Benefits and harms of statin therapy for persons with chronic kidney disease: a systematic review and meta-analysis
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CRD summary
This well-conducted review concluded that statins decreased mortality and cardiovascular events in persons with early stages of chronic kidney disease, had little or no effect in people who received dialysis and had uncertain effects in kidney transplant recipients. The authors’ conclusions reflect the evidence available and appear likely to be reliable.

Authors' objectives
To assess the benefits and harms of statin therapy for adults with chronic kidney disease and examine whether effects varied by stage of disease.

Searching
Studies were identified from a previous review published by the authors in 2008. Additionally, EMBASE, Cochrane Central Register of Controlled Trials (CENTRAL) and Cochrane Renal Group's Specialised Register were searched from inception to February 2012 without language restrictions. Search strategies were not reported but were available from the authors on request.

Study selection
Eligible studies were randomised trials that compared the effects of statins with placebo, no treatment, standard care or another statin in patients with any stage of chronic kidney disease. Studies had to report on mortality and cardiovascular outcomes. Studies with a follow-up period of less than eight weeks were excluded.

Most trials were of doses equivalent to or less than 20mg of simvastatin (a range of statins were studied). Most patients had not undergone dialysis or kidney transplant. Mean ages of patients and the proportion with diabetes varied widely across studies. The commonest comparator treatment was placebo.

Two reviewers independently selected studies for inclusion.

Assessment of study quality
Two or more authors independently evaluated risk of bias for sequence generation, allocation concealment, blinding, intention-to-treat analysis, completeness of outcome data, selecting outcome reporting and other threats to validity. The quality of evidence was summarised using Grading of Recommendations Assessment, Development, and Evaluation (GRADE) guidelines.

Data extraction
Data were extracted to enable calculation of relative risks (RR) or mean differences, with 95% confidence intervals (CI). Three population classifications were made according to use (or not) of dialysis (dialysis or chronic kidney disease) and receipt of kidney transplant.

Two reviewers independently extracted data.

Methods of synthesis
Meta-analyses were performed to calculate pooled relative risks or mean differences (with 95% confidence intervals) using a random-effects model. Publication bias was assessed using funnel plots and Egger's test. Heterogeneity was assessed using the Cochran Q test and the I² statistic. The authors prespecified subgroup analyses to investigate heterogeneity. Absolute effects per year of treatment per 1,000 treated were calculated using meta-analysis results along with event rate estimates from observational studies.

Results of the review
Eighty trials (51,099 participants) were included. Most studies were unclear in their reporting of randomisation and
allocation concealment methods. Around one third of studies were at high risk of bias with respect to blinding, intention-to-treat analyses and reporting of incomplete outcome data. More than half of the studies were at risk of bias due to other threats to validity. Around three-quarters of the studies were at high risk of bias due to selective outcome reporting. Two studies had a low risk of bias for all assessments. Follow-up ranged from two months to 5.5 years.

Moderate to high quality evidence suggested statins reduced all-cause mortality (RR 0.81, 95% CI 0.74 to 0.88; 11 studies, I²=32%), cardiovascular mortality (RR 0.78, 95% CI 0.68 to 0.89; eight studies, I²=0%) and major cardiovascular events (RR 0.76, 95% CI 0.73 to 0.80; 14 studies, I²=30%) in participants who did not receive dialysis. There was an indication that publication bias affected the major cardiovascular events analysis.

Moderate to high quality evidence indicated that statins had no statistically significant effects on all-cause mortality, cardiovascular mortality and major cardiovascular events in participants who received dialysis. There was no evidence of heterogeneity.

Low quality evidence suggested uncertain effects of statins in kidney transplant recipients.

Meta-regression analyses for all-cause mortality suggested that heterogeneity was related to disease stage, statin type, estimated glomerular filtration rate, baseline cholesterol and the proportion of patients with diabetes.

Statins had little or no effect on cancer, myalgia, abnormal liver function or withdrawal from treatment (adverse effects were evaluated in fewer than half of the trials).

Further results were reported.

**Authors' conclusions**
Statins decreased mortality and cardiovascular events in persons with early stages of chronic kidney disease, had little or no effect in people who received dialysis and had uncertain effects in kidney transplant recipients.

**CRD commentary**
The review addressed a clear question and was supported by reproducible inclusion criteria. The authors attempted to identify relevant studies in any language by searching electronic databases and checking trial registers; several studies were published only as conference proceedings. Suitable methods were employed to reduce the risks of reviewer error and bias throughout the review.

Study quality was assessed comprehensively and the results were used when interpreting the results of the review (although study quality results for individual studies were not presented). Study details were provided and appropriate methods were used to synthesise data and to assess and investigate heterogeneity.

The authors' conclusions reflect the evidence available and appear likely to be reliable.

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

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