Author's response to reviews

Title: Interventions in randomised controlled trials in surgery: issues to consider during trial design

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Author's response to reviews: see over
Dear Professor Altman

Thank you for the opportunity to resubmit the above manuscript. We are grateful for the valuable comments given by the reviewers. Below we have responded to each of the issues raised. The manuscript also contains the proposed revisions in **bold text**.

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**Editorial requests**

1. **Please include the full names and email addresses of all authors on the title page. Please note that only those individuals who qualify for authorship should be included on the author list of the manuscript.** More information on the criteria for authorship can be found at the following link: [http://www.icmje.org/recommendations/browse/roles-and-responsibilities/defining-the-role-of-authors-and-contributors.html](http://www.icmje.org/recommendations/browse/roles-and-responsibilities/defining-the-role-of-authors-and-contributors.html). Please move the contributors who do not qualify for authorship to the Acknowledgements section.

**Reply:** We thank the editor for this comment. All of the individuals listed on the cover page qualify for authorship of this paper. Whilst the ‘front line’ authors designed and coordinated the workshop, everyone attended the workshop, gave presentations and were engaged in subsequent discussions. The paper reflects these discussions and, therefore, contains contributions from all authors. All authors read and approved the final manuscript.

**Revisions:** All authors’ email addresses have now been included on the cover page.

2. **Please provide a title of ‘Review’ for the main body of text (between the Background and Conclusions sections).**

**Reply:** The word ‘review’ has been added to the main body of text.

**Revisions:** The subheading now reads: **“Review: Designing surgical interventions within RCTs”**

3. **Please include a list of abbreviations used and their meanings, after the Conclusions section.**

**Reply and revisions:** A list of abbreviations has now been added, as requested.
4. Please move the tables below the reference list.

Reply and revisions: In the revised manuscript, tables appear below the reference list.

Reviewer 1

Major Compulsory revisions: None

Minor Essential Revisions: None

Discretionary revisions:

1. Designing surgical interventions within RCTs: Section 2: first paragraph “A recent systematic review examining reporting standards for surgical interventions found that 30% of trials only reported the name of the intervention under investigation and gave no further written detail” might read better as “A recent systematic review examining reporting standards for surgical interventions found that 30% of trials reported only the name of the intervention under investigation and gave no further written detail” to avoid any confusion that only 30% of trials reported the intervention.

Reply: We thank the reviewer for this comment and completely agree with this re-wording.

Revisions: The first paragraph of Question 2: ‘What are the surgical interventions under evaluation?’ now reads: “A recent systematic review examining reporting standards for surgical interventions found that 30% of trials reported only the name of the intervention under investigation and gave no further written detail.”

2. Designing surgical interventions within RCTs: Section 2: It will be useful to add that any planned second operations and the interval between the first and second operation should be included in the details of the intervention. For example, elective two-staged liver resection involves two planned operations but the interval may vary between 2 weeks and 6 weeks. Second look laparotomy may be performed at 24 hours, 48 hours, or 72 hours after the initial laparotomy. It is necessary for authors to state clearly this is a planned second operation and also clearly state the interval between the first and second operations.

Reply: We thank the reviewer for this helpful comment and completely agree that this detail is very important to document.
Revisions: The following sentences have been added to the end of the first paragraph of Question 2: ‘What are the surgical interventions under evaluation?’: “This identification process should also include any planned further operations; for example, elective two-staged liver resection involves two operations with an intervening interval of between two and six weeks. It is necessary to clearly state that there is a planned second operation, as well as the anticipated interval between the first and second operations.”

3. Designing surgical interventions within RCTs: Section 4: Before stating how the explanatory and pragmatic trial designs differ in terms of standardisation of the intervention, it will be helpful to describe these terms briefly (for example, explanatory trials are designed to investigate the causal relationship between an intervention and physiological process.

Reply: We thank the author for pointing this out and agree that more information about pragmatic and explanatory trials would be useful. Some details are already provided in the text and we have therefore added further information to Table 2 (see below). Table 2 is now signposted within this section of the paper.

<table>
<thead>
<tr>
<th>Pragmatic trial</th>
<th>A trial which is designed to answer the question ‘How well does the intervention work in comparison to the control when delivered under usual conditions?’(^{25}) (i.e. effectiveness focused, usually aiming to influence health policy)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Explanatory trial</td>
<td>A trial which is designed to answer the question ‘How well does the intervention work in comparison to the control when delivered under ideal conditions?’(^{25}) (i.e. efficacy focused, usually aiming to investigate the causal relationship between an intervention and physiological processes)</td>
</tr>
</tbody>
</table>

Reviewer 2

Thank you for asking me to review this article. It is well written and clearly meets its aims of describing the prior limitations of surgical procedural trials and how these should be handled moving forward. This article should be of interest to everybody about to start a surgical based trial.

Reply: We thank the reviewer for their support.