RR=0.84	0.50 to 1.42	0%	No evidence that relative risk is associated with publication year

Table 7

Results of univariate meta-regression analysis for PTCA

Explanatory variable	Exp (slope)*	95% Confidence interval*	Proportion of variation explained	Interpretation
Case mix (% MI patients)	RR=0.99	1.00 to 1.01	3.5%	No evidence that relative risk is associated with case mix

Explanatory variable	Exp (slope)*	95% Confidence interval*	Proportion of variation explained	Interpretation
Dose of exercise (dose=duration in weeks × number of sessions × number of sessions per week)	RR=1.00	1.00 to 1.00	0%	No evidence that relative risk is associated with case mix
Type of rehabilitation (exercise only vs comprehensive rehab)	RR=0.99	0.39 to 2.54	0%	No evidence that relative risk differs between types of rehabilitation
Follow up (months)	RR=1.00	0.99 to 1.02	0%	No evidence that relative risk is associated with case mix
Publication year (pre 1995 vs post 1995)	RR=0.92	0.42 to 2.06	0%	No evidence that relative risk is associated with publication year

WHAT'S NEW

Last assessed as up-to-date: 13 June 2010.

Date	Event	Description
4 July 2011	Amended	Author (Neil Oldridge) details updated

HISTORY

Protocol first published: Issue 3, 1999

Review first published: Issue 4, 2000

Date	Event	Description
7 June 2011	New search has been performed	The searches were updated and re-run in December 2009, identifying an additional 17 studies for inclusion. Fourty-seven trials in total have been included
7 June 2011	New citation required and conclusions have changed	The inclusion criteria have been revised for this update. Five out of the 35 formerly included studies (in the review) have therefore been excluded
The conclusions have changed based on the analysis of 47 included studies and have focused more on the impact of exercise-based cardiac rehabilitation on clinical events and HRQL outcomes
1 November 2000	New citation required and conclusions have changed	Substantive amendment

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

Changes in this update review

Given its policy focus, in addition to updating the original Cochrane review, this update review:

1. Excluded exercise capacity and cardiac risk factors outcomes and added costs.

2. Limited the inclusion to those studies that assess outcomes at six months or longer.

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Indicates the major publication for the study

PLAIN LANGUAGE SUMMARY

Regular exercise or exercise with education and psychological support can reduce the likelihood of dying from heart disease

Coronary heart disease (CHD) is one of the most common forms of heart disease. It affects the heart by restricting or blocking the flow of blood around it. This can lead to a feeling of tightness in the chest (angina) or a heart attack. Exercise-based cardiac rehabilitation aims to restore people with CHD to health through either regular exercise alone or a combination of exercise with education and psychological support. The findings of this review indicate that exercise-based rehabilitation reduces the likelihood of dying from heart disease and there is moderate evidence of an improvement in quality of life in the predominantly middle aged, male patients included in these studies. More research is needed to assess the overall health impact of exercise-based rehabilitation in a broader range of patients.
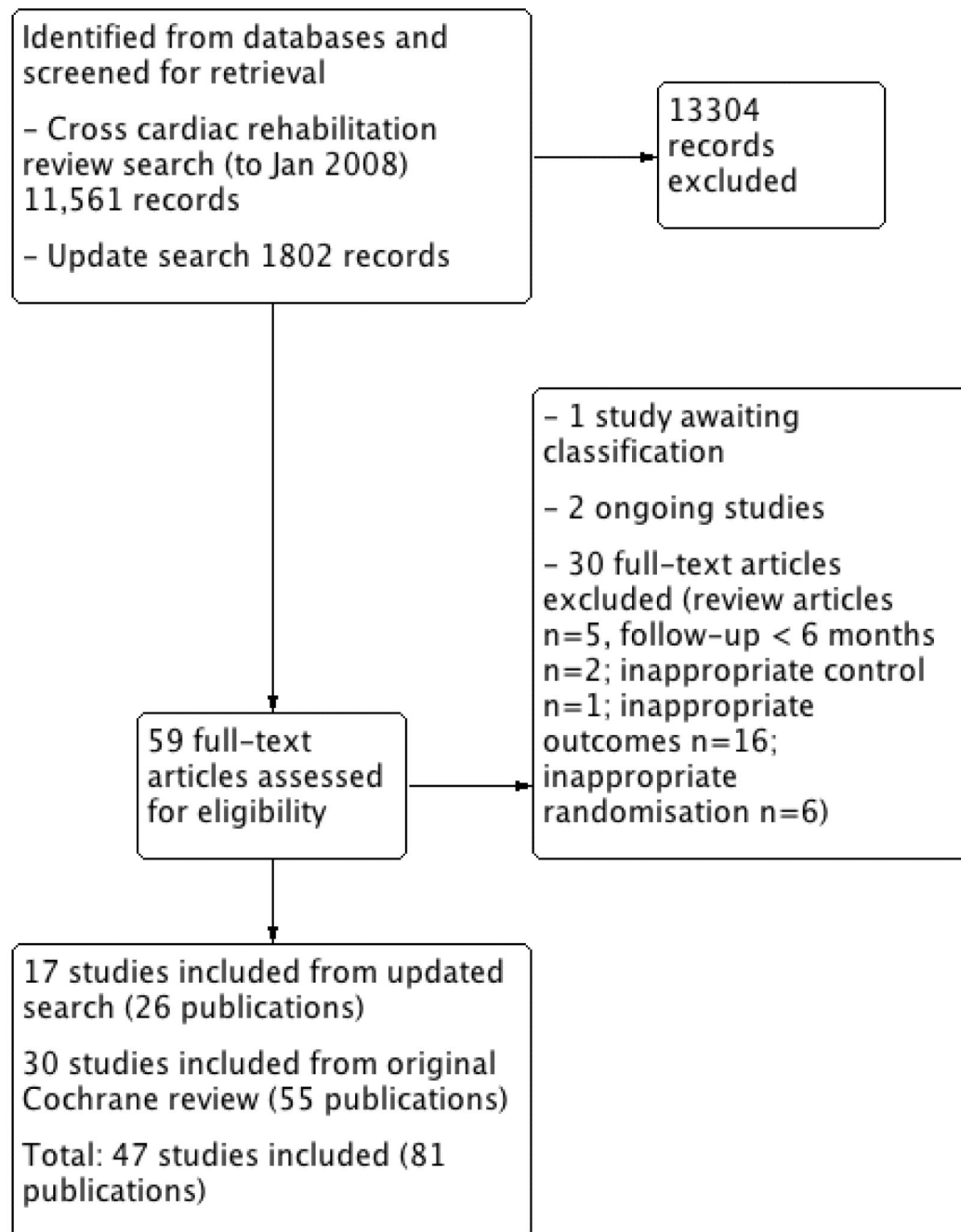
Identified from databases and
screened for retrieval

