Author's response to reviews

Title: Diagnostic Randomised Controlled Trials: The Final Frontier

Authors:

Marc Rodger (mrodger@ohri.ca)
Tim Ramsay (tramsay@ohri.ca)
Dean Fergusson (dafergusson@ohri.ca)

Version: 3 Date: 25 April 2012

Author's response to reviews: see over
Response to Reviews:

We thank the Reviewers for their helpful comments. We did our best to incorporate suggestions into our manuscript or explain and justify why we have not done so. A point by point response is provided below.

Reviewer 1:

1. abstract/background – unclear what “lag far behind” means for non-therapeutic interventions. Is that lagging behind ‘in number’?

Response: We agree it was unclear and have revised

2. The value of the diagnostic RCT design – “indeterminate rate is often omitted in diagnostic cohort studies”. Need a reference (is that true?)

Response: References have been added.

3. Potential limitations of diagnostic RCT
   - A discordant test RCT – ethics and timing of trial consent could have been described here. The purported limitation of influencing participation would be minimised if consent is taken after discordant status is known.

Response: We have added that we believe consent and enrollment may be further hampered, rather than improved, as patients or treating physicians would be influenced by discordant results and opt for treatment or retest.

   - It is not clear why different clinical and demographic details in the diagnostic study using discordant pairs is a particular issue compared to the diagnostic RCT design. All RCTs have a similar concern regarding the generalisability of the study result to clinical practice.

Response: We agree and have revised the manuscript. The concern is generalisability not internal validity.

4. In my opinion, an additional paragraph to describe some of the decision processes that researchers should undertake before deciding on the type of diagnostic study to conduct would be warranted.

Response: We felt that including an additional paragraph on the decision processes for considering when to undertake diagnostic RCTs goes beyond the scope of our paper. Our primary aim was to raise awareness on why diagnostic RCTs are needed and their value.
Reviewer 2:
The authors present a novel manuscript that argues the point for conducting diagnostic randomised controlled trials. Overall, the article addresses an important issue, is well structured and balanced. The following comments are provided as suggestions for further strengthening the manuscript.

Major Compulsory Revisions
1. The authors make the comment that “While randomized trials of non-therapeutic interventions such as surgical procedures and behavioural interventions lag far behind those of drugs, randomized trials of diagnostic procedures are an even rarer species.” Can the authors provide some insight into as to why this is so?

Response: We have added our thoughts as to why they have not been conducted. Unfortunately, we are not aware of any empirical evidence.

2. The authors describe the diagnostic randomised controlled trial (RCT) as a comparison of two diagnostic interventions (one standard and one experimental) with identical therapeutic interventions based on the results of competing diagnostic interventions... Several figures are also provided with the manuscript, however these are not referred to in the manuscript. Please incorporate/refer to Figures 2, 3 and 4 when describing the proposed diagnostic RCT, as these figures would greatly clarify for readers the proposed methodology.

Response: We agree and have added references to Figures 1, 2 and 3.

3. The paragraphs under the section titled “The value of the diagnostic randomized controlled trial design” lack any references to support the statements. Please include appropriate references to support statements.

Response: We agree and have added references.

Discretionary Revisions
4. The authors dedicate a section explaining the value of the diagnostic RCT using their venography and clot tri-corder example. Is it possible to construct a figure that may visually describe some of the concepts discussed within this section? e.g. selection bias etc...

Response: We found it difficult to visually describe in a concise manner the concepts using our venography example. We felt it best to list potential biases in a table and text.