Author’s response to reviews

Title: Patterns of traumatic brain injury and six-month neuropsychological outcomes in Uganda

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Author’s response to reviews:

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Dear Editor,

We have received comments to our manuscript titled 'Patterns of traumatic brain injury and six-month neuropsychological outcomes in Uganda' which have been very helpful. Below are our responses to the comments in bold italics.

Technical Comments:

1. Please include, at minimum the names, institutions, countries and email addresses of all authors, and the full postal address of the submitting author in the Title page.

Email addresses which were missing in the initial submission have been added for all authors.

Reviewer reports:
This paper describes characteristics of, and 6 month outcomes in a cohort of 171 persons with TBI compared to a group of non-injured controls.

The findings are interesting, and show some striking differences in demographics of TBI compared to the literature from Europe and the US. Some issues are still worth remarking:

In the introduction (p. 4, line 24) the authors state that 6 month outcome is necessary to determine persisting symptoms. I would say that even 6 months is early in the recovery course, and that this should me mentioned. The patients can expect substantial spontaneous recovery for a long time after this.

We have added a statement to this effect stating that the 6 month time point maybe too early to predict persistent outcomes since recovery may occur after 6 months. Line 78

Re inclusion criteria and sample: only patients able to provide informed consent before leaving the hospital are included. The paper does not state how long their admissions were, but I would think this gives a sample bias in the direction of losing the most severe injuries. Consent could have been provided at the 6 month follow-up. Also, it seems that patients with the mildest injuries do not seek hospital treatment, as more than 70% of patients had intracranial injuries on radiological examinations. These sampling issues should be duly noted in the discussion.

It is indeed correct that severely injured patients not able to consent on admission were not included which could have resulted in a sample of moderately injured patients mainly. We have however clarified that those initially too injured to give consent but did so after recovery were included in this study. Therefore some severely injured patients were included in the study. This is mentioned in the methods section (line 106) and in the discussion (line 278)

We have also added in the results the duration of admission (line 181) and added this in table 2.

It was impossible to seek consent at 6 months as this would have made it impossible to trace the patients six months after discharge since location and contact details are not routinely collected in detail in emergency cases as we did.
Regarding the test battery, the authors say it has been validated in Ugandan children, but it seems we do not know much about how they serve adult patients. This is quite important, as the dichotomization into impaired/non-impaired is based on these norms, with a rather strict cut-off of 2 SD. Please comment. Also, the battery does not seem to assess executive functions much, while we know that problems with regulation of cognition, but also emotions and behavior, are core long-term symptoms of TBI.

The CogState battery has not been used among Ugandan adults but has been used extensively among adults in the USA and other Western countries. In addition, it employs easy to use, non-culturally biased stimuli that make it easy to use. We have now mentioned this in the manuscript on lines 119 and 123.

The 2SD cut-off is based on existing conventions to diagnose neurocognitive impairment as used in the DSM-5 and in other studies in this region. We now have mentioned this on line 164.

The maze learning task of the CogState does measure aspects of executive function that include working memory and error monitoring. We have now mentioned this in the manuscript on line 135.

Throughout the manuscript the word "cases" is systematically used. Please change to "persons with TBI" or patients, as the terms seems somewhat objectifying.

This has been corrected from 'cases' to 'patients' throughout the manuscript.

I am quite surprised that only 8% displayed physical disability, in such a severe sample, and with many motorcycle accidents. What do the authors think is the reason for this?

We now mention in the discussion that exclusion of those who were severely injured to give consent and failure of those who had physical disability to return to the hospital at 6 months led to the low rates of physical disability. Line 278

Regarding PTSD, many more persons were assault victims compared to what would have been the case in Europe and the US. I would like to invite the authors to discuss this in relation to PTSD symptom burden.
We have discussed PTSS burden with a focus on the nature of assessments used to explain why we observed a high PTSS rate. We now also show that the rate of PTSS in our study is within the ranges seen in European and US studies. Line 244

Also, as the authors note, they have not diagnosed PTSD. I would recommend to use the term post-traumatic stress symptoms instead of PTSD which is a reference to a specific diagnosis.

We have now used the term posttraumatic stress symptoms (PTSS) to describe our outcome in place of PTSD throughout the manuscript.

I found the big difference from Europe and the US in cause of injury intriguing, ie that such a large proportion of the traffic accidents were motor cycle incidents, and that violence was so common. It would be interesting to see the authors compare their findings in relation to demographics to other studies in more detail in the Discussion.

We have added a few lines in the discussion explaining that a high crime rate characterized by 'iron bar robbers' and the popular use of motorcycle transport were the reasons for this difference. Starting from line 230

Reviewer 2 (Reviewer 2): PEER REVIEWER COMMENTS: To view the full report from the academic peer reviewer, please see the attached file.

REVIEWER COMMENTS FROM REPORT: This is a timely controlled, observational clinical study to characterize six-month neuropsychological outcomes after traumatic brain injury (TBI) in a Ugandan tertiary hospital. This study addresses an important gap in the literature linking TBI with long-term psychological outcomes. The area of investigation is important and the study appears to have been conducted with high standards. The writing is clear, the data is well presented, and the conclusions are well justified.

REQUESTED REVISIONS:

The work is technically sound. I only have a few minor points for the authors to consider/clarify.
I only have two comments regarding potential places of improvement. First, the inclusion/exclusion criteria could be more clearly defined. As stated, the inclusion criteria includes patients with TBI that were able to self-consent. This would suggest a skew toward mild TBI with few moderate-severe TBI patients, as the latter are either unconscious or lack the mental capacity to self consent during the early evaluation period.

We have clarified in the inclusion criteria that we also recruited severely injured patients who were initially unable to give consent but later recovered and were able to give consent. Line 105

Given this, it may be useful to correlate the Glasgow Coma Scale (GCS) score (see Table 2) for all patients with outcomes. The inclusion of Glasgow Outcome Scale scores would also be a relative simple addition that could help readers across the world to extrapolate these findings.

Unfortunately we did not use the Glasgow Outcome Scale in this study. However did run T-Tests comparing GCS scores with all our categorical outcomes as stated on line 167

Given this patient population, the authors may want to consider the addition of information in the title and/or abstract stating this study was performed in mild/moderate TBI patients, which seems to be a more accurate description of the work.

Given the clarification on the inclusion above where we state that even severely injured patients were recruited after recovery (Line 107), we do not think defining the study sample as mild/moderate would be a true reflection of the patients we recruited.

A second very minor point, is the prevalence of men in the TBI group; however, PTSD is more prevalent in females. While not a criticism of this study, some discussion of this point may be warranted as the study population may actually underestimate the rate of PTSD after TBI.

Indeed patients were predominantly males however there were no sex differences in rates of PTSS or any of the neuropsychological outcomes. This is mentioned on line 205

Despite these few minor points, the study overall is well done and there is enthusiasm for the work.

Thank you, we appreciate this feedback and the earlier comments.

Paul Bangirana PhD