Author's response to reviews

Title: A systematic review protocol for measuring comorbidity in inpatient rehabilitation for non-traumatic brain injury

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Author's response to reviews: see over
Cover letter for systematic review revisions; MS: 5221445841404559 - A systematic review protocol for measuring comorbidity in inpatient rehabilitation for non-traumatic brain injury

Dear Drs. Maya O’Neil and Martin Rohling and the Systematic Reviews Editorial Board,

We sincerely thank both reviewers for their thorough review, time, and helpful comments, which have strengthened our submission entitled “A systematic review protocol for measuring comorbidity in inpatient rehabilitation for non-traumatic brain injury”. The encouraging positive comments were appreciated. We have indicated below how we have addressed all the reviewer comments and hope that our manuscript is now suitable for publication. In the text below, the reviewer’s comments have been copied and pasted, and prefixed with the initial letter of their surname and italicized. Reviewer suggestions on similar topics been listed in series. Our response to the comments follows each comment in bold font, with references to the line numbers in the revised manuscript where appropriate.

O: First, please have all authors review the protocol to ensure that the writing is edited for clarity and parsimony throughout.

All authors have reviewed the protocol to ensure the protocol is edited for clarity and parsimony.

O: The background section needs to be more concisely and clearly written, while methods-related sections need to be significantly expanded to provide needed detail.

We have edited the background section for clarity and conciseness and have expanded on the methods sections to provide more detail, particularly in areas that were noted by the reviewers.

R: I have not liked the term non-TBI (nTBI) as it has been used in the literature. I understand that these researchers are simply using the term that has been more commonly used by others in the field. Nevertheless, I prefer the term “acquired non-traumatic brain injury” or AnTBI. I find it more descriptive of the population to which these authors refer.

Despite the helpful suggestion on terminology and use of ‘AnTBI’ instead of ‘nTBI’ for non-traumatic brain injury, we have chosen to use nTBI because we have used it in previous publications whereas we are unfamiliar with ‘AnTBI’. A Google search confirmed that ‘nTBI’ is an acceptable term. Whereas relevant results were found for acquired non-traumatic brain injury by searching ‘nTBI’ and ‘brain injury’, searching ‘AnTBI’ and ‘brain injury’ shows no results.

O: I would recommend that the overall purpose of the proposed systematic review be clarified throughout the protocol.

We have clarified the overall objective of the proposed systematic review, which is to identify the current methods used to measure comorbidities in the nTBI population in inpatient rehabilitation and if available, the predictive validity of these comorbidity measurements. This is explicitly stated in the background – please see
O: Currently, the protocol describes a rationale for understanding comorbidities as being related to evaluation of the effectiveness of rehabilitation. Though this is clearly part of the rationale, this alone does not provide adequate support for the review (for example, evaluating the effectiveness of rehabilitation methods can be reasonably investigated through RCTs, and therefore there is less concern about describing comorbidities in a group of participants who can be randomly assigned to intervention vs. control conditions).

We apologize for this misunderstanding. The purpose is not to study the effectiveness of specific clinical or rehabilitation interventions but to inform efforts to develop a predictive multivariable model of rehabilitation outcomes (e.g., function independence measure efficiency) for health services research based on population-based administrative health data.

O: It is also unclear in places whether the focus is on describing the types of methods used to assess comorbidities, or on describing the comorbidities themselves (prevalence, etc.). This, too, should be clarified throughout, and a strong research and clinical rationale provided for the chosen focus of the review.

We have clarified the focus of the systematic review.

The primary purpose is to identify the types of methods used to measure comorbidities.

The secondary objective is to assess the face and predictive validity of the measurements if possible, i.e., if the authors conducted predictive validity assessment in their study or cite other studies that have assessed the predictive validity. This is important for developing risk adjustment and predictive models used in health services research because the predictive validity of a given comorbidity measurement method differs by the population in which it is measured and the outcome which it is used to predict (Sharabiani et al. 2012, reference 11).

The tertiary objective is to profile the comorbidities in patients with nTBI within rehabilitation settings. The data extracted for the systematic review will provide the opportunity to assess specific comorbidities/describe the comorbidities, which is of clinical interest.

R: Under the heading DISCUSSION – The authors make an argument as to why their systematic review is needed. Yet, they provided no data or citations to support their position. The reader is left to assume that the authors’ have accurately assessed reality, despite the fact that we have no information upon which to base a judgment.

R: Under the heading DISCUSSION – The researchers try to persuade the reader of the need for such a review to be completed. However, the essence of their argument seems
too circular to me and is essentially unsupported. What they claim as a justification for their project is that prior data may not be valid. Yet, again, they have provided the reader with no evidence to support such an assertion.

