
Study protocol: A systematic review of trials of statins for primary prevention of cardiovascular diseases

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BACKGROUND

Cardiovascular disease constitutes a major public health challenge, and its contribution to the global burden of disease is expected to increase over the coming decades (1).

Hyperlipidaemia is an important modifiable risk-factor for developing cardiovascular diseases (2).

We will conduct a systematic review of evidence from randomised controlled trials on the effects of the most commonly used lipid-lowering drugs, HMG-CoA-reductase inhibitors (statins), for the primary prevention of cardiovascular disease.

METHODS

This analysis will be based on an update of the literature search, article-selection and data-extraction that we carried out as part of a recent systematic review commissioned by the Norwegian Directorate for Health (3).

Searching

We will conduct a broad, updated search for randomised controlled trials of interventions for primary prevention of cardiovascular disease in the following databases: CENTRAL, MEDLINE, EMBASE and AMED. We also search for systematic reviews in The Cochrane Library, in which we will examine reference lists for further references. We will not apply any language restrictions.

Selection

Since we are focussing on primary prevention, we will exclude trials where more than half the participants have experienced a myocardial infarction, stroke or other significant cardiovascular event. Our main outcomes are total mortality, myocardial infarction and stroke. We will also report on the following outcomes: angina and heart failure.

Validity assessment

We will use a stepwise approach for validity-assessment. Firstly, titles and abstracts will be assessed for relevance. Potentially relevant articles will be assessed in full text, and those deemed relevant assessed for internal validity using standardised criteria (4). At each step two reviewers will make independent assessments of each article. Disagreements will be resolved through discussion, e.g. through e-mail discussions or at plenary meetings for the whole group of reviewers.

Data extraction

Data extraction will be done independently by two reviewers.

Study characteristics

Disagreements regarding study design, characteristics of study participants, intervention, outcomes and clinical heterogeneity will be resolved on an ad hoc basis through plenary discussions and, if necessary, by making compromises.

Data synthesis

We will conduct meta-analyses in RevMan 4.2 (5) and present results as relative risks with 95% confidence intervals. We will use fixed-effects models as our starting point for all analyses.

Sub-group analyses will be conducted for women and men, and for younger and older trial-participants. We will also consider comparing results from trials with large, medium or small proportions of hypertensive participants.

Grading the evidence

We will assess the quality of the evidence for each outcome using the GRADE-instrument (6).

References

- (1) The World Health Organization. World Health Statistics 2008. 2008. Geneva, The World Health Organization.
- (2) The World Health Organization. The World Health Report 2002. Reducing Risks, Promoting Healthy Lives. 2002. Geneva, The World Health Organization.
- (3) Håheim L, Fretheim A, Brørs O, Kjeldsen SE, Kristiansen IS, Madsen S et al. Primærforebygging av hjerte- og karsykdom, med særlig vekt på medikamentelle tiltak. 2008. Oslo, Norwegian Knowledge Centre for the Health Services.
- (4) Harbour R, Miller J. A new system for grading recommendations in evidence based guidelines. *BMJ* 2001; 323:334-336.
- (5) Review Manager (RevMan). Version 4.2 for Windows. Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2003.
- (6) Atkins D, Best D, Briss PA, Eccles M, Falck-Ytter Y, Flottorp S et al. Grading quality of evidence and strength of recommendations. *BMJ* 2004; 328:1490.