Article

# Comparing cardiac rehabilitation programmes for people with coronary heart disease

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**Title** Cardiac rehabilitation for Coronary Heart Disease: a comparison of programmes including exercise and non-exercise

A commentary on: Huang R, Palmer SC, Cao Y et al. Cardiac Rehabilitation Programs for Chronic Heart Disease: A Bayesian Network Meta-analysis. Can J Cardiol. 2021;37(1):162-171. doi: 10.1016/j.cjca.2020.02.072.

**Key Points**

- Cardiac rehabilitation programmes including exercise are the most successful in improving outcomes for cardiovascular mortality, morbidity and hospitalisation in patients with Coronary Heart Disease.
- Comprehensive cardiac rehabilitation (exercise plus educational and behavioural support) is associated with a lower risk of all-cause mortality.
- Cardiac rehabilitation programmes including exercise should be offered to patients through a range of options such as home-based tele-rehabilitation.

## Introduction

In the UK, coronary heart disease (CHD) is the second highest cause of death and 2.3 million people currently live with the disease (BHF 2021). Secondary prevention of cardiovascular events and the reduction of risk factors are important strategies for managing the disease. Cardiac rehabilitation (CR) is a multi-disciplinary intervention to address modifiable risk factors related to CHD and is associated with reduced mortality and hospitalisation (Ambrosetti et al. 2020). There are several core components involved in delivering CR including health-behaviour change and education, lifestyle risk factor management such as supervised exercise and nutritional counselling, management of psychosocial health and medical risk (British Cardiovascular Society, 2017).

The evidence base suggests that CR may reduce all-cause mortality (Kabboul et al. 2018, Xia et al. 2018) and cardiovascular mortality (Anderson et al. 2016, Kabboul et al. 2018, Xia et al. 2018), improve health-related quality of life (Francis et al. 2019) and reduce hospital admissions (Anderson et al. 2016, Kabboul et al. 2018). The evidence is limited in some instances by exercise only trials, a focus on individual components and quality of life outcomes or potential biases such as selective outcome reporting. The network meta-analysis by Huang et al. (2021) aimed to address these limitations by comparing the benefits of all CR programmes including exercise and non-exercise, across a range of cardiovascular and mortality outcomes.

## Methods

A robust multi-database search was undertaken (Embase, MED-LINE, and the Cochrane Central Register of Randomized Trials [date of inception to May 2019]). Only randomised controlled trials (RCTs) which compared CR programmes to usual care or a second CR strategy for adults who have had a myocardial infarction (MI), angiography, percutaneous coronary intervention (PCI), or coronary artery bypass grafting (CABG) were included. Additionally, the

RCTs needed to have a minimum of a six-month follow-up period. Primary clinical outcomes reported were all-cause mortality, cardiovascular mortality, major adverse cardiovascular events (MACE), nonfatal MI, heart failure, and nonfatal stroke or TIA. The secondary outcome measures were PCI or CABG revascularization, all-cause hospitalisation, cardiovascular hospitalisation, and depression.

Screening, data extraction and assessment of bias (Cochrane risk of bias the assessment) were undertaken by two reviewers independently. A score of bias was given for each individual study by adapting the grades of low, high or unclear risk of bias to derive an overall quality score. An overall level of evidence quality for each outcome (rating of certainty) was given using the grading of recommendations assessment, development and evaluation (GRADE). Data synthesis was undertaken to compare programmes using a pairwise and Bayesian network meta-analysis using standard mean differences (SMD) or odds ratios (OR) and credibility intervals (CrI). The assumption of transitivity (similarity between different sets of trials) was assessed using effect modifier analyses. Ranking probability for the best treatment was assessed using the surface under the cumulative ranking curve (SUCRA). A larger SUCRA score indicated a treatment is more effective with scores close to 100% indicating superiority.

**Results**

The network meta-analysis included 134 RCTs that compared comprehensive CR, CR without exercise, exercise only CR or standard care (121 studies, 90%). Included studies were published between 1975-2017 and had a median follow up of 1 year. There were 62,322 participants included, with a mean age of 81.8 and 85% were male. There were 20 studies assessed to have a high risk of bias (15%), 68 with a moderate risk (51%) and 46 with a low risk (34%). Results are described below and in Table 1.

**Comprehensive cardiac rehabilitation** (exercise plus education, counselling, risk-factor modification and/or psychosocial management) was the only programme associated with a lower risk of all-cause mortality when compared to standard care (moderate quality evidence). This programme was also associated with lower risk of MACE (low quality evidence) and lower revascularization (moderate quality evidence) compared to standard care. SUCRA scores showed that comprehensive CR ranked highest in the categories of all-cause mortality, MACE, PCI and CABG revascularization and depression. Outcomes that did not show evidence of effect were cardiovascular mortality, non-fatal MI, heart failure, non-fatal stroke/TIA, all-cause/cardiovascular hospitalisation and depression.