As comorbidities may confound results and interpretation of such models, it is important to control for them. However, due to specificity in the methods of developing comorbidity tools (i.e., validity and reliability are typically studied in a specific population for a specific outcome) it is uncertain as to which comorbidity measures will perform the best for a given outcome in a given population (e.g., functional outcome after inpatient rehabilitation in patients with nTBI).

Several studies have recently been published which show differing comparative validity of comorbidity measures (e.g., ADG, Elixhauser, and Charlson) for mortality in different populations (e.g., schizophrenia and COPD). Thus it is important to validate measures of comorbidity when developing predictive models for health services research.

The goal of this systematic review is to address the research gap stated above, which is to identify the current methods that are used to measure comorbidity for nTBI patients in inpatient rehabilitation. We hypothesize that there are currently no studies that assess the comparative validity of various comorbidity measurement methods specifically in patients with nTBI for rehabilitation outcomes such as functional outcome and length of stay. In this case, this systematic review will document measures that have been used so that we can assess the face validity and then perform a validation study. If it has already been accomplished, it would be less necessary to perform a validation study ourselves.

References (Austin, Stanbrook, Anderson, Newman, & Gershon, 2012; Berlowitz & Stineman, 2010) have been included, which demonstrate the importance of selecting validated measurements of comorbidity in health services research, particularly for improvement of rehabilitation service quality (page 8, line 637 and 639).

R: Under the heading METHODS with the subheading of Study Selection - The researchers note that their review will not include studies that they have decide to exclude. This is circular reasoning and is potentially dangerous in the researchers’ attempt to complete an unbiased review. The researchers might want to cite a more concrete or definitive inclusion criteria; possibly one that has been proposed by others on this issue.

R: I do not think the authors did a very good at explaining how the data they propose to collect will be gathered in an unbiased manner and how the data extracted from the literature will be interpreted to benefit the field. This is an area in which improvements could be made.
Cover letter for systematic review revisions; MS: 5221445841404559 - A systematic review protocol for measuring comorbidity in inpatient rehabilitation for non-traumatic brain injury

We have more specifically listed acceptable study designs that will be included or excluded and the reasons for doing so (pg. 5 line 250-357).

We hypothesized that there may not be many comparative validity studies on comorbidity measurement methods in relation to functional outcome after inpatient rehabilitation in patients with nTBI. As such, any form of studies that have assessed rehabilitation outcome in nTBI patients in inpatient rehabilitation and have used comorbidity information in any way would be eligible, including cohort studies, case-control studies, or RCTs. This would also allow us to capture comparative validity studies as they use retrospective cohort data.

R: Under the heading METHODS with the subheading of Quality Assessment - The researchers refer to their expected use of the Critical Appraisal Skills Program (CASP), which will be used to guide their assessment of study quality. I believe a reference is needed here for the CASP and it is missing. I would also like to see some description of why the CASP is the best measure available for this purpose, as I am not sure that it is.

We have chosen the CASP partly because of the availability of tools for various study designs since we have chosen to liberally include various study designs. The overall purpose of the study is to survey the currently used methods of measuring comorbidity for patients with nTBI in inpatient rehabilitation settings, and if possible (i.e., if it is a validation study or if the study cites a validation study) determine the most valid method of measuring comorbidity, which can be applied to predictive (or risk adjustment) models. The quality of the study will influence whether the results can be used – i.e., whether we will choose to apply a comorbidity measurement method in our predictive model of rehabilitation outcome in patients with nTBI and whether the data should be used in a meta-analysis (if it is possible to conduct a meta-analysis based on the included studies).

Moreover, if studies also report the effect of comorbidities on rehabilitation outcome, these could be used in a meta-analysis, though again the choice of inclusion would depend on the quality of the studies. Thus, the purpose of using the CASP is to guide critical appraisal of the studies for both the use of a specific comorbidity measurement method or for inclusion in a meta-analysis to understand the effect of comorbidities on rehabilitation.

O: Specifically, the quality assessment section lists a general group of tools (CASP), yet doesn't clarify which tool(s) will be applied based on design factors. This may be because included study designs also need to be more clearly specified in this protocol. More information is needed on which study factors are important to critically appraise this body of literature, particularly since the topic is focused on validity of assessment methods (quality considerations for this type of literature are less common/well known than RCTs, for example). Are sample selection factors important? What about participant attrition? Factors related to generalizability? Other study design factors specific to this clinical topic and research question? These key quality factors should be listed and
Cover letter for systematic review revisions; MS: 5221445841404559 - A systematic review protocol for measuring comorbidity in inpatient rehabilitation for non-traumatic brain injury explained.

