Lipid-lowering interventions in angiographic trials
Rossouw J E

Authors' objectives
To pool the data from 14 published angiographic trials in order to examine the overall effects of lipid reduction on angiographic outcomes and on clinical events, and to determine whether the effects are related to the type of intervention used to obtain the lipid modification or to the baseline or in-trial lipid levels.

Searching
The author does not provide details of the sources searched or the strategies used.

Study selection
Study designs of evaluations included in the review
All randomised angiographic trials published at May 31st 1995, studying lipid lowering interventions. Trials with multifactorial interventions were included, provided that lipid reduction was one of the interventions used.

Specific interventions included in the review
Lifestyle interventions (diet, exercise and other interventions), drug therapy (subclassified as resins, statins and combinations) and surgery (partial ileal bypass).

Specific drugs studied: cholestyramine, lovastatin, simvastatin, pravastatin, colestipol, niacin, gemfibrozil, probucol.

Participants included in the review
Patients with high levels of low density lipoprotein (LDL) and clinically- or angiographically-evident coronary artery disease (CAD).

Outcomes assessed in the review
Angiographically determined disease changes were examined as categorical variables (progression, no change or regression). 'No change' included mixed change, i.e. progression and regression in the same patient. Cardiovascular events (fatal coronary artery disease, non-fatal myocardial infarction, coronary angioplasty, coronary bypass surgery and stroke). Lipid results.

How were decisions on the relevance of primary studies made?
The author does not state how the papers were selected for the review, or how many of the reviewers performed the selection.

Assessment of study quality
The author does not report the method used to assess validity, or how the validity assessment was performed.

Data extraction
The author does not state how the data were extracted for the review, or how many of the reviewers performed the data extraction.

Methods of synthesis
How were the studies combined?
Results of the treatment/control comparison and also cardiovascular events were pooled to obtain a summary estimate of the overall treatment effect, expressed as the summary odds ratio (OR) and 95% confidence interval (CI). For trials with more than one intervention, the intervention arms were analysed both separately (by type of intervention) and in
How were differences between studies investigated?
The author acknowledges that the studies differed with respect to type of intervention, baseline lipid levels and “other characteristics of participants”, the degree and pattern of lipid modification obtained, and the methods used for measuring and classifying the angiographic outcome. Sample sizes and length of follow-up also varied between studies.

Correlation analyses were performed to assess whether the odds ratio for disease change were related to baseline or in-trial LDL levels or to relative or absolute differences between treatment and control groups during the trial. For trials with more than one intervention, the intervention arms were examined separately.

Results of the review
Fourteen randomised controlled trials (RCTs) with 16 intervention arms were included. Total participants: n= 3,961. Those with exit angiograms: n=3,141.

Lipid results: on average, treatment reduced LDL levels by 25.7% (from 16.3% in the lifestyle study to 37.3% in the surgical arm) compared with controls. High density lipoprotein (HDL) levels increased modestly on most treatments; however, in the lifestyle arms it decreased by 6.3% on average. Triglyceride levels increased on lifestyle and resin treatments and decreased on all other treatments.

Angiographic outcomes: the overall incidence of disease progression decreased by about 49% (odds ratio 0.51, 95% CI: 0.45-0.59), the incidence of no change increased by about 33% (odds ratio 1.33, 95% CI: 1.15-1.53) and the incidence of disease regression increased by about 219% (odds ratio 2.19, 95% CI: 1.78-2.69). All classes of intervention significantly reduced disease progression; however, surgery appeared to be more effective than drugs, except resins. For the no change category, only surgery had a significant effect among the individual classes of intervention. The results for disease regression were similar across treatment classes, with all classes except resins showing significant increases in the odds ratios for regression.

Cardiovascular events: overall incidence of cardiovascular events was 24% in the control groups and 15% in the treatment groups. The lowest incidence of cardiovascular events was observed in the lifestyle trials (12%) and the highest incidence was observed in the surgical trial (52%). The meta-analysis confirms a highly significant reduction in cardiovascular events of the order of 47% (odds ratio 0.53, 95% CI: 0.45-0.63).

Relations of angiographic outcomes to lipids: Baseline levels of LDL had a modest inverse correlation with the odds ratio for progression: the higher the baseline LDL level, the greater the inhibition of progression (r=-0.420). For regression, the correlation with baseline LDL levels was weakly positive (r=0.123).

Authors' conclusions
All interventions reduced LDL cholesterol levels (average reduction 26%), whereas the effects on HDL cholesterol and triglycerides varied by type of intervention. Lipid reduction is effective for modifying the angiographic outcome and for reducing the incidence of coronary artery disease events. It is hypothesised that lowering LDL levels by 30 mg/dl is sufficient on average to modify the angiographic outcome, with modest gains from further reductions in LDL levels.

CRD commentary
No search method or strategy was given and the quality of studies was not discussed in detail. The method by which studies were assessed was not described, nor whether the data extraction procedure was subject to checking by one or more additional reviewers.

In nine of the studies, the baseline LDL levels were either at the upper normal limit, or borderline.

Bibliographic details
Rossouw J E. Lipid-lowering interventions in angiographic trials. American Journal of Cardiology 1995; 76(9 Special
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.