Impact of statins on risk of stroke: a meta-analysis
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CRD summary
The authors concluded that statin therapy significantly reduced the risk of developing all cerebrovascular events and ischaemic stroke, but was associated with a non-significant increased risk of haemorrhagic stroke. Overall, this review appeared to be well conducted, but it was difficult to assess the reliability of the findings without further information about the quality of the studies.

Authors' objectives
To evaluate the effect of statin therapy on all cerebrovascular events, ischaemic stroke and haemorrhagic stroke.

Searching
MEDLINE, EMBASE, CINAHL and Web of Science were searched for English-language publications from June 1975 to September 2006; search terms were reported. The authors searched abstracts of meetings of the American College of Cardiology, the American College of Clinical Pharmacy and the American Stroke Association from 2001 to 2006. The reference lists of review articles were checked.

Study selection
Randomised controlled trials (RCTs) of statins versus placebo that compared the incidence of cerebrovascular events (ischaemic and haemorrhagic stroke) in patients at risk of stroke were eligible for inclusion in the review. Studies that included an active therapy or standard care control group and studies of cerivastatin were excluded from the analysis. Studies were also excluded from the analysis if there were no events in either group.

Included studies were mostly a mixture of primary and secondary cardiovascular disease prevention trials using a placebo run-in period. Statins included atorvastatin (dose range from 10 to 80mg/day), simvastatin (dose range from 20 to 40mg/day), lovastatin (dose range from 20 to 80mg/day), fluvastatin (dose range from 40 to 80mg/day) and pravastatin (dose range from 10 to 40mg/day). Most included participants were white males with a history of hyperlipidemia. Approximately 21% of the overall sample population were current smokers. Mean age ranged from 50 to 75 across studies. Two trials also included numbers of transient ischaemic attacks when assessing cerebrovascular events. The length of follow-up ranged from six months to six years.

The authors did not state how many reviewers selected the studies for inclusion.

Assessment of study quality
The quality of the included studies was assessed using the criteria of randomisation, allocation concealment, blinding and withdrawals. Three reviewers independently assessed quality; any disagreements were resolved by consensus.

Data extraction
Relative risks with 95% confidence intervals were calculated. Data on transient ischaemic attacks were not extracted for inclusion in the analysis of all cerebrovascular events (when reported separately). Three reviewers performed the data extraction; any disagreements were resolved by consensus.

Methods of synthesis
Meta-analyses examining pooled relative risks with 95% confidence intervals (CIs) were performed using the DerSimonian and Laird random-effects model. The data were also examined using a Mantel-Haenszel Rothman-Boice fixed-effect model. Statistical heterogeneity was evaluated using Cochran's Q statistic (using p<0.1 to indicate heterogeneity). Publication bias was assessed through visual inspection of funnel plots and using Egger's regression method.

Results of the review
Twenty-seven RCTs (n=100,683) were included in the review. The sample sizes ranged from 100 to 20,536 participants.

The authors reported that 25 studies were double-blind. No other quality assessment criteria were reported.

Statin therapy significantly reduced the risk of all cerebrovascular events in the treatment group compared to control group (relative risk 0.83, 95% CI: 0.76 to 0.91; 26 trials, n=100,560). There was no statistical heterogeneity between the trials. No publication bias was evident.

Statin therapy significantly reduced the risk of ischaemic stroke in the treatment group compared to control group (relative risk 0.79, 95% CI: 0.63 to 0.99; six trials, n=37,292). There was statistical heterogeneity between the trials (p=0.03). No publication bias was found.

There was no significant difference in the incidence of haemorrhagic stroke between statin and control. No significant heterogeneity was reported. No publication bias was evident.

Authors' conclusions
Statin therapy significantly reduced the risk of developing all cerebrovascular events and ischaemic stroke. It was also associated with a non-significant increased risk of haemorrhagic stroke.

CRD commentary
The review addressed a clear question and was supported by clear inclusion criteria. Attempts to identify all relevant studies were undertaken by searching electronic databases and other sources, including conference abstracts. The authors did not find any publication bias. As the search was limited to English-language publications, language bias may have been introduced. Some quality assessment criteria were assessed, but were not adequately reported. Although the overall sample sizes were large, sensitivity analyses of better-quality studies would have provided more confidence in the summary results. Three reviewers were involved in some aspects of the review process, which reduced the risk of reviewer bias. The studies were appropriately summarised in a meta-analysis, but the authors did not discuss potential sources of statistical heterogeneity in one of the analyses. Overall, this review appeared to be well-conducted, but it was difficult to assess the reliability of the findings without further information about the quality of the studies.

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

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