We have explicitly listed areas of particular importance in these studies - i.e., methodological quality, such as the use of appropriate statistical tests and accounting for confounding, and also the sample/population selection which affects the generalizability of the results (pg. 7 line 393-396).

The reviewers do not provide an alternate to the CASP, though we welcome suggestions for a more appropriate quality assessment tool if our rationales provided in the revised protocol and our response above are not deemed suitable by the reviewers.

R: Under the heading METHODS with the subheading of Study Selection - I do not see the logic of excluding “stroke” while simultaneously including “vascular conditions.” It would seem that the only reason stroke will be excluded is because the database would be too large and it would be too time consuming to collect the relevant data and complete the review. Maybe this is a legitimate position to take, but it is a practical argument and not a scientific one. I am concerned that such exclusion will result in the data collected being far less of interest to rehabilitation professionals.

O: I also have questions about the proposed scope: It makes sense to separate TBI from nTBI, but the inclusion criteria for this review seem a bit narrow in scope. As a systematic reviewer, I am very sympathetic to the need to scope reviews in order to be feasible; however, the rationale for such scoping decisions should be supported by methodological and clinical decisions. You do not provide a strong clinical or research rationale for excluding stroke from the nTBI category, particularly because included brain injuries don’t share etiologies, symptoms, etc. I am wondering if consultation with a research librarian could help expand the scope while maintaining feasibility of the review? Many research librarians have expertise in refining searches to increase specificity without sacrificing sensitivity, and perhaps this could enable feasible inclusion of stroke-related literature. Because you propose that the body of literature will be relatively small and not often include validation studies, I imagine that the main hurdle in terms of size of the literature will be at the abstract review stage, rather than at the data extraction/synthesis stage. If a large body of literature is identified, it may be possible to select only studies meeting important methodological criteria relevant to the research questions and clinical topic rather than restricting the scope to exclude stroke.

There is no universally agreed upon definition of nTBI. As such, stroke may or may not be included in the definition. Our research program has excluded stroke due to the existence of research networks dedicated specifically to studying stroke (e.g., reference 2, reference 3)

Given the vast amount of established research on stroke versus other forms of nTBI, we believe that a systematic review focused exclusively on stroke is warranted but not necessarily within this study. A focus on nTBI outside of stroke would be more
of a unique contribution to the field. We propose that a separate systematic review protocol be developed specifically to study stroke. We have provided further justification for excluding stroke in the revised protocol (pg. 6, line 265-273).

O: The analysis (or synthesis) section also needs significant clarification: Rather than simply stating that narrative synthesis is likely, you should provide information about what the synthesis will entail. For example, will studies be grouped by any key factors such as diagnosis or assessment tool? How will you synthesize studies of various designs? Will certain tools or items be grouped? Etc.

Regarding the analysis or synthesis, we have expanded on what the synthesis will entail. Specifically, we have identified the grouped by key factors and how these will be used in a narrative synthesis (pg. 7 lines 402-498).

R: The review proposed does not describe in great detail any statistical procedures planned for the data. Here I quote, “Extracted data will be grouped into clusters based on empirically important variables, such as the type of data used, population stratification, and type of co-morbidity measurement.” These are not inferential statistics per se. Rather, the proposed analyses might best be labeled descriptive statistics. As a meta-analyst, I am biased toward calculating effect sizes after so much time and energy has been expended on the data collection and extraction. I am worried that the current proposal may miss the opportunity to have an even bigger impact on the field than their current proposal is likely to have.

R: I would like to see more explanation in the statistical section of the protocol as to what might be gleaned from the results and how these might improve services to the relevant population of patients.

The primary purpose is to survey the currently used methods for measuring comorbidity in the nTBI population for rehabilitation outcomes. For this purpose, inferential statistics would not apply.

The secondary objective is to assess the predictive validity of these measurement methods. Assessing the comparative validity of comorbidity measurement methods for a given population and outcomes is useful for in selecting the most appropriate variable to be included in risk adjustment models. In this case, a met-analytic technique applied in Sharabiani et al. (2012) could be applied if relevant studies are identified.

The tertiary objective is to profile the comorbidities as identified in the studies included in the systematic review. Meta analyses will be considered to synthesize information from similar study designs that use similar measurement tools (pg. 8, lines 499-515). It will not be possible to combined information from various tools, as they will capture different information on comorbidity. This information would be useful to health care professionals that work with the patients.
Cover letter for systematic review revisions; MS: 5221445841404559 - A systematic review protocol for measuring comorbidity in inpatient rehabilitation for non-traumatic brain injury

We hope that these revisions have addressed the concerns of the reviewers and make our protocol suitable for publication.

Sincerely,

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