Cholesterol lowering with statin drugs, risk of stroke, and total mortality: an overview of randomized trials

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Authors' objectives
To assess the effectiveness of statin drugs to reduce the risk of stroke and total mortality.

Searching
A computerised literature search was performed from 1985 to 1995. Data from the Cholesterol and Recurrent Events (CARE) Trial was added when the report was published in late 1996. The search was limited to English language articles. Principal researchers of the included trials and their respective funding bodies were contacted for details of unpublished reports.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs) testing statin drugs with an average follow-up of 3.3 years, were included.

Specific interventions included in the review
Simvastatin (2 studies), pravastatin (8 studies) and lovastatin (6 studies).

Participants included in the review
The majority of trials recruited patients with elevated lipid levels, although one study was designed to evaluate coronary events in post-myocardial infarction (MI) patients with usual cholesterol levels. Most trials contained a mixture of patients who were either disease-free or post-MI. Treatment groups included both male and female patients whose mean ages ranged from 53 to 63 years.

Outcomes assessed in the review
Stroke; total deaths; deaths due to cardiovascular disease (CVD and non-CVD); occurrence of cancer; lipid lowering.

How were decisions on the relevance of primary studies made?
The authors do not state how the papers were selected for the review, or how many of the authors performed the selection. All studies had to meet the following selection criteria: lipid lowering was attained only by statin drugs; and data were presented for deaths and/or strokes.

Assessment of study quality
The authors discuss important characteristics of each included trial by narrative discussion. The authors do not state how the papers were assessed for validity, or how many of the authors performed the validity assessment.

Data extraction
Two researchers extracted the data.

Methods of synthesis
How were the studies combined?
The overall odds ratios were calculated. Subgroup analyses were carried out to assess the effectiveness of dose, duration of treatment, and primary versus secondary prevention.

How were differences between studies investigated?
Chi-squared statistics were employed to test for heterogeneity.
Results of the review
Sixteen trials (29,008 participants) were included.

Average reductions in total and low-density lipoprotein cholesterol were 22 and 30%, respectively.

Reductions in risks of stroke: 29% (95% confidence interval, CI: 14, 41).

Reductions in deaths due to CVD: 28% (95% CI: 16, 37).

Reduction in total mortality: 22% (95% CI: 12, 31).

Non-CVD mortality unchanged: relative risk 0.93 (95% CI: 0.75, 1.14).

Cancer risk unchanged: relative risk 1.03 (95% CI: 0.90, 1.17).

Authors’ conclusions
Statin use is associated with large reductions in cholesterol levels and benefits in reduced risk of stroke and total mortality. There is a significant decrease in CVD mortality, but no significant increase in either non-CVD deaths or cancer.

CRD commentary
A timely review of the efficacy and associated risk of statin use. This study, whilst providing a valuable contribution to the debate over statin use, fails to report important design characteristics that are required to assess the methodological rigour of this review. The authors do not provide comprehensive search details, without which it is difficult to assess how complete this review is, and validity of the primary studies was not assessed quantitatively. However, the large number of participants included in the analysis (greater than 29,000) would tend to suggest that the authors’ conclusions are sound.

Implications of the review for practice and research
Statin use is effective at lowering lipid levels and reducing the attack rate of strokes, total mortality and CVD deaths. There is no evidence that statins are associated with non-CVD deaths.

Bibliographic details

PubMedID
9228438

Other publications of related interest


Indexing Status
Subject indexing assigned by NLM

MeSH
Anticholesteremic Agents /therapeutic use; Arteriosclerosis /prevention & control; Cardiovascular Diseases /epidemiology; Cerebrovascular Disorders /epidemiology; Enzyme Inhibitors; Humans; Hydroxymethylglutaryl CoA Reductases; Hydroxymethylglutaryl-CoA Reductase Inhibitors /therapeutic use; Hypercholesterolemia /drug therapy; Mortality; Neoplasms /epidemiology; Randomized Controlled Trials as Topic; Risk

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