Reviewer's report

Title: Statins in hypercholesterolaemia: A dose-specific meta-analysis of lipid changes in randomised, double blind trials

Version: 3 Date: 9 October 2003

Reviewer: Paul Hopkins

Reviewer's report:

General
The authors have appropriately responded to most of the prior comments. This remains a well written and potentially valuable manuscript with generally sound conclusions. They have appropriately now cited the excellent review by Law which provides data which most clinicians can generally expect to see using dose-response studies. They further differentiate their study as reflecting only longer lasting studies. These may or may not actually reflect what most people will experience long term as titration studies were included in the analysis (see below).

Discretionary Revisions (which the author can choose to ignore)

Minor Compulsory Revisions
It appears that titration studies are reported separately from the fixed-dose studies in the figures. It is not clear that the results are no different. This reviewer strongly disagrees that the titration studies would be expected to show greater reductions. Instead, it is more likely that those who required titration to higher doses are enriched in relatively unresponsive persons. It is therefore more likely that smaller reductions in LDL would be seen at the same dose in a titration study than a fixed-dose study. At the very least, the authors must make clear in the figure legends whether the studies with a dose range are indeed titration-type studies and what the basis of the titration is (being increased because participants did not reach a pre-specified goal, or whether there was forced titration). Titration to goal versus forced titration will also likely make a large difference in response. Ideally, the authors should do a formal analysis of these types of studies separately from the other types of studies to see whether this particular difference in study design made a significant difference in the estimate of response.

Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

What next?: Accept after minor compulsory revisions

Level of interest: An article of importance in its specialized field or of broad interest

Quality of written English: Acceptable

Statistical review: No

Declaration of competing interests:
We have performed studies for Merck, Pfizer, Abbott, and Astra-Zeneca.