Author's response to reviews

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

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PDF covering letter
Response to Reviewers

We understand what the reviewer is saying. First, we checked again that the papers using dose titration did not recruit patients that were any different than those in other studies where dose titration was not used. No differences were stated. We now say that in a new paragraph in discussion (below). Second, we have not performed a separate analysis for the dose titration studies using a fixed escalation and those using target LDL or total cholesterol, because there is insufficient information. Instead, and to help, we have changed the colours of the symbols in Figures 1-4, so that dose escalation to target cholesterol is now shown in red, allowing a visual interpretation. We make some comments on this in a new paragraph (below).

New paragraph in discussion

In dose titration studies, the dose of statin could be increased up to daily maximum, either according to a prescheduled incremental regimen (blue symbols in Figures 1-4), or to achieve specific reductions in LDL or total cholesterol (red symbols in Figures 1-4). For no single statin and dose range was there sufficient information to assess whether either regimen achieved better results because of limited numbers of studies and patients. Overall, however, there appeared to be no major difference between these two dose titration regimens or use of a fixed dose in the longer duration studies. There was no indication in the individual studies that patients who had been recruited for dose titration studies differed in any way from those who were recruited for fixed dose studies.

In addition, we understand how one particular sentence may have caused a problem for the reviewer in the next paragraph of the discussion. This sentence is speculation, and we have chosen to omit it in this update.

Omitted sentence

This was surprising, because the use of higher doses in dose titration would be expected to recruit more patients with larger reductions in total and LDL cholesterol, and therefore larger reductions in the whole randomised cohort.