Author’s response to reviews

Title: Registration of randomized controlled trials in nursing journals

Authors:

Richard Gray (r.gray@latrobe.edu.au)
Ashish Badanapurkar (ABadanapurkar@hamad.qa)
Eman Mohamed (EMohamed8@hamad.qa)
Dona Thomas (DThomas13@hamad.qa)
Laileah Baraguir (LBaraguir@hamad.qa)
Annie Topping (ATopping@hamad.qa)
Martin Jones (Martin.Jones@unisa.edu.au)
Daniel Bressington (dan.bressington@polyu.edu.hk)
Ellie Brown (Eleanor4.Brown@live.uwe.ac.uk)
Charley Baker (charlotte.l.baker@nottingham.ac.uk)

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Author’s response to reviews:

In addition to addressing the reviewers comments, please address the following two editorial comments:

1. For transparency, where you cite your previously published editorial analysing some overlapping studies (reference 6), please explain in the manuscript how this relates to the current study.

Response: We have added additional context that hopefully explains the progressing of thinking that led to this study.

2. When responding to point 8 from reviewer 2 (regarding whether it is justified to divide retrospectively registered studies by registration before and after the submission date) please also consider that for JAN and JPM, submission date was not known. Subtracting 90 days from the publication date would appear not to differentiate between studies that were
registered retrospectively because the editor of the journal they were published in asked for them to be versus studies that had already been rejected from another journal where the authors had been asked to register or had read in the Instructions for Authors that trial registration was necessary.

Response: We have amended the text to hopefully address this point.

Reviewer #1: This is an important study that looked at registration of RCTs in nursing journals. While not original (there have been many such investigations in other fields) it is important to establish the extent of the problem in order to determine how to go forward in the field. On this note, it is worth citing other authors who have conducted very similar types of investigations in other fields. eg: http://onlinelibrary.wiley.com/doi/10.1111/acps.12647/pdf and http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0133718.

Response: We have amended our literature view to include these studies.

These results suggest that people who do research in nursing need to be educated on the importance of trial registration to prevent bias in the field.

In the methods, the authors describe the search strategy. They need to be specific that they did not look at all clinical trials (eg they didn't look at open label trials or quasi experimental trials like ABAB) so they can't declare that they looked at "all clinical trials".

Response: We have amended the text.

I wondered if the search term "RCT" would actually capture the stepped wedge trials -shouldn't that term have been included in the search? Same with feasibility trials.

Response: We have amended the text.

How were the journals chosen? Did the authors use a website to find the highest impact journals for nursing? What impact were these journals?

Response: We have added additional details about the data that informed the decision to select the included journals.
I am concerned about the grouping that was created, in particular "retrospectively registered after and before submission to journal". The problem here is that there is an assumption that the journal where the trial was published was the first journal where the trial was submitted. This is highly unlikely. So it makes this categorization significantly problematic. Unless this choice can be defended, it might be best to collapse and not look at the registration status based on submission to the journal.

Response: We have added additional text to the discussion to reflect this concern. The criteria that we used were not ours rather were those described by Harriman and Patel (2016).

For the "not registered" trials - did the authors follow up with emails to the authors of the studies to confirm that the trial was indeed not registered?

Response: We have added clarification and contacted corresponding authors by email to check that trials were not registered.

There are some spelling errors throughout the manuscript.

Response: We have carefully proof read the manuscript to eliminate any typographical errors that may have occurred.

Reviewer #2: The objective of this study was to determine the proportion of randomized controlled trials (RCTs) published in top nursing journals that were registered and to determine the proportion that were registered prospectively. 137 trials published between September 2011 and August 2016 were included, and of these, 54 were registered. Of the registered trials, less than half were registered prospectively. The discussion focused on different factors that may drive researchers and editors in the field of nursing to forgo trial registration. The authors conclude that the rate of trial registration in top nursing journals is suboptimal, and that greater attention should be given to issues of trial registration and reporting by nursing researchers. There are concerns, however, about the study design and quality of reporting that make it difficult to confidently interpret and generalize the results.

