Reviewer's report

Title: Continuous wound infusion of local anesthetic and steroid after major abdominal open surgery: a multicenter, double blind, phase III clinical trial

Version: 3 Date: 26 May 2015

Reviewer: Jo Dumville

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1. The author should follow the headings used in protocols published in Trials Journal for example Background rather than Rationale etc. Could the authors go through and re-structure as required.

2. All abbreviations need to be defined at first use – for example – CWI in the background. It is defined in the abstract but I think needs to be defined again in first use in the main text.

3. Overall I think that the number of abbreviated terms could be reduced – there are quite a lot – I would suggest only abbreviating 2 or 3 key terms and having the rest of terms written in full through-out.

4. The background is relatively clear although it does need proof reading and copy edit will be required to enhance readability so that the flow and meaning of the text is crisp and clear. There are issues with switching between past and present tense in some places through-out text.

5. I think that the background could be improved by the additional of one or two sentences at the end to link the background material to the proposed trial. For example there is discussion of how individual’s genetics might impact on pain. This suggests that there will be a genetic element to the trial but this is not apparent at the background stage – nor from the study title. I think the relevance of this material to the prosed study needs to be highlighted. The aims of the study currently appear mid-way through the paper – essentially they need to be moved upwards.

6. When discussing inclusion criteria can the authors be more specific about what is defined as major abdominal surgery?

7. The discussion of how randomisation occurs needs to be moved up I think to when randomisation is first mentioned. The authors state that they will use opaque, sealed envelopes: could they clarify that these will also be sequentially numbered. Whilst they discuss how the allocation will occur I don’t think there is any discussion of how the randomisation sequence is actually generated.

8. I think that information about the outcomes should be presented separately from the aims. I also think that the wording around the outcomes needs to be reconsidered. I would not use the word verify. I also think that the wording needs
to be clearer – so the primary outcome as I understand it is amount of rescue analgesics required – is this correct? I think this needs to be stated more clearly.

9. The author then talk about primary endpoints and secondary end points. I was not clear what the difference between outcomes and endpoints were. This needs to be made clearer. It was also not clear to me what measures were being used to assess ‘pain values’ and other elements of pain.

10. Also related to secondary outcomes/endpoints – the authors state that they will measure side effects. I think more detail is required. Earlier on in the test monitoring of wound healing and infection are mentioned – are these related to outcomes/side effects. In general I think all the information about outcomes needs to be put in one place with a clear specification of what outcomes are and how and when they are measured.

11. The sample size calculation needs more detail – if possible any further detail about how the difference was decided on would be useful. The authors note clinical experience – was this recorded in some way – e.g. via an audit of use of pain meds. Is there any data from other studies that support this difference of 50% (which is large and leads to a small sample size). Further justification would be useful. The attrition rate used in the calculation would also be useful.

12. The discussion of drop-outs is brief and unclear. The authors note that they consider anyone not complete the treatment as a drop-out. It would be reassuring if the authors can confirm that they will be conducting an intention to treat analysis and that all participants will be analysis where possible. Any approaches that will be taken to deal with missing data could usefully be discussed here.

13. The analysis section is very brief. I think more detail about the analyses planned for the primary outcome and then each secondary outcome would be clearer. Again I think that the detail around the use of repeated measures is too limited. At this stage the protocol should be able to contain the same level of analytical detail as the final paper would.

14. At the end of the protocol I remained unclear about how the genetic data, the IR data and the Oxidative stress data was going to be used. The aims suggest that they will be assessed to see if they are biological markers that help modulate post-operative and persistent pain. I think the analysis section could pre-specify the analysis that will be done as part of this exploration.