Everolimus-eluting versus sirolimus-eluting stents: an updated meta-analysis of randomized trials

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CRD summary
This review concluded that everolimus-eluting stents had a similar incidence of clinical events to sirolimus-eluting stents, but they may have had a lower risk of definite stent thrombosis. The uncertain quality of the evidence, the short follow-up, and the differences in the definition and measurement times of major adverse cardiac events, limit the reliability of the results.

Authors' objectives
To compare the clinical outcomes of everolimus-eluting stents, with those of sirolimus-eluting stents, in patients with coronary artery disease, who were undergoing percutaneous coronary intervention.

Searching
Cochrane Central Register of Controlled Trials (CENTRAL), and PubMed were searched to September 2011. Five clinical trial internet sites and five conference sites were searched. Reviews and editorials from major medical journals that were published within the last year were screened for relevant trials. Experts were contacted for unpublished trials.

Study selection
Randomised controlled trials (RCTs) of everolimus-eluting stents versus sirolimus-eluting stents, in patients with coronary artery disease, who were undergoing percutaneous coronary intervention, were eligible for inclusion. The primary outcome was the composite of major adverse cardiac events (MACE) at the longest follow-up. Secondary outcomes included target lesion revascularisation, and the composite of probable and definite stent thrombosis. Other clinical outcomes were considered.

In the included trials, the patients' mean age ranged from 63 to 69 years. Some trials specifically defined MACE as including cardiac death, whilst others simply stated death. One trial included definite stent thrombosis in the definition of MACE. The percentage of male patients ranged from 59 to 80. The duration of clopidogrel therapy ranged from six to 12 months or more.

The authors did not state how many reviewers selected studies.

Assessment of study quality
A formal quality assessment was not undertaken, but the trials were assessed for allocation concealment, performance of the analysis according to the intention-to-treat principle, and blinded assessment of the outcomes of interest. The authors did not state how many reviewers assessed quality.

Data extraction
Data were extracted on the MACE and other clinical outcomes, and used to calculate hazard ratios, with 95% confidence intervals. If one trial group experienced no events, the estimate of the treatment effect, and its standard error, were calculated after adding 0.5 to each cell of the 2x2 table for the trial.

The authors did not state how many reviewers extracted the data.

Methods of synthesis
DerSimonian and Laird random-effects meta-analysis was used to calculate pooled hazard ratios and 95% confidence intervals. \( \hat{I}^2 \) and Cochran Q were used to assess statistical heterogeneity. \( \hat{I}^2 \) values under 25% were deemed low, 25 to 50% were moderate, and over 50% were high. Sensitivity analyses were conducted for primary and secondary outcomes, by removing each trial consecutively.

Results of the review
Eight RCTs were included in the review, with 11,167 patients (range 150 to 3,197). Follow-up ranged from nine to 36 months. No quality details were reported.

There was no significant difference in the rate of MACE (HR 0.91, 95% CI 0.79 to 1.04; I²=0; eight RCTs) between everolimus-eluting stents versus sirolimus-eluting stents. There was no significant difference in repeat revascularisation (eight RCTs; I²=0), and the composite of probable and definite stent thrombosis (eight RCTs; I²=0). There were no significant differences in all-cause deaths, and myocardial infarction.

There was a statistically significant decrease in definite stent thrombosis with everolimus-eluting versus sirolimus-eluting stents (HR 0.49, 95% CI 0.27 to 0.91; I²=0; six RCTs).

The sensitivity analysis was reported as not significantly altering the results.

**Authors’ conclusions**

Everolimus-eluting stents had a similar incidence of overall clinical events, compared with sirolimus-eluting stents, but they may have had a lower risk of definite stent thrombosis.

**CRD commentary**

The inclusion criteria were clearly defined and several relevant data sources were searched. Publication bias was not assessed, but two unpublished trials were included. It was not clear if any attempts were made to reduce reviewer error and bias during data extraction, quality assessment, and study selection. Quality assessment was not undertaken using a standard checklist, and the results were not presented, which makes it difficult to assess the reliability of the included trials.

The data were combined using meta-analysis and no substantial statistical heterogeneity was indicated. The authors noted that the definition of MACE was not consistent across trials, and they were reported at different follow-up times across the trials. They also acknowledged that the follow-up periods in the trials might not have been sufficient to detect important outcomes. They stated that the power of the review to detect rare events, such as stent thrombosis, might have been limited.

The uncertain quality of the evidence, the relatively short follow-up, and the differences in the definition and measurement times of MACE across the included trials, limit the reliability of the overall results. The authors appropriately stated that their findings should be interpreted with caution and may warrant further investigation.

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

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

**Research:** The authors stated that their results should be investigated further.

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