**Exercise-only cardiac rehabilitation** (guided exercise only) was associated with a lower risk of cardiovascular mortality, MACE and non-fatal MI compared to standard care. It was also the only programme associated with lower risk of all-cause hospitalisation. There was a lower risk of cardiovascular hospitalization compared to both standard care and CR without exercise (moderate quality evidence). There was very low-quality evidence for a lower risk of non-fatal stroke/TIA compared to standard care and other programmes. SUCRA scores showed that exercise-only CR ranked highest for reducing risk of non-fatal MI/stroke, all-cause and cardiovascular hospitalization. Outcomes that did not show evidence of effect were all-cause mortality, heart failure, revascularization and depression.

**Cardiac rehabilitation without exercise** (education, counselling, risk factor modification and psychosocial management) was associated with a lower risk of cardiovascular mortality (low quality evidence) and lower non-fatal MI compared to standard care (moderate quality evidence). CR without exercise was the only programme associated with lower depression compared to standard care based on moderate quality evidence. SUCRA scores showed that CR without exercise ranked highest in reducing cardiovascular mortality and heart failure. Outcomes that did not show evidence of effect were all-cause mortality, MACE, heart failure, non-fatal stroke/TIA, revascularization and all-cause/cardiovascular hospitalisation.

**Commentary**

Using the Amstar2 critical appraisal tool for systematic reviews (Shea et al. 2017), the network meta-analysis satisfied twelve of sixteen criteria. The four criteria lacking were assessment of the potential impact of risk of bias (from individual studies) on the results, subsequent discussion of the risk and the impact of heterogeneity and publication bias. The network meta-analysis included studies with a high risk of bias and their potential impact on the results was not investigated. In addition, the proportion of studies achieving risk of bias criteria (blinding assessment etc.) was discussed but the proportion of studies obtaining low, moderate or high risk of bias status (using an adapted quality score) was not. Using the supplementary material, we were able to report these characteristics with most studies in the moderate to low risk category (85%). It is also worth noting that the Cochrane tool is not designed to produce a score, as individual items have different levels of effect and are therefore not comparable. Potential sources of heterogeneity and publication bias were investigated but their impact on results was not discussed in any detail. Overall, the network meta-analysis provided an accurate and comprehensive summary of the results from available studies but an analysis of the impact of bias and heterogeneity would have been favourable.

The findings of this network meta-analysis suggest that CR programmes containing exercise are the most successful in improving outcomes for mortality and hospitalisation in patients with CHD, consistent with previous findings (Anderson et al. 2016, Kabboul et al. 2018, Xia et al. 2018). The analysis also found broader cardiovascular benefits in less well reported outcomes such as MACE, non-fatal MI and PCI. Only comprehensive CR showed a reduction in overall mortality. Given the evidence base, it is important to promote CR to patients and current UK guidelines suggest that all adults admitted with an MI should be offered and encouraged to attend a CR programme with an exercise component as soon as possible (NICE 2020).

Despite the positivity of the evidence base, there are still issues with low referral and participation rates. In one US study, 62% of patients were deemed eligible for CR referral after MI and of those only 33% attended at least one session (Doll et al. 2015). Referral and uptake of CR also remains low in Europe (Ambrosetti et al. 2020). Factors for low uptake of CR include being female, older, of non-white ethnicity, more likely to smoke, greater comorbidity, elective revascularization compared to acute, unstable angina pectoris and the provider being too far away (Doll et al. 2015; Mariëtte van Engen-Verheul et al. 2013).

Barriers that have been reported specifically to women include a lower level of education, non-english first language, multiple comorbidities, decreased social support, and a high burden of family responsibilities (Supervia et al. 2017).

Automatic referral to CR and assisted enrolment may help to improve referral and participation rates (Supervia et al. 2017). To encourage uptake, guidance also suggests that adults referred to a CR programme are offered sessions during and outside working hours and the choice of undertaking the programme at home, in the community or in a hospital setting (NICE 2015). Promising and novel modes of delivery have been developed which may help with participation including cardiac telerehabilitation (undertaken at home using web-based applications/wearable monitoring devices) and loyalty programmes which reward attendance (Vromen et al. 2021). A network meta-analysis reported that home or tele-based programmes were not superior to centre-based CR (undertaken in hospital or a suitable centre) in reducing all-cause and cardiovascular mortality when compared to usual care (Xia et al. 2018). However, home-based cardiac tele-rehabilitation was placed in the spotlight during the covid-19 pandemic due to the suspension of centre-based settings. The effectiveness of the home-based model for patients with CHD has since been appraised and found to have associations with increased functional capacity, physical activity behaviour, depression and quality of life compared to usual care. When compared to centre-based models, it was comparably effective (Ramachandran et al. 2021).

Future research trials within this field should aim to use standardised protocols of CR to help improve consistency and similarity in reporting outcomes. Individual patient factors (age, obesity, etc.) should also be considered for their potential impact on outcomes. Data were found to be lacking for cost-effectiveness and trials specific to women and this should be considered in future research design.

**Reflective Questions**

- What are the main limitation of the network meta-analysis presented?
- What are the main differences between the cardiac rehabilitation programmes?
- What factors should be considered to improve referral and participation rates?

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