Author's response to reviews

Title: Implementing evidence-based recommended practices for the management of patients with mild traumatic brain injuries in Australian emergency care departments: study protocol for a cluster randomised trial

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Author's response to reviews: see over
Dear Editors,

Thank you very much for reviewing our manuscript with the Title “Implementing evidence-based recommended practices for the management of patients with mild traumatic brain injuries in Australian emergency care departments: a CRT study protocol”.

Please find below our responses (in **bold**) to the comments we received.

**Editorial requests:**

1. Please ensure the title conforms to journal style for study protocol articles. The title should follow the format “___________: study protocol for a randomized controlled trial.”

   Thank you, we have changed the Title to read: “Implementing evidence-based recommended practices for the management of patients with mild traumatic brain injuries in Australian emergency care departments: study protocol for a cluster randomised trial”

2. Please mention each author individually in your Authors’ Contributions section. We suggest the following kind of format (please use initials to refer to each author’s contribution): “AB carried out the molecular genetic studies, participated in the sequence alignment and drafted the manuscript. JY carried out the immunoassays. MT participated in the sequence alignment. ES participated in the design of the study and performed the statistical analysis. FG conceived of the study, and participated in its design and coordination and helped to draft the manuscript. All authors read and approved the final manuscript.”

   We have now listed contributions of each author in more detail (please see page 33 of the manuscript).

3. Please include an additional file title and legend section after your figure legend.

   We have included additional file titles and legend sections after our Figure legend on page 49. All abbreviation are included in the main manuscript, and therefore not repeated in the Figure legends. Please, let us know if this is incorrect.

   We have also uploaded versions of the figures with higher resolution.

**Reviewer comments:**

**Major Compulsory Revisions**

1. As your selection of patients will be after their care, to avoid selection bias please specify how you will differentiate the patients that were unable “to participate in a phone interview” (page 13) from those who were unable because of previous impairment or because of their current mTBI. Also, how will you consider the latter in the analysis?
The possibility of selection bias for patient participants in the NET trial can arise through the following four processes:

1. Identification of eligible patients through the chart audit.
2. The ED staff members’ decision of whether to contact a patient to ask for their consent to participate in a follow-up phone call.
3. The application of exclusion criteria by the researcher who undertakes the phone interview.
4. The patient’s decision of whether to participate.

We have tried to minimise potential bias arising through these processes in designing the trial. For process 1, chart auditors (who are responsible for identifying eligible patients) will be independent, and blind to the hospital’s intervention allocation, where possible. In circumstances where it not possible to have a chart auditor independent of the hospital, a solution will be discussed with the hospital that aims to minimise any risk of selective identification of patients. For process 2, it is not possible to blind the ED staff member to the hospital’s allocation. However, ED staff will be expected to contact most patients, and in rare instances where they make a decision not to phone a patient, the reason for this will be recorded. These reasons will be reviewed by the trial research team, and discussed with the ED staff member if there is concern that too many patients are not being phoned. For process 3, the researcher who undertakes the follow-up phone call will be blind to the intervention that the patient’s medical team has received (i.e., blind to the hospital’s allocation). Therefore, there is no risk that the researcher’s application of the exclusion criteria can be modified by knowledge of the hospital’s allocation. Finally, for process 4, the patient will be blind to the intervention that their medical team has received, and so the patient’s decision to participate cannot be influenced by this knowledge.

Given the methods we have implemented, we expect that the risk of bias from selective identification and recruitment of patients to be low. We will present summary statistics that allow readers to judge the risk of selective identification of patients (presenting summary statistics by group of the cluster size (e.g. number of patients attending over the two month identification period)) (process 1), and the risk of selective recruitment (e.g. presenting summary statistics by group of the number of patients who complete the follow-up phone interview, age, sex, and presenting Glasgow Coma Scale score) (processes 2 – 4).

Minor essential Revisions

1. Please, consider if “evaluation” (or similar) is the right word instead of “selection” in page 14, blinding section.

We are using the categorisation of biases for clinical trials as outlined in Higgins et al and are referring to both selection (where the characteristics of participants identified may differ if the person responsible for the identification has knowledge of the hospital’s allocation) and detection (where the outcome measurement may be affected by knowledge of the hospital’s allocation) biases. We hadn’t previously noted detection bias, but have now changed the sentence to “To
limit the possibility of selection and detection bias, chart auditors will be independent, where possible, of the hospital.”


2. As your design has a formal sample size calculation within the decision framework of Neyman and Pearson, please consider highlighting a main efficacy analysis.

We have now identified a primary effectiveness analysis through the addition of the following sentence in the ‘Effectiveness analysis’ section: “Our primary effectiveness analysis will be the model (as described above) that estimates the intervention effect on the primary outcome, appropriate PTA screening.” In addition, interpretation of our results will be based on the estimated intervention effects and their confidence intervals. We now note in the ‘Sample size’ section the expected width of the confidence interval for the primary outcome (both on the risk difference and odds ratio scales), and note in the ‘Effectiveness analysis’ section that all estimates will be reported with 95% confidence intervals.

Discretionary revisions

1. To improve readability, please consider changing the primary outcome description in the abstract (“the percentage of patients for which a prospective measure of post-traumatic amnesia using a validated tool is performed in the emergency department, until a perfect score is achieved before the patient was discharged home (or the patient was transferred or admitted)”); and in aims, page 8 (“increasing the percentage of patients for which a prospective measure of PTA using a validated tool is performed in the ED until a perfect score is achieved or the patient is transferred or admitted”) to something shorter and clearer, such as “increasing the percentage of patients with appropriate screening” as in primary outcome, page 13. In other words, specify the details later, and be shorter and direct at the beginning.

Thank you for this suggestion. We have made the suggested change to the abstract section. However, in our aims section, we kept the longer version, because we distinguish between primary and secondary aims (which correspond to the primary and secondary outcomes). This means it is hard to use short descriptions without raising questions (e.g. what is the difference between “appropriate PTA screening” (primary aim), and “other assessment methods to screen for PTA” (secondary aim).

2. Please note that the gain of efficiency reported by Senn in his 1989 paper applies only to numerical outcomes.

We have clarified this sentence to make it clear that we are referring to continuous outcomes. The sentence now reads “Adjustment for the baseline measure of a continuous outcome yields
unbiased estimates of intervention effect in circumstances where there is baseline imbalance, and has the benefit of providing the most powerful analysis [89].”

3. As your paper has a considerable amount of methodological reflections, but there is no statistician in the acknowledgement section, please consider specifying in the contributions the name of the responsible for the statistical design.

Thank you for reflecting on this issue. We have now provided more detail in the author contributions section.