Multifactorial lifestyle interventions in the primary and secondary prevention of cardiovascular disease and type 2 diabetes mellitus: a systematic review of randomized controlled trials

Angermayr L, Melchart D, Linde K

CRD summary
This review concluded that multifactorial lifestyle programmes may reduce harmful events and mortality in people with or at risk of coronary heart disease or diabetes. Evidence was limited and it was not possible to say what types of interventions were most effective. Data came from trials of limited quality. Many trials were small. The authors' conservative conclusions appear reasonable.

Authors' objectives
To assess the effects of lifestyle interventions in people with, or at increased risk of, coronary heart disease or type 2 diabetes.

Searching
PubMed was searched to January 2010 and EMBASE, PsycINFO, SOMED and The Cochrane Library were searched to July 2007. The search terms were reported online. No language restrictions were applied. Reference lists of identified studies and reviews and two trials registers were checked in January 2010.

Study selection
Randomised controlled trials (RCTs) that compared lifestyle interventions in people with or at increased risk of type 2 diabetes or coronary heart disease to a less intensive intervention or usual care were eligible for inclusion. Trials needed a minimum follow-up of six months. Interventions had to consist of elements aimed at diet, exercise and stress management/relaxation. The primary outcomes of interest were mortality, cardiovascular events and diabetic secondary complications. Secondary prevention studies were included if they reported on body mass index (BMI), serum lipids, glycated haemoglobin (HbA1c) or blood pressure. Primary prevention studies were included if they reported incidence of manifest disease or overall coronary heart disease risk scores.

Participants in the included studies were men and women. Mean ages ranged from 50 to 67 years. Reported BMI ranged from 25 to 35. Most studies on people with diabetes recruited participants from registries and one included newly diagnosed people. People with coronary heart disease had recent acute myocardial infarction, percutaneous coronary intervention (PCI), coronary artery surgery or proven coronary heart disease. Some studies included a residential element (2.5 to 45 days). Overall contact time ranged from one to 596 hours. Intervention duration ranged from 1.5 to 48 months. Delivery of the intervention included group sessions, individual sessions and telesupport. Most also included interventions aimed at smoking cessation, education on disease and techniques to increase adherence. Adherence was measured in some studies. Concomitant treatments were not reported. Follow-up ranged from six to 60 months. Most trials were undertaken in Europe and North America.

One reviewer screened search results and excluded all clearly irrelevant papers. Remaining publications were checked independently by two reviewers. Disagreements were resolved by discussion and consensus.

Assessment of study quality
Study quality was assessed by two reviewers independently using Cochrane Collaboration methods for assessing risk of bias based on items such as allocation concealment, allocation sequence, blinding of outcome assessment, completeness of data and selective reporting.

Data extraction
Interventions were classified according to intensity of interventions: very low (up to 10 hours), low (10 to 30 hours), moderate (30 to 100 hours), high (more than 100 hours). Follow-up times were classified as four to six months, seven to 12 months, 13 to 24 months and more than 24 months.
Standardised mean differences were calculated for risk scores. For other continuous data, weighted mean differences and 95% confidence intervals (CI) were calculated. Missing standard deviations were imputed. Where baseline standard deviations were available, these were used for later time points or changes from baseline. Where they were not available, an average of available standard deviations was used. Relative risk (RR) and 95% CI were calculated for dichotomous outcomes.

Two reviewers extracted data independently. Disagreements were resolved by consensus. Authors were contacted for additional information.

**Methods of synthesis**

Pooled realative risks and mean differences with 95% CIs were calculated using a random-effects model. Heterogeneity was assessed using $\chi^2$, $\chi^2$ and $I^2$. Sensitivity analyses were based on removal of the largest trial from analyses and by using changes from baseline for the outcomes of BMI and HbA1c. Subgroup analyses investigated the intensity of the intervention, inclusion of a smoking cessation element and study quality (at least four risk of bias criteria met).

Publication bias was assessed using funnel plots and Egger's test.

**Results of the review**

Twenty-five RCTs (7,703 participants) were included. One study had 3,241 participants and others ranged from to 28 to 591 participants. Three trials were primary prevention and 22 were secondary prevention.

Study quality was limited. Only four trials reported adequate methods of randomisation and allocation concealment. Only six trials reported blinding of outcome assessors for clinical outcomes. Bias because of high or unbalanced losses to follow-up were unclear or high in more than half of the studies. Losses to follow-up ranged from zero to 44%. Eight trials reported more than 60% attendance on available sessions.

Tests did not suggest publication bias, but may have been inconclusive given the clinical variation in the included studies.

Seven trials with moderate or high intensity intervention and three out of 13 trials with low or very low intensity intervention reported significant improvements in self-reported risk behaviour in at least two aspects.

Clinical event rates were low. Compared to control, the intervention was associated with a lower risk of acute myocardial infarction (RR 0.53, 95% CI 0.35 to 0.80, $I^2$=0%; six trials) and cardiovascular events (RR 0.68, 95% CI 0.50 to 0.93, $I^2$=42%; seven trials). There was no statistically significant effect on mortality ($I^2$=0%; 12 trials), PCI ($I^2$=23%; seven trials) and coronary artery surgery rates ($I^2$=10%; nine trials).

Compared to control, the intervention was associated with no statistically significant or small changes in laboratory and surrogate outcomes (results reported in full).

Subgroup analyses failed to show any clear indications that results were affected by intensity of intervention, disease status and components of the programme.

**Authors' conclusions**

Available evidence suggested that multifactorial lifestyle interventions may reduce major harmful events and mortality in people with or at increased risk of coronary heart disease or diabetes. Evidence was limited and it was not possible to say what types of interventions were most effective in defined populations.

**CRD commentary**

The aims of the review were clearly stated in terms of the inclusion criteria. The search covered a number of relevant sources and there were no language restrictions, which were likely to have reduced the possibility of language bias. There was a three-year difference between the dates of searching different databases. It was possible that studies, including unpublished studies, were missed. The authors' tests suggested no evidence of publication bias, but these were...
limited by the numbers of studies available for individual outcomes. It was possible that publication bias affected the review. The review methods were aimed at reducing reviewer error and bias. The methods of synthesis appeared generally appropriate. Heterogeneity was investigated. Data came from trials of limited quality. Many trials were small.

The authors’ conclusions are suitably conservative and are reasonable.

Implications of the review for practice and research

Practice: The authors did not state any implications for practice.

Research: The authors stated a need for large-scale longer-term trials of multifactorial lifestyle interventions in people with, or at risk of coronary heart disease or diabetes. Trials should include improved methods and reporting and include a clear description of the intervention. Clear reporting of adherence to interventions, reporting of lifestyle changes and laboratory or clinical outcomes was needed.

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