Reviewer's report

Title: The use of LiDCO based fluid management in patients undergoing hip fracture surgery under spinal anaesthesia: Neck of femur optimisation therapy - targeted stroke volume (NOTTS)

Version: 1 Date: 7 July 2011

Reviewer: Charlie Goldsmith

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The plan for this trial could be improved and better understood by readers by paying attention to the issues raised in the following comments.

1. P(age) 2, p(aragraph) 1, l (ine) 1. Suggest inserting [in the United Kingdom] after [hip].

2. P 2, p 2, l 2. Insert [concealed] between [generated] and [tables].

3. P 2, p 2, l 4. Rewrite as [> 65 years]. Include a space between the inequality and the number and insert the age units.

4. P 2, p 2, l 10. Insert [is determined by a blinded team of clinicians] after [stay].

5. P 2, p 3, l 1. Insert the date of registration as well as the date the first patient was randomized. P 5 claims that patents are being recruited; however, it does not mention the date of randomization of the first patient. Was the first patient randomized on September 9, 2009? Has recruiting ceased? If so, include the date the last patient was randomized.

6. P 3, p 1, l 2. Insert [United Kingdom [ between [the] and [UK] and ]] after the latter.

7. P 3, p 1, l 7. Insert [likely] between [will] and [increase].

8. P 3, p 2, l 4. Replace [significant] by [clinically important] or some such phrase, reserving significant for statistical judgments in clinical trials.

9. P 3, p 2. These facts should be supported by suitable references if they are available.

10. P 3, p 2, l 6. Suggest rewriting as [For these reasons most …] as more than one is mentioned.

11. P 4, p 1, l 9. Does R(eference) 18 support all the points raised in the this p? If not, provide other Rs as well as it.

12. P 4, p 1, l 9. Claiming the [never been studied] without a viable search strategy is not sufficient. This may be the authors’ opinions, and so should be toned down unless a recent published search can be cited. Also P 4, p 2, l 2.
13. P 5, p 2, l 3. Was this the same day the first patient was randomized? See 5.

14. P 5, p 3. Include the allocation ratio somewhere here. Presumably it is 1:1; if so, say so.

15. P 5, p 3, l 4 to 6. Using the NHFS to stratify the patients looks as if there are exactly 2 strata: Low and High risk; however, this should be stated as 2 levels. Also, where do you put those with = 10%? The stratification factor has not been considered in the analysis as it seems as if the NHFS is to be used continuously and not as 2 categories that are constraints on the randomization.

16. P 5, p 5, l 6. This statement seems incorrect. The study is not complete until the last patient randomized has been discharged (your primary outcome measure). Otherwise you will not have data on the last few patients and no mention has been made about a censored analysis. It would also be helpful to follow patients until discharge to record any adverse effects that may accrue during the trial and be recorded in their chart.

17. P 5, p 6, l 3 and 4. Subjects randomized should not be able to have you delete their fact/date of death (if it happens) and the date of their discharge as these are important to the proper analysis of your data. However, other secondary data might be erased. It seems to this reviewer that the former 2 variables should be available for all who are randomized. It might be helpful to have ruling on this form your ethics committee, so as not to allow patients randomized to compromise your study credibility. See P 6, last p for more details where this is relevant. Allowing patients to opt out once randomized means you cannot do an intent-to-treat (ITT) analysis on your primary outcome.

18. P 6, p 1, l 2. Replace [significant] by [large] or some other suitable phrase.

19. P 6, last p, l 3 to end and p 1 on next p. Suggest having a selected use of the data, instead of complete withdrawal, ie, 1) death date and discharge date, 2) all other relevant outcomes, and then 3) the remaining data not used for the study outcomes.

20. P 7, p 2, l 1. Replace [parameters] by [variables]. A parameter is a characteristic of a distribution of a variable in a population and not another name for a variable in a sample, as used in this trial. Also P 7, p 4, l 6 and 7.

21. P 7, p 2, l 4. The manufacturer of LiDCOplus should be specified with a location.

22. P 7, p 2 and 3. Too many items are stated without references. Please try to cite suitable references for the things stated here.

23. P 8, p 1, l 4. Please cite the manufacturer’s guidelines.

24. P 8, p 3, l 7. Suggest replacing [significantly] by [clinically important].

25. P 8, p 3. Are the discretionary interventions recorded? This could lead to
serious co-interventions. If they are recorded, then there is a possibility to take them into account in the trial report.


27. P 8, p 5, l 4. Cite the pathway.

28. P 8, p 5, l 8 and 9. Is this report citable?

29. P 9, p 3. It is not clear that the stratification factor is considered in all analyses, since there is a lack of the correct analyses that take this into account. Also, no references are provided for unusually analyses. Consideration should be given to multiple imputation for missing data and suitable censored analyses for things like death and incomplete data. Sensitivity analyses will likely not be powerful enough to measure the impact of changes specified here. Any choices such as these should be documented with suitable references.

30. P 9, p 4. These analyses also do not take the stratification into account and are more complicated than stated as a result. Software such StatXact can handle these analysies using stratification while SPSS can not currently.

31. P 9, p 4, l 11. Unpaired t test does not take the stratification into account. ANOVA could.

32. P 10, p 2, l 3. Rewrite as [\# = 0.05] rather than [p \# 0.05].

33. P 10, p 2. My use of PASS version 11 determined that a sample size of 60 per group would be needed, and the inflation for dropouts should be 60/0.9 = 66.6 or 67 before inflating for stratification. This reviewer suggests adding 1 to get 68 per group or 136 for the trial. If this is challenged, the authors should cite suitable software used to get their sample size, and a case why they did no take dropouts into account properly as well as the inflation for stratification.

34. P 10, p 3. This p has not mentioned ITT analysis. This means you have to analyse all who are randomized with no other criteria. Otherwise your testing is not valid. Other analyses could also be done and should be specified, ie, as per protocol, etc.

35. P 10, p 6. Provide Rs for these.

36. P 11, p 1. Provide dates either here or on P 2 or 5. See earlier issues.

37. P 11, p 2, l 5. Replace [significant] by [important].


39. P 11, p 3. Mention the blinding of your team to get more credit for this with length of stay.

40. P 11, p 3, l 6. Replace [significant] by [clinically important].

41. P 11, p 5, l 2. Replace [significant] by [important].
42. P 12, p 1. Suggest mentioning your choice of LiDCOplus again.
43. P 12, p 2, l 1. Replace [significant] by [important].
44. P 12, p 2, l 8. Suggest that you delete [significant].
45. P 12, p 3, l 2. Replace [significant] by [high].

A random sample of 10 Rs was checked for citation accuracy. Also this reviewer likes to see issue numbers as they make the R easier to find on many databases.

46. P 13, R 4 seems to require payments so could not be verified.
47. P 13, R 12, l 3. Insert [(1)] after [88].
48. P 13, R 13 seems correct.
49. P 13, R 14, l 2. Insert [(1)] after [92].
50. P 14, R 18, l 1. The fifth author is [Grounds], and in l 3, insert [(6)] after [9].
52. P 14, R 22, l 2. Insert [(3)] after [79].
53. P 14, R 26, l 1. The authors are [Hamilton TT, Huber LM, Jessen ME] and on l 2 insert [(4)] after [74].
55. P 15, R 35, l 2. Insert [(5)] after [75].