Reviewer's report

Title: Baseline characteristics and Statistical Analysis Plan for the 'Prevention Of Decline in Cognition After Stroke Trial' (PODCAST) trial

Version: 2  Date: 6 July 2015

Reviewer: Sarah Pendlebury

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General comments

The investigators have clearly put a large effort into this trial designed to examine the feasibility of aggressive vascular factor management to prevent cognitive decline in patients post-stroke. Although the target recruitment population was not reached, the findings will inform the design and recruitment method of future trials in this important area. There are a few issues requiring clarification as outlined below.

Compulsory revisions

1. Abstract, introduction. It would be helpful to the reader to have a sentence in the Background clarifying the specific focus of the current paper.

2. Abstract, Methods/Results. The maximum total scores of the ACE(/100) and MoCA(/30) should be given. The definition of the figures in brackets eg (sd) would aid clarity.

3. Abstract, Methods. The time at which the primary outcome was to be measured should be given.

4. Abstract, Results. The NIHSS and Rankin should be given as important characteristics of the trial population.

4. Methods. I am not sure if I have misunderstood but under interventions, it states that all patients were randomised to intensive vs guideline blood pressure lowering and yet later it appears that only 300/600 total participants were to be recruited to the BP group.

5. Eligibility. Not all readers will be familiar with the telephone MMSE, it would be helpful to give the maximum achievable score and the cut-off considered indicative of dementia (ie the score equivalent to <24 in face-to-face testing). Telephone scores of 17 would appear quite low – how was dementia excluded in eligible patients? I understand the DMS-IV criteria were used but how were these criteria applied in practice?

6. Conclusions. The numbers quoted for dementia at 1-year post-stroke from the literature include patients who develop dementia early after stroke whereas in the current trial, these patients are excluded. Given that the post-stroke dementia risk is relatively low after the immediate post-stroke period, any treatment effect might be expected to be small. Further, the available data do not show a strong association between vascular risk factors and post-stroke dementia. Finally, the
NIHSS and cognitive scores show that the trial population had mild events and were relatively high functioning thus further reducing the risk. Some discussion of these issues in relation to the risk of dementia in the trial population and in relation to the earlier statement made by the authors that the inclusion/exclusion criteria were designed to select a high risk population would be helpful.

7. References. Refs 8 and 9 appear to be duplicates.

8. Table 3. How was “memory problem” defined?

9. Protocol references. The references for the telephone MMSE should be given. Also the references should be given for the validation of the ACE-R in cerebrovascular populations (particularly since this is the main outcome measure) and also for the MoCA and TICSm (there are more recent refs than the one given for TICSm) since all these tests were in fact developed and originally validated in non-vascular populations. The cut-offs used should be justified with some background information.

10. Please clarify how the IQCODE was used, the instructions are confusing - the protocol would suggest that the informant compares how the patient is now with how they were at the last follow-up but also suggests they make the judgement over the past year. The original IQCODE requires that the informant compares how the patient is now with how they were 10 years previously. The IQCODE method described in the paper would thus appear to be significantly different from the original – has this been validated? The change from the original should be acknowledged and discussed.

11. The proposed statistical analysis plans would appear appropriate and take into account confounding and adjustment for multiple comparisons.

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

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I declare that I have no competing interests