Reviewer's report

Title: Methodology of the Prospective Economic Evaluation of the Prophylaxis for ThromboEmbolism in Critical Care Trial (E-PROTECT)

Version: 3  Date: 1 August 2014

Reviewer: Christopher Longo

Reviewer's report:

Is this protocol suitable for publication in Trials?
Yes suitable for publication. No completing interests.

1. Will the study design adequately test the hypothesis?
Yes I believe the design will adequately test the hypothesis

2. Are sufficient details provided to allow replication of the work or comparison with related analyses: if not, what is missing?
Yes there is sufficient detail to replicate the study, but I believe some detail can be omitted by referring to standard procedures in health economics texts and health economic guideline documents.

3. Is the planned statistical analysis appropriate?
Yes

4. Is the writing acceptable?
I find overall the paper is a bit hard to follow. The abstract does not adequately cover the content of the paper, and the use of past and present term is mixed in the manuscript. I also think it could be shortened substantially without losing the key points.

• Major Compulsory Revisions
NONE

• Minor Essential Revisions
(1) OVERALL- Although the description of methods is quite important, I find this paper difficult to read. I can see some of the work has already been done and other portions have yet to be done. I would make those distinctions a bit clearer. Perhaps labels/headings: Completed work, work in progress, work yet to be completed. It appears that the main trial is complete, the systematic review is complete, some of the costing is complete, but the full analysis has yet to be undertaken. I believe your focus is, and should be, on the work that has not yet been done and would make this clear both in the abstract and intro.

Details
(2) Abstract - I believe the purpose of this manuscript is to describe the planned
methodology for a prospective economic evaluation of LMWH and UFH, yet in reading it I don’t really get this message. I believe there should be a key statement in the introduction and/or in the methods/design that highlights this as the main purpose of the paper. Within the methods/design the authors use the term “data-rich time horizon” which is a term that I am unfamiliar with. I would suggest that they define this more clearly or use alternate terminology. I would have expected to see an actual time horizon (1 month, 3 months) but am unclear what data-rich means.

(3) Pg. 15 last paragraph – the use of data-rich time horizon appears again.

(4) Pg. 17 1st paragraph - you refer to an Appendix, but provide no Appendix number. I would encourage you to break down your Appendix, which is quite extensive, into parts and number them.

(5) Pg. 18 2nd paragraph – details about funding can be left in the acknowledgements, it does not need to be in the methods.

(6) Pg. 18 last paragraph – comment about “no patients were lost to follow-up”. This is where it is easy to be confused as you read through this document. If you leave the “work already done” in one section and the “work to be done” in another you will not have both past tense and future tense in the same paragraph which is hard to read.

(7) Pg. 20 2nd paragraph - Statement “Direct and indirect costs were be sought from 23 of 67 hospitals” has some errors in grammar.

(8) Pg. 21 1st paragraph – AS an example both past and future terms in this paragraph, but this is because some of the work has been done and other aspects have not. A different structure to your paper would eliminate this.

(9) Pg. 26 last sentence, & pg. 27 first sentence - I find it unusual that if you have a dominant scenario (lower cost, similar outcomes) that you would do a cost-minimization analysis. If you are doing a cost-effectiveness analysis you first check for dominance and if present report it. I think you are saying IF the costs are less AND outcomes are similar we would undertake a cost minimization analysis, but would you not also do a cost minimization analysis if the costs were higher and the outcomes were similar?

(10) Pg. 32 2nd paragraph – Much of this paragraph would be very helpful to highlight in the introduction, and provide justification for why you are doing this work rather than presenting it at the end.

• Discretionary Revisions
NONE

Level of interest: An article of importance in its field

Quality of written English: Needs some language corrections before being published

Statistical review: No, the manuscript does not need to be seen by a statistician.
Declaration of competing interests:

I have no stocks, patent interests, financial connections or competing interests as it relates to this manuscript