Major comments:

1. On page 4, the authors state that the ICMJE has published a policy called the "Uniform Requirements for Manuscripts". However, no citation is provided. The authors should include a citation for this policy.
Response: we have included the following link in the text

2. The authors state "this journal was selected in part because it is a leading mental health nursing journal but also because two of us (RG and CB) are editors". Thus, currently, the criteria for including journals is (1) being one of the top 2 journals based on impact factor, or (2) being managed by 2 people with a particular interest in this topic and who are conducting a study on the topic. It is unclear why the status of two of the authors as editors for this journal would influence journal selection. If the goal of the study is to assess trial registration practices in leading nursing journals, then the top journals from the field should be included, regardless of who the editors are. The authors should either include a comprehensive set of nursing journals or only the top journals based on some objective criterion, such as impact factor.

Response: We have amended the text setting out the bibliometric data that were used as the basis for selecting the included Journals

3. The manuscript states that two authors reviewed all article titles and abstracts independently, but provide no details for how coding discrepancies were resolved. The authors should clarify how disagreements were resolved (i.e., through discussion, with a third author, etc.).

Response: We have amended the text accordingly (page 7)

4. The selection of studies at the title-abstract review stage was completed by looking for the phrase "randomized controlled trial" or RCT. However, it is possible that some studies used random assignment but were not described as randomized controlled trials, as has been described in previous studies of nursing journals (for example, Jull & Aye, Int J Nurs Stud, 2015). Thus, some eligible studies may have been incorrectly omitted from the study. In a similar vein, the authors do not provide a definition for the term RCT. Previous studies have used the definition provided by the ICMJE (see, for example, Azar et al., PloS One, 2015; Riehm et al., J Psychosom Res, 2015; and Mathieu et al., JAMA, 2009). To ensure transparency and comparability to other studies, the authors should define "RCT", ensure that all included studies are consistent with this definition, and review excluded studies to ensure that no RCTs were omitted from the pool of included studies.

Response: we have amended the text and checked included studies.
5. Trials were classified as "not registered" if no information about trial registration was available in the manuscript. However, registration details are not always included in published articles, and previous studies have therefore used rigorous methods to determine the registration status of a trial (see Mathieu et al., JAMA, 2009; Azar et al., PloS One, 2015; Riehm et al., J Psychosom Res, 2015). These methods include identifying key words from the published article and searching clinicaltrials.gov, ISRCTN, and the trial registry for the country of the corresponding author. In addition, authors of previous studies have attempted to contact trialists and inquire about study registration via email. To improve the accuracy of trial registration identification, the authors of the current manuscript should conduct thorough database searches and inquire with trialists as to whether their studies were registered or not.

Response: we manually searched the two most frequently used trial registries (CTG and ISRCTN) to check if any trials were registered but this was not reported in the manuscript. We also contacted the corresponding authors by email to check if the trial was registered.

6. The fifth classification for trials in this study was called "timely registration". However, the requirements for meeting this criterion are described in different ways throughout the manuscript. On page 6, the authors state that they extracted information regarding whether the trial registration number is "in the PubMed citation (abstract)", but on page seven this is referred to as the "PubMed field". Were the authors assessing if the trial registration number can be found in the abstract, in a specific text field designated for trial numbers, or in the abstract specifically on PubMed? The authors should clarify this issue.

Response: we have amended the text accordingly.

7. The authors state that they extracted trial start dates from the trial registry. However, this information may have also been reported in the published article, and may be different from the dates specified in the registration. The authors should clarify whether they examined dates reported in the article, and if so, how they prioritized dates reported in the article versus the trial registry.

Response: we have added clarification in the discussion section of our manuscript.

8. The authors divide the classifications of registrations based on whether they were registered before or after the estimated submission date, but the justification for doing so is unclear.
The only rationale provided is in the discussion, which states "we felt it was important to try to estimate to what extent journal editors are intervening to ensure trial registration". This statement implies that any registration completed after submission is a result of editorial intervention. This may be the case for some journals, such as the BioMed Central journals, for which post-hoc registration is encouraged. However, as numerous articles highlight (see Azar et al., PloS One, 2015; Riehm et al., J Psychosom Res, 2015), the value of post-hoc registrations in countering publication or selective reporting bias is negligible. Thus, some journal policies may give the impression that all registrations are useful in addressing publication and selective reporting biases, regardless of when they were completed. The authors should elaborate their rationale for separating articles by when the registration was completed relative to the submission date, as well as expand their discussion of the relative value of a priori compared to post-hoc registrations.

