Reviewer’s report

Title: The effect of long-term homocysteine-lowering on vascular structure and function in stroke: a randomized controlled trial and meta-analysis

Version: 2 Date: 30 May 2008

Reviewer: Petra Verhoef

Reviewer’s report:

The paper reports on original data of an RCT that investigated effects of long-term homocysteine lowering treatment on carotid artery intima thickness and flow mediated dilation. Next to it includes two meta-analyses of homocysteine-lowering RCT: one with FMD as endpoint, and one with IMT as endpoint. A limitation of the study is the fact that there are no baseline measurements of IMT and FMD, but it is a fair assumption that these were similar for the two treatment groups.

- Discretionary Revisions

1) Proposal for title: The effect of long-term homocysteine-lowering on carotid artery intima-media thickness and flow-mediated vasodilation in stroke patients: a randomized controlled trial and meta-analyses

In my view, it is always better to mention the specific measurements in title than rather vague terms.

2) It would be nice to give some information on the expected moment for VITATOPS trial to report. How many patients are currently included? When will it end?

3) The abstract should mention that these were patients subgroup from VITATOPS.

4) On page 7, under heading ‘Outcomes’, the authors state that CIMT and FMD were the primary outcome measures. That may be true for this substudy, but these participants were also part of the bigger VITATOPS study, where primary outcomes were not IMT and FMD, but vascular events.

- Minor Essential Revisions

1) In the description of the methods, it is not clear right away that no baseline measurements of FMD and IMT were obtained. Can this be stated clearly, early on in the methods?

2) On page 11, under ‘Outcomes and estimation’. The authors state “The estimated effect size (corrected for bias) was 0.06 (95% CI –0.25, 0.37)” . It is unclear to me what is meant by “estimated effect size (corrected for bias)”, and
how this analysis was done. Please elaborate.

3) Figure 3 could be removed as these findings are also given in table 3.

4) Could figure 5 maybe use different sizes of ‘points/balls’ for the studies, dependent on size of study?

- Major Compulsory Revisions:
  None

**Level of interest:** An article of importance in its field

**Quality of written English:** Acceptable

**Statistical review:** Yes, but I do not feel adequately qualified to assess the statistics.

**Declaration of competing interests:**

'I declare that I have no competing interests'