Reviewer's report

Title: Design and rationale for the 6S - Scandinavian Starch for Severe Sepsis/Septic Shock trial - A double-blinded, randomised clinical trial comparing the effect of hydroxyethyl starch 130/0.4 with balanced crystalloid solution on mortality and kidney failure in patients with severe sepsis

Version: 2 Date: 19 July 2010

Reviewer: Charlie Goldsmith

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Goldsmith 2010-07-15 \BMCTrial\Review
Review of BMC Trials MS: 1655458402401270
Design and Rationale for the 6S Study
Perner A et al

The following comments are offered to improve the presentation of this protocol.

1. Page 2, paragraph 4, line 1. Insert the date that the trial was registered, ideally using the yyyy-mm-dd format. Also include the date that the first patient was randomized, in the same format.

2. Page 5, paragraph 1, line 2. Since [or] logically includes [and], drop [and/]. Also Page 11, paragraph 4, line 6,7.

3. Page 5, paragraph 2, bullet 4, line 1. Replace [mls] by [ml] as metric is not used in a plural way. Also Page 10, bullet 5, line 1.

4. Page 5, paragraph 3. Include a restatement of the 3 blocking factors here.

5. Page 6, paragraph 2, line 10. Is it planned to record all other interventions, in case they matter to the outcome?

6. Page 7, paragraph 2, bullet 6. Will the interim analyses be decided by statistical criteria, or clinical criteria or both? Who will decide on the clinical criteria? The DSME?

7. Page 8, paragraph 6. This reviewer thinks that the first analysis should be taking the blocking and randomization into account with a logistic model, the second analysis could be a simple Chi-square without the blocking and the third could be a logistic model including the listed patient characteristics. Presumably this blocking logistic model that was the one that was justified in the sample size calculations.

8. Page 9, paragraph 2, line 3. Please include the reference to the Haybittle-Peto criteria in the reference list.

9. Page 9, paragraphs 4, bullet 1, line 1. Replace [Parameters] by [Variables]. A parameter is a characteristic of a distribution of a variable and not another name for a variable. Also Page 10, bullet 4.
10. P 9, last l. It seems to make sense to use the 2 hours before randomization, however, why use the time after since variables could be changed by the intervention. This suggests it could not be used as a covariate in future analyses.

11. P 10, b 5, l 1. Spell out [incl.] to [including]. Also P 11, p 2, l 2.

12. P 12, p 1, l 2. Include the date of trial registration and the date the first patient was randomized.

13. P 13, p 6, l 1. Replace [definite] by [definitive].


15. P 15,16. A random sample of 10 references was checked for accuracy with a PubMed search for each.

16. P 15, R(eference) 1, 8 13 were correct.

17. P 15, R 7. Since this is a set of letters and replies in correspondence, either the page numbers are not correct, or other authors should be cited.

18. P 15, R 9. After the 4th author, the [CRYCO Study Group] is listed.

19. P 16, R 17. The authors listed here are not listed as authors in PubMed, yet a study group is listed as the author.


23. Trial Fluid Chart. The [mls] should be replaced by [ml]. See 3 above.

24. Additional File 1, Criteria (2) 1., l 4; 2. l 4; 3. l 2 and 4. l 2. This reviewer could not find a definition for [deranged]. Would it be better to use another term to make it clear to recorders?

25. A(dditional) f(ile) 3, P 1, p 2 under Primary, l 1. Rewrite as [… the Steering Committee (SC).].

26. A f 3, P 5, p 5. This reviewer finds it strange that an ethical issue is decided by members of the DMSC about itself. An external person or committee not involved in the trial should have this responsibility.

27. A f 3, P 6, p 3, l 3. Drop [In order] and capitalize [To], as the 2 words are redundant.


30. A f 5. Define all short forms such as Map and CPAP.