Response: we have amended the text accordingly.

8. The authors reviewed all articles published in the included journals across a five-year period, but no flow diagram is provided to document the number of articles reviewed at each stage. Per the PRISMA guideline, the authors should outline how many articles were reviewed at the title-abstract and full-text stages and include the number of articles excluded on the basis of each exclusion criterion.

Response: we have added a PRISMA flow diagram as suggested (figure 1).

9. 137 articles were included for review in this study, but these articles are neither cited nor listed in any part of the manuscript. Thus, the accuracy of the methods used to identify eligible trials cannot be evaluated. To ensure transparency, the authors should provide an online appendix that lists the included articles and coding decisions.

Response: we have generated a reference list of included studies.

10. It is unclear how the results of the data extraction process were tracked. For example, did the authors use Excel, SPSS, or another database software? The authors should describe how they stored and managed their data.

Response: we have amended the text accordingly (page 8)
11. The results section does not clearly delineate the findings of this study. For example, the overall proportion of registered trials is not stated, despite this being the key objective of this study. In addition, exact calculations are not presented in numerous locations; for example, the authors state that "around a quarter of trials were registered retrospectively" (page 8) without specifying the exact number. To improve the transparency of the results section and better convey their findings, the authors should highlight the main findings of the study and provide exact calculations and numbers whenever possible.

Response: we have amended the results section accordingly (page 10-11)

12. The results section of the paper includes numerous analyses that are not outlined in the methods section. For example, analyses examining the proportion of registered trials in Asia, as well as descriptive analyses of conflicts of interest, are not mentioned in the manuscript prior to the results section. The authors must outline the methods used to conduct these analyses. Furthermore, if these analyses were not planned prior to obtaining the results, the authors should specify that these were post hoc exploratory analyses.

Response: We have added text stating that these were post hoc exploratory analyses.

14. In the discussion, the authors suggest that journal editors audit and publish the proportion of prospectively registered trials in order to focus the attention of editors, reviewers, and authors. Is this realistic? Some journals do not even have a policy. Others have only suggestions to register. Others still have a policy that they do not enforce. Given that they have not taken these steps, how likely is it for them to report their compliance? One could just as easily recommend that they adhere to pre-enrolment registration policies, but again, this isn't being done. Journal editors in this field are simply not doing what needs to be done, even though they have the basic knowledge that experts are urging a priori trial registration. What can be done to realistically improve the situation in this context. More thought is needed on this issue.

Response: we have amended the conclusion to address this point (page 16)

15. There were a number of grammatical errors throughout the manuscript. For example, on page 7, "there were some inconsistency across registries..." There were many other errors throughout the manuscript. The authors should carefully review and edit the manuscript to correct grammatical errors and improve readability.
Response: We have carefully copy edited the manuscript to eliminate typographical/gramatical errors.

16. The main objective of this study was to determine the proportion of nursing RCTs that were registered. Although registering trials is important in and of itself, the extent to which registrations reduce selective outcome reporting bias is dependent on the quality of registrations. Previous studies have shown that the quality of trial registrations is very poor (see for example Killeen et al., Ann Surgery, 2014; Azar et al., PloS One, 2015; Riehm et al., J Psychosom Res, 2015; Milette et al., J Psychosom Res, 2011; Mathieu et al., JAMA, 2008), that most registrations do not provide information that can be easily used to compare registered and published outcomes and outcome classification (e.g., primary, secondary), and that even when they do, registered and published outcomes are often discordant. Because the current study did not compare registered to published outcomes, the authors cannot comment on the quality of registrations in nursing journals. The authors should either incorporate methods that will allow them to comment on the adequacy of trial registration or include a discussion of this as a major limitation in the limitations section of their study.

Response: we have attended the text accordingly (page 16).

Minor comments:

1. There are numbered notes located at the bottom of Table 1, but they are no numbers in the table that refer to these notes. The authors should clarify what these numbers refer to in the table.

Response: we have attend to the text accordingly (Table 1)