A meta-analysis of clinical trials of paclitaxel- and sirolimus-eluting stents in patients with obstructive coronary artery disease
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CRD summary
This review compared the effects of sirolimus and paclitaxel drug-eluting stents in people with obstructive coronary disease. The authors concluded that major adverse cardiac events, restenosis rates and late loss of arterial lumen diameter were less with drug-eluting stents than with bare metal stents. Problems with the review methodology and reporting mean that the conclusion should be treated with caution.

Authors' objectives
To compare the effects of paclitaxel and sirolimus drug-eluting stents with bare metal stents in people with obstructive coronary artery disease.

Searching
MEDLINE and EMBASE (to June 2004) and the Cochrane Library (2003) were searched for studies published in the English language; the search terms were given. The reference lists of retrieved articles and Index Medicus were handsearched. Conference abstracts detailed in journals and online were also checked.

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 the effects of paclitaxel or sirolimus drug-eluting stents with bare metal stents were eligible for inclusion. One study assessing QP2, a taxane derivative-eluting stent, was also included in the analysis. Both polymer- and non polymer-coated stents were used in the included studies. Concomitant medication varied across the studies and included aspirin, clopidogrel, heparin, cilostazol, glycoprotein IIb/IIIa inhibitors and ticlopidine.

Participants included in the review
Studies on people with de novo coronary lesions, stable or unstable angina, or silent ischaemia were eligible for inclusion. No further details were reported on those evaluated in the included studies.

Outcomes assessed in the review
The outcomes of interest were incidence of major adverse cardiac events (not defined), restenosis rates and late loss of arterial lumen diameter. The studies had to report data as the relative risk or odds ratio (OR) or mean difference for one or more of these outcomes to be eligible.

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

Assessment of study quality
Each study was assigned a quality score using published guidance that included items such as randomisation, baseline comparability, eligibility criteria, cointerventions, blinding, withdrawals and use of intention-to-treat analysis. Details on how each component was scored were not reported in the paper. The authors did not state how the papers were assessed for quality, or how many reviewers performed the quality assessment.
Data extraction
The authors did not state how the data were extracted for the review, or how many reviewers performed the data extraction. The OR and 95% confidence intervals (CIs), or data to enable the calculation of the OR, were extracted from each individual study for restenosis rates or major adverse cardiac events. For late loss of lumen diameter, data were extracted on the mean differences between treatment groups in each study.

Methods of synthesis
How were the studies combined?
For studies reporting restenosis or major adverse cardiac events, a pooled OR with 95% CI was calculated using both fixed-effect (Mantel-Haenszel) and random-effects (DerSimonian and Laird) models. For studies reporting lumen diameter loss, a pooled standardised mean difference (SMD) with 95% CI was calculated. Publication bias was assessed using a funnel plot and Rosenthal's file drawer method.

How were differences between studies investigated?
Statistical heterogeneity was assessed by calculating the Q statistic (P<0.05 was considered statistically significant). For restenosis rates, the analysis was repeated with and without the study in which a taxane derivative was used in the drug-eluting stent group.

Results of the review
Thirteen RCTs (4,379 participants) were included.

The study quality scores ranged from 0.45 to 0.76. The funnel plot did not exclude the possibility of publication bias. At least 31 negative trials would have been required to change the statistically significant results with drug-eluting stents into non significant results.

Drug-eluting stents significantly reduced the incidence of major adverse cardiac events (random-effects OR 0.35, 95% CI: 0.24, 0.50) and of restenosis rates (random-effects OR 0.27, 95% CI: 0.15, 0.47) in comparison with bare metal stents. The results of the fixed-effect analyses were similar.

The likelihood of restenosis remained significant when excluding the results of the trial that evaluated QP2 eluting stents from the analysis (OR 0.24, 95% CI: 0.19, 0.31).

The late loss of lumen diameter was significantly less with the drug-eluting stents than with bare metal stents (SMD 0.57, 95% CI: 0.49, 0.68).

Authors' conclusions
Compared with bare metal stents, paclitaxel- and sirolimus-eluting stents significantly reduce major adverse cardiac events, restenosis rates and late loss of arterial lumen diameter.

CRD commentary
The inclusion criteria for this review were stated. Several relevant sources were searched to identify studies, although only English language studies were eligible for inclusion. In addition, the assessment of publication bias suggested that it was possible that some studies were missed. No details of methods used to minimise reviewer bias and error in the review process (i.e. study selection, data extraction, quality assessment) were given. One of the included studies did not appear to meet the inclusion criteria because a different drug was used in the stents. It was unclear why it was decided to include this study, given that it accounted for most of the heterogeneity in the analysis of restenosis. Furthermore, the authors did not say if they sought or found any similar studies. The quality of each included study was assessed using established criteria and used to produce a summary score. However, it was unclear how the individual components were scored and the results for the individual studies were not reported.

There was very little detail of the included participants (i.e. age, severity of disease, concomitant illness of participants.
evaluated in the included studies) and this could affect the generalisability of the results. In addition, the authors gave no details of the length of follow-up for the results of the review. In view of these comments, the results of the review should be treated with caution.

**Implications of the review for practice and research**
The authors did not state any implications for practice or further research.

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