– Cross cardiac rehabilitation
review search (to Jan 2008)
11,561 records

– Update search 1802 records

13304
records
excluded

– 1 study awaiting
classification

– 2 ongoing studies

– 30 full-text articles
excluded (review articles
n=5, follow-up < 6 months
n=2; inappropriate control
n=1; inappropriate
outcomes n=16;
inappropriate
randomisation n=6)

59 full-text
articles assessed
for eligibility

17 studies included from updated
search (26 publications)

30 studies included from original
Cochrane review (55 publications)

Total: 47 studies included (81
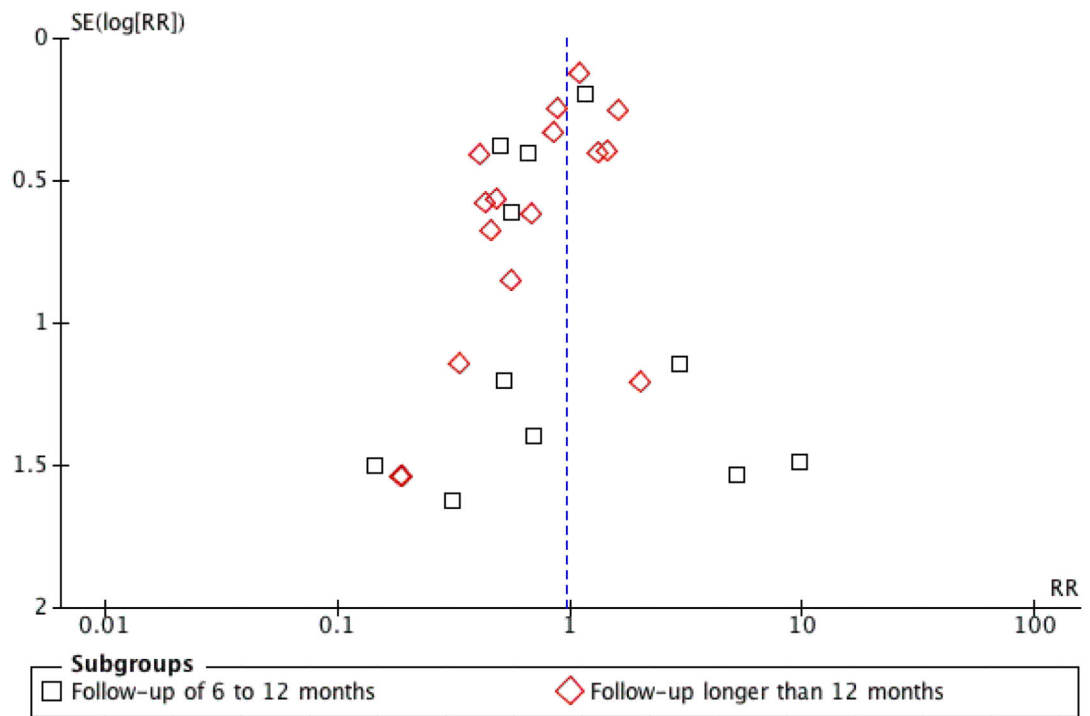publications)

Figure 1. Study flow diagram

Figure 2. Funnel plot of exercise-based rehabilitation versus usual care for fatal and/or nonfatal MI