Pharmacologic lipid-lowering therapy in type 2 diabetes mellitus: background paper for the American College of Physicians
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CRD summary
This review assessed the effectiveness of pharmacologic lipid-lowering therapy in preventing cardiovascular events in patients with type 2 diabetes. Lipid-lowering agents were found to reduce cardiovascular risk. However, the authors warned that recommendations for primary prevention therapy could not be made for diabetics with relatively low cardiovascular risk. The evidence was not assessed for quality, hence the conclusions may not be reliable.

Authors' objectives
To assess the effectiveness of pharmacologic lipid-lowering therapy in patients with type 2 diabetes mellitus.

Searching
MEDLINE (searched in September 2002) and the Cochrane Library were searched using the search terms listed in the review. Further studies were sought through contact with experts and by scanning references of identified articles, meta-analyses and reviews.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs) were eligible for inclusion.

Specific interventions included in the review
Studies of pharmacologic lipid-lowering therapies were eligible for inclusion. The treatments included in the review were lovastatin, pravastatin, gemfibrozil, simvastatin, atorvastatin and fluvastatin; all of which had varied doses. Most of the studies compared the lipid-lowering drug with placebo.

Participants included in the review
Studies of patients with diabetes were eligible.

Outcomes assessed in the review
Studies that measured total mortality and major cardiovascular events, such as cardiovascular mortality, myocardial infarction and stroke, were eligible. Only the reported primary outcome in the studies was included in the review.

How were decisions on the relevance of primary studies made?
The authors did not state how the papers were selected for the review, or how many reviewers performed the selection.

Assessment of study quality
The authors did not state that they assessed validity.

Data extraction
One reviewer extracted the data, with the accuracy of the extraction being confirmed through re-extraction and comparison with the original extraction. The studies were divided into two categories: studies that evaluated the effects of lipid management in primary prevention (patients without known cardiovascular disease) and studies that evaluated the effects in secondary prevention. The relative risk (RR) and absolute risk reduction (ARR), with confidence intervals (CIs), and the numbers-needed-to-treat (NNT) for benefit were calculated for each study.
Methods of synthesis
How were the studies combined?
The studies were combined in meta-analyses using absolute and relative risks and NNT. The studies were summarised under primary prevention trials or secondary prevention trials. In the absence of heterogeneity a fixed-effect model was applied.

How were differences between studies investigated?
Differences between the studies were investigated using the Mantel-Haenszel test. Owing to substantial heterogeneity, the random-effects model of DerSimonian and Laird was used to pool the analyses of secondary prevention. Sensitivity analyses were performed by excluding outlying studies.

Results of the review
Twelve RCTs with at least 11,923 participants (not all patient numbers were reported) were included in the review.

Primary prevention (6 RCTs). There was a significant reduction in the risk of cardiovascular events with lipid-lowering drugs (RR 0.78, 95% CI: 0.67, 0.89; ARR 0.03, 95% CI: 0.01, 0.04). The pooled estimate of NNT to prevent an event was 34.5 for a weighted trial average of 4.3 years. There was no significant heterogeneity between the studies. The sensitivity analysis changed the estimates of effect only slightly.

Secondary prevention (8 RCTs).
There was a significant reduction in the risk of cardiovascular events with lipid-lowering drugs (RR 0.76, 95% CI: 0.59, 0.93; ARR 0.07, 95% CI: 0.03, 0.12). The pooled estimate of NNT to prevent an event was 13.8 for a weighted trial average of 4.9 years. There was significant heterogeneity between the studies. The sensitivity analysis found that the removal of one study eliminated the heterogeneity and slightly reduced the estimates of effectiveness.

Authors' conclusions
Lipid-lowering agents reduce cardiovascular risk in patients with type 2 diabetes.

CRD commentary
The review question was well-defined with clear inclusion criteria. The literature search was limited and it was unclear over what time period the search was conducted. Publication bias was not assessed and it was unclear whether the authors considered non-English language papers, therefore it was not possible to assess language bias. There was no information on the number of reviewers who selected the studies, and the validity of the included studies was not assessed; it is therefore not possible to comment on the likelihood of bias, or on the quality of the included studies. The studies were pooled regardless of the individual drug used. Assuming the reliability of the analyses and adequate quality of the included studies, the authors' conclusion appears reliable.

Implications of the review for practice and research
Practice: The authors stated that there was insufficient evidence to make strong recommendations for primary prevention therapy for people with diabetes with relatively low cardiovascular risk. Aggressive management of lipids provided substantial benefit for people with elevated risk for cardiovascular events, namely type 2 diabetics. The use of statins should be nearly universal in this population.

Research: The authors stated the need for reanalysis of the lipid-lowering trials using multivariable risk stratification prediction tools.

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Other publications of related interest

This additional published commentary may also be of interest. Gami AS. Review: Lipid-lowering agents reduce cardiovascular events in type 2 diabetes. ACP J Club 2004;141:65.

Indexing Status
Subject indexing assigned by NLM

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Record Status
This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.