PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	Challenges in the acute identification of mild traumatic brain injuries: results from an emergency department surveillance study
AUTHORS	Pozzato, Ilaria; Meares, Susanne; Kifley, Annette; Craig, Ashley; Gillett, Mark; Vu, Kim Van; Liang, Anthony; Cameron, Ian; Gopinath, Bamini

VERSION 1 - REVIEW

REVIEWER	Fiona Lecky Universities of Sheffield and Manchester and Salford Royal Hospital UK CENTER TBI Investigator TARN Research Director NICE Head Injury Guideline Chair
REVIEW RETURNED	11-Oct-2019

GENERAL COMMENTS	This single centre study used a retrospective chart review to estimate the prevalence of mild TBI in Emergency Department attendees aged 16-65 over a recent 9 month period. Over 30,000 records were screened with symptoms of mild TBI according to WHO criteria being present in 1.15% with uncertainty in a further 0.6%. The authors highlight an important issue with diagnostic coding with mild TBI only being flagged as a coded discharge diagnosis in 23% of cases where the chart suggested mild TBI was highly likely In general I enjoyed reading this study and commend the authors on their efforts to screen and reliably identify cases according to predetermined criteria using two authors. My recommendations for improvement are minor and relate to clarity. At the end of the introduction, I was unsure of what the issue was that the study was trying to address – mild TBI prevalence or highlighting diagnostic and coding challenges, the language should be tightened up here to formalise an aim(s) or research questions. The first results table is much too long should be split into 3especially, demographics co morbidity, mechanism alcohol and drug use in the first Clinical features of mild tbi and scan findings second Care in third I don't think tables 2 and 3 are easy to interpret ? redo as pie charts or omit Finally the discussion should acknowledge the challenge of making this diagnosis in the ED under time pressure and with intoxication being a major confounder (36% of cases) as alone it

	can cause all of the mild TBI features. This is likely to be the major cause of the coding issues. ED is crying out for a brain injury blood biomarker and the recent TLN paper by Yue et al could be referenced.

REVIEWER	Cameron Jeter The University of Texas Health Science Center at Houston, United States of America
REVIEW RETURNED	18-Oct-2019

GENERAL COMMENTS	This thorough and well-written manuscript retrospectively determined the accuracy of mild traumatic brain injury (mTBI) diagnoses in an emergency department. The research meets a need of the field to determine the incidence of mTBI in an Australia ED, and whether standardized diagnostic criteria generate a similar rate as reported in studies from other countries. The specific goals of this study were to establish the number of documented mTBI diagnoses in an emergency room (chart notes or diagnostic codes), determine the actual incidence of mTBI, and identify assessments associated with positive mTBI diagnosis. Comments are below. Major 1. Diagnostic criteria of the standardized assessment method used is unclear. Although it is clear the WHO definition is used and what their four clinical manifestations for mTBI diagnosis are, nowhere does the article explicitly state how many of these criteria must be met for mTBI diagnosis and with what assessments. This is key to understanding the manuscript. Thus, in the third paragraph of the Introduction, please more clearly explain the diagnostic criteria, including naming the WHO criterion to which each objective measures listed (i.e., CT, GCS, PTA) here or in the Tables (could) belong. 2. Further confusion on the diagnostic criteria can stem from the inclusion of more than four mTBI WHO criteria in the tables. Please link each assessment in the Introduction to the WHO criterion it fulfills, and in the Tables, list them in the order of the four WHO criteria. Minor 1. The abstract Conclusion is that mTBI is prevalent in the ED. Is <2% considered prevalent? 2. Edit the third strength and limitation bullet to be a complete sentence. 3. As part of the final strength and limitation bullet, consider adding that this limitation of information about mTBI means that mTBI is in fact more prevalent than is possible to confirm here – that mTBI may be underreported. 4. In the second paragraph of the Discussion, consider pointing out that although confirmed mTBI diagnosis rate was low, your work confirms the single most effective assessment for increasing accuracy of mTBI diagnosis is of PTA. 5. In the second paragraph of the Discussion, line 49, consider clarifying “(i.e., meeting 2 of the 4 WHO criteria).” 6. In Table S1, is Backache a disorder, finding, or neither?

REVIEWER	Carl Marincowitz Hull York Medical School UK
REVIEW RETURNED	05-Nov-2019

GENERAL COMMENTS	This is a valuable piece of work and I apologise for the delay in providing a review. I do have the following queries. 1) You do raise in the limitations section that your population and site may not be generalisable. Is it possible to provide a description of the study setting and provide some insight into whether the findings are likely to be applicable to the rest of Australia. 2) You highlight the proportion of all attendances which should have been diagnosed with TBI by the WHO criteria. Do you have any percentage of attendances which presented with head trauma? 3) You rightly highlight that post-traumatic amnesia is a particularly hard marker of TBI to record and measure. I personally feel that any retrospective chart review is likely to under-estimate this symptom and bias your estimate of the point prevalence of TBI over the 9 month period. Have you any prospective studies you can reference to compare your findings to? 4) Do you have any insight into what TBI is being diagnostically coded as instead? 5) I think this is an interesting and well written study, but the implications or so what could be brought out better. I struggled to really find an implication for future practice or research other than highlighting that TBI is poorly coded, but as you reference this has already been demonstrated previously.

VERSION 1 – AUTHOR RESPONSE

Reviewer #1:

This single centre study used a retrospective chart review to estimate the prevalence of mild TBI in Emergency Department attendees aged 16-65 over a recent 9 month period. Over 30,000 records were screened with symptoms of mild TBI according to WHO criteria being present in 1.15% with uncertainty in a further 0.6%. The authors highlight an important issue with diagnostic coding with mild TBI only being flagged as a coded discharge diagnosis in 23% of cases where the chart suggested mild TBI was highly likely In general I enjoyed reading this study and commend the authors on their efforts to screen and reliably identify cases according to predetermined criteria using two authors. My recommendations for improvement are minor and relate to clarity.

1) At the end of the introduction, I was unsure of what the issue was that the study was trying to address – mild TBI prevalence or highlighting diagnostic and coding challenges, the language should be tightened up here to formalise an aim(s) or research questions.

Author response: Agreed. Study aims have now been rephrased to improve clarity (pp 7, second para): ‘Given the current challenges in mTBI diagnosis and limitations of existing epidemiological research, this study primarily aimed to establish: (i) the occurrence of mTBI diagnosis among ED attendances (i.e. meeting standard diagnostic criteria) and the proportion of these that received a clearly recorded mTBI diagnosis (i.e. based on clinical notes and/or diagnosis codes). A secondary aim was to describe challenges in acute identification and management of mTBI, such as the implementation of a validated measure for PTA screening in ED.’

2) The first results table is much too long should be split into 3 especially, demographics co morbidity, mechanism alcohol and drug use in the first Clinical features of mild tbi and scan findings second Care in third I don’t think tables 2 and 3 are easy to interpret? redo as pie charts or omit

Author response: Agreed. As suggested, Table 1 has now been split into three tables (i.e. Table 1: clinical features of mTBI, Table 2: sociodemographic and injury-related information, Table 3: acute hospital management details. Previous Tables 2 and 3 are now provided as online supplementary material (i.e. Table S1 and S2 respectively).

3) Finally the discussion should acknowledge the challenge of making this diagnosis in the ED under time pressure and with intoxication being a major confounder (36% of cases) as alone it can cause all of the mild TBI features. This is likely to be the major cause of the coding issues. ED is crying out for a brain injury blood biomarker and the recent TLN paper by Yue et al could be referenced.

Author response: The following sentence was added in the Discussion (pp 15, second para): ‘These findings confirm intoxication is a major confound affecting accurate identification of mTBI in busy ED settings, with day of injury blood alcohol levels being associated with: failure on PTA assessment, [20] a longer duration of LOC, and decreased GCS scores. [32] Differentiation of mTBI in these individuals in the ED setting is likely to be facilitated by the potential implementation of blood based biomarkers., [33]

The following Yue et al (2019) paper has also been referenced in the manuscript (pp 15, second para, ref [33]): Yue JK, Yuh EL, Korley FK, Winkler EA, Sun X, Puffer RC, Deng H, Choy W, Chandra A, Taylor SR, Ferguson AR. Association between plasma GFAP concentrations and MRI abnormalities in patients with CT-negative traumatic brain injury in the TRACK-TBI cohort: a prospective multicentre study. The Lancet Neurology. 2019 Oct 1;18(10):953-61.

Reviewer #2:

This thorough and well-written manuscript retrospectively determined the accuracy of mild traumatic brain injury (mTBI) diagnoses in an emergency department. The research meets a need of the field to determine the incidence of mTBI in an Australia ED, and whether standardized diagnostic criteria generate a similar rate as reported in studies from other countries. The specific goals of this study were to establish the number of documented mTBI diagnoses in an emergency room (chart notes or diagnostic codes), determine the actual incidence of mTBI, and identify assessments associated with positive mTBI diagnosis.

Comments are below.

Major

1) Diagnostic criteria of the standardized assessment method used is unclear. Although it is clear the WHO definition is used and what their four clinical manifestations for mTBI diagnosis are, nowhere does the article explicitly state how many of these criteria must be met for mTBI diagnosis and with what assessments. This is key to understanding the manuscript. Thus, in the third paragraph of the Introduction, please more clearly explain the diagnostic criteria, including naming the WHO criterion to which each objective measures listed (i.e., CT, GCS, PTA) here or in the Tables (could) belong.

Author response: Thank you for the opportunity to clarify this important point. We have now modified the second paragraph of the Methods section (pp 8): 'A confirmed mTBI diagnosis was ascertained based on the presence of any of the four mTBI manifestations (i.e. level of consciousness, confusion/disorientation, post-traumatic amnesia, transient neurological abnormalities), as expressed by the corresponding WHO criteria (Table 1 and Online Supplementary Table S1): (i) a GCS of 13–15 30 minutes after injury or on later presentation to healthcare; and/or loss of consciousness of ≤30