Author’s response to reviews

Title: Flexible trial design in practice: stopping arms for lack-of-benefit and adding research arms mid-trial in STAMPEDE: a multi arm multi stage randomised controlled trial

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Author’s response to reviews: see over
15-Aug-2012

Charlie Goldsmith
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Dear Dr Goldsmith,

ID:     MS:1452242310692318

Title:  Flexible trial design in practice: stopping arms for lack-of-benefit and adding research arms mid-trial in STAMPEDE: a multi arm multi stage randomised controlled trial

Thank you for provisionally accepting our manuscript for publication in Trials and for the further helpful and constructive comments. We have addressed these three points and the subsequent table lists how we have done this.

We include clean and tracked versions of the manuscript. We hope that we have correctly understood the instructions and have structured and formatted the manuscript correctly. We have now removed the line numbers from the clean version.

We hope that you will be able to accept this revised version for publication in Trials as is but will be happy to address any remaining questions and make further changes.

Yours sincerely,

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<th>REVIEWER’S COMMENTS</th>
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<td><strong>Reviewer:</strong> Charlie Goldsmith</td>
<td><strong>Authors Responses</strong></td>
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<td>1. In the replies to Goldsmith # 53, the reference to the Landis and Kock paper has taken the citation from PubMed rather than the paper in Biometrics. Indeed JR Landis is a friend and his citation of the R standfs fro Richard. He is known as Dick to his friends. I still think the Biometrics citation should rule.</td>
<td>We have added the [R] to [J Landis] in deference both to editorial opinion and personal knowledge. We agree that the (1977) Biometrics paper mentioned in the left column includes his middle initial in PubMed, but neither PubMed nor Nature Reviews Drug Discovery include it in the Kola and Landis (2004) paper that we are referencing as reference 11; the journal does list his full name [John Landis] instead.</td>
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<tr>
<td>2. Page 15 of 40, line 318. Since November 2012 has not even happened, the date should likely be changed from 2012 to 2011.</td>
<td>Thank you for detecting this typographic error. We have corrected this.</td>
</tr>
<tr>
<td><strong>Reviewer:</strong> Allan Donner</td>
<td><strong>Authors Responses</strong></td>
</tr>
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<td>The authors have satisfactorily responded to my comments, However I believe more detail is required in responding to comment #2 of the other reviewer, as this is an important methodological issue. Thus it should be indicated how the issue of subjects &quot;counted twic&quot; will be specifically dealt with, if only by conductig a sensitivity analys.</td>
<td>We believe this comments refers to Goldsmith’s original comment #22. We would understand from the reviews above the Goldsmith was satisfied with the response and action taken. However, we have updated line 252 from [No patient will contribute more than once to any comparison.] to [No patient will contribute more than once to any comparison; sensitivity analyses will be considered.] We will defer to editorial opinion on whether this statement should be removed.</td>
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