Percutaneous coronary interventions for non-acute coronary artery disease: a quantitative 20-year synopsis and a network meta-analysis

CRD summary
This review compared percutaneous coronary interventions to each other or medical therapy for the treatment of non-acute coronary artery disease. The authors concluded that there was support for the use of medical therapy as an initial management strategy. Review limitations make the reliability of the pooled results uncertain, but the overall conclusion was suitably cautious and appears appropriate.

Authors' objectives
To evaluate the effectiveness of percutaneous transluminal balloon coronary angioplasty (PTCA), bare metal stents and drug eluting stents for the treatment of non-acute coronary artery disease.

Searching
MEDLINE was searched to April 2008 for publications in English. Search terms were reported. Reference lists of previous meta-analyses were searched for additional studies.

Study selection
Randomised controlled trials (RCTs) of PTCA, bare metal stents or drug eluting stents compared to each other or medical therapy in patients who had symptomatic or asymptomatic non-acute coronary artery disease were eligible for inclusion. Included trials had to have at least 10 patients in each group, comparing at least two of the treatments of interest. Trials were excluded if they: recruited patients within 72 hours of a myocardial infarction (MI); were restricted to patients with diabetes; focused on venous bypass grafts, in-stent restenosis, or left main disease; compared two techniques of the same type (for example, two bare metal stents); used different types of percutaneous coronary intervention in the same group unless at least 85 per cent of the comparator group were given one type. Outcomes of interest were mortality, MI, revascularisation and coronary artery bypass graft (CABG). Where reported, the mean age of participants ranged from 52 to 69 years, 59 to 100 per cent were male, 0 to 56 per cent had diabetes and 10 to 100 per cent had multi-vessel disease. Most trials compared bare metal stents with PTCA or drug eluting stents with bare metal stents. Trials comparing PTCA with medical therapy tended to have younger patients and fewer patients with unstable angina than other comparisons.

The authors did not state how studies were selected for the review, or how many reviewers performed the study selection.

Assessment of study quality
The authors did not state that they systematically assessed validity; blinding was the only quality criteria stated as being assessed.

Data extraction
The number of patients experiencing each outcome was extracted, and a relative risk (RR) and 95% confidence intervals (CI) were calculated for each study.

Data were extracted by one reviewer and checked by a second; discrepancies were resolved by consensus.

Methods of synthesis
Pooled RR and 95% CI were calculated from the RCTs with direct comparisons using a random-effects model. A mixed treatment analysis was conducted which combined direct and indirect evidence, using a two-level linear mixed effects model with heteroscedastic errors. Heterogeneity was assessed using the I² statistic. Subgroup and sensitivity analyses were conducted investigating: type of drug eluting stents; the proportion of patients with unstable angina;
timing of MI prior to randomisation; and the inclusion of mixed interventions in the percutaneous coronary intervention group. Where event rates were zero, 0.5 was added to all cells for these analyses.

**Results of the review**

Sixty three RCTs were included (n=25,388; range 41 to 2286); median follow-up was 12 months (interquartile range 6 to 24 months). One trial was reported as being triple-blind, 12 as double blind, seven reported blinding the outcome assessor, one was open label; blinding was not reported in the other trials.

No direct comparison showed a significant difference between groups in terms of mortality or MI. The only direct comparisons to show a statistically significant results were a reduction in CABG with drug eluting stents compared to bare metal stents (RR 0.56, 95% CI: 0.36, 0.88; 12 trials) and target vessel/lesion revascularisation with bare metal stents compared to PTCA (RR 0.68, 95% CI: 0.60, 0.77; 32 trials). Statistically significant heterogeneity was observed for the revascularisation outcomes, and MI in PTCA versus medical therapy.

When indirect evidence was taken into account, there was a significant reduction in: revascularisation with bare metal stents compared to medical therapy (RR 0.71, 95% CI: 0.58, 0.87); CABG with drug eluting stents compared to medical therapy (RR 0.58, 95% CI: 0.38, 0.88); target vessel/lesion revascularisation (RR 0.68, 95% CI: 0.60, 0.77) and revascularisation (RR 0.77, 95% CI: 0.61, 0.99) with bare metal stents versus PTCA; CABG (RR 0.55, 95% CI: 0.37, 0.81) and target vessel/lesion revascularisation (RR 0.30, 95% CI: 0.17, 0.51) with drug eluting stents versus PTCA; and CABG (RR 0.56, 95% CI: 0.39, 0.80) and target vessel/lesion revascularisation (RR 0.44, 95% CI: 0.35, 0.56) with drug eluting stents versus bare metal stents. No direct evidence was available for drug eluting stents versus PTCA or medical therapy.

Subgroup and sensitivity analyses did not alter the results of the main analyses (data not reported).

**Authors' conclusions**

The results of the review support the current recommendations to optimise medical therapy as an initial management strategy in patients with non-acute coronary artery disease. Catheter-based treatment shows no evidence of an effect on death or MI compared to medical therapy.

**CRD commentary**

The authors addressed a clear research question with detailed inclusion criteria. Only a single electronic database was searched, which could lead to missed studies, although the review did have a large number of studies included with a substantial patient population. Unpublished studies were not sought and this may lead to publication bias affecting the results of review, despite the large numbers of studies involved, as a result of selective reporting. Data were extracted in duplicate; however it was unclear whether a similar precaution was used to avoid selection bias during study selection. Study quality was not systematically assessed and therefore the reliability of the results from individual studies is not clear. Supplementary study details were available in tables online, although the methodological and population details provided were sparse, making an assessment of clinical heterogeneity difficult. Statistical heterogeneity was observed for all except one of the outcomes assessed, using traditional meta-analytic techniques that went on to produce statistically significant effects when the indirect comparison was made. The authors state that the results from the network of evidence should be interpreted with caution in patients with unstable angina. Given the above concerns, the reliability of the pooled results is uncertain, although the overall conclusion was suitably cautious and seems appropriate given the lack of evidence for a benefit of invasive percutaneous coronary interventions over medical therapy.

**Implications of the review for practice and research**

Practice: The authors did not state implications for practice beyond the recommendation for the use of current guidelines.

Research: The authors stated that a direct comparison of drug eluting stents with medical therapy was required.

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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.