Meta-analysis: secondary prevention programs for patients with coronary artery disease

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CRD summary
This review found that programmes involving education/counselling and/or exercise reduced the risk of death and heart attack in patients with coronary artery disease. The authors' conclusions are likely to be reliable, particularly for the relatively young male patients who formed the majority of participants in the included studies.

Authors' objectives
To determine the effectiveness of interventions with and without an exercise component for the secondary prevention of cardiac events.

Searching
MEDLINE (1966 to 2004), the Cochrane CENTRAL Register (Issue 4, 2004), EMBASE (1980 to 2004), CINAHL (1982 to 2004), SIGLE (1980 to 2004) and PubMed (January to December 2004) were searched; the search terms were reported. The authors also searched Web of Science (1999 to 2004) for items citing an earlier review on a similar topic, and handsearched reference lists of identified studies, review articles and references provided by subject experts. The searches were limited to English language material.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs) were eligible for inclusion.

Specific interventions included in the review
Studies comparing secondary prevention interventions with usual care were eligible for inclusion. Interventions delivered to in-patients and interventions not provided by health professionals were excluded, as were single-modality interventions other than exercise. The interventions included in the review involved:

- education and counselling together with supervised exercise;
- education and counselling alone; and
- supervised exercise alone.

The duration of the intervention ranged from 0.5 to 48 months and the follow-up from 0.75 to 72 months.

Participants included in the review
Eligible participants were patients with coronary artery disease (CAD). The participants in studies in the review included patients who had suffered a myocardial infarction (MI), undergone an intervention such as angioplasty or coronary artery bypass grafting, or had documented CAD. The proportion of men in the included studies ranged from 0 to 100%, but the majority of the participants in most studies were male. The mean age of the participants ranged from 48 to 76 years.

Outcomes assessed in the review
Studies were eligible for inclusion if they reported rates of mortality, MI or hospitalisation. The included studies assessed all-cause mortality, MI and a range of other outcomes including cardiovascular risk factors, use of effective medications, quality of life and functional status. The outcomes were defined as in the primary studies.

How were decisions on the relevance of primary studies made?
Two reviewers independently assessed studies for relevance. Any disagreements were resolved by consensus.
Assessment of study quality
Validity was assessed according to whether the method of randomisation was described and appropriate, whether withdrawals or losses to follow-up were described, and the adequacy of allocation concealment. The studies were also allocated a quality score based on the Jadad scale. Two reviewers independently assessed validity. Any disagreements were resolved by consensus.

Data extraction
Two reviewers independently extracted the data. Any discrepancies were resolved by consensus. For the primary outcomes (mortality and MI), the numbers of events in each group were used to calculate the risk ratio (RR) and its 95% confidence interval (CI).

Methods of synthesis
How were the studies combined?
For mortality and MI, the studies were combined in a meta-analysis using the random-effects model of DerSimonian and Laird. The results for the other outcomes were discussed in a brief narrative. Egger's method was used to assess publication bias.

How were differences between studies investigated?
The I-squared statistic was used to assess heterogeneity. Data for three follow-up periods (12, 24 and 60 months) were pooled in a priori sensitivity analyses.

Results of the review
Sixty-three RCTs with 21,205 participants were included in the review. Twenty-four studies (n=5,654) evaluated education or counselling combined with exercise, 23 studies (n=13,167) evaluated counselling or education without exercise, and 17 studies (n=2,566) evaluated exercise alone.

In terms of study quality, none of the included RCTs was double-blind and few described their randomisation methods. Only 15 RCTs had adequate allocation concealment.

Mortality.
The overall RR was 0.85 (95% CI: 0.77, 0.94), suggesting a significant benefit of secondary prevention programmes. The overall RR varied with time of follow-up; it was not significant at 12 months (RR 0.97, 95% CI: 0.82, 1.14), but was significant at 24 months (RR 0.53, 95% CI: 0.35, 0.81) and 60 months (RR 0.77, 95% CI: 0.63, 0.93). The benefit of interventions combining education and counselling with exercise was not statistically significant (RR 0.88, 95% CI: 0.74, 1.04), whereas education and counselling alone (RR 0.87, 95% CI: 0.76, 0.99) and exercise alone (RR 0.72, 95% CI: 0.54, 0.95) showed statistically significant benefits.

MI.
The overall RR was 0.83 (95% CI: 0.74, 0.94), suggesting a significant benefit of secondary prevention programmes. The benefit of interventions combining education and counselling with exercise was statistically significant (RR 0.62, 95% CI: 0.44, 0.87), whereas education and counselling alone (RR 0.86, 95% CI: 0.72, 1.03) and exercise alone (RR 0.76, 95% CI: 0.57, 1.01) did not show statistically significant benefits.

Other outcomes.
Most RCTs that reported these outcomes found that secondary prevention programmes improved quality of life or functional status, but the effect sizes were small.

There was no statistically significant heterogeneity in the meta-analysis and no evidence of publication bias.
Cost information
One study reported an incremental cost of £1,097 per quality-adjusted life-year for a nurse-led clinic.

Authors' conclusions
Secondary prevention programmes improved health outcomes in patients with CAD.

CRD commentary
The review question was clear, although the inclusion criteria for the interventions were broad. The authors searched a wide range of appropriate sources. They limited the search to articles in English and did not search for unpublished material, so it was possible that some relevant studies could have been missed. The authors used standard methods to assess validity and noted that weaknesses in many of the included studies would tend to overestimate treatment effects. Two reviewers independently carried out the study selection, validity assessment and data extraction processes, thus reducing the risk of bias and errors in the review process.

The authors carried out a meta-analysis for the primary outcomes; statistical heterogeneity was assessed and the effects of follow-up time on the results for mortality were included in a sensitivity analysis. The limitations of the review were made clear, particularly an inability to comment on the value of the different components of the interventions. Overall, the authors' conclusions are likely to be reliable, particularly for the relatively young male patients with CAD who made up the majority of participants in the included studies.

Implications of the review for practice and research
Practice: The authors stated that the large-scale implementation of secondary prevention programmes for patients with CAD is justified.

Research: The authors stated that there is a need for research to evaluate the cost-effectiveness of programmes.

Funding
Agency for Healthcare Research and Quality, contract number 290-02-0023.

Bibliographic details

PubMedID
16263889

Original Paper URL
http://www.annals.org/cgi/content/full/143/9/659

Other publications of related interest
These additional published commentaries may also be of interest. Lancaster T. Review: secondary prevention programmes with and without exercise reduce all cause mortality and recurrent MI. Evid Based Med 2006;11:87.

Indexing Status
Subject indexing assigned by NLM

MeSH
Cause of Death; Coronary Artery Disease /mortality /prevention & control /therapy; Counseling; Exercise Therapy;
Health Status; Humans; Patient Education as Topic; Quality of Life; Recurrence; Risk Factors

**AccessionNumber**
12005008551

**Date bibliographic record published**
31/03/2006

**Date abstract record published**
31/03/2006

**Record Status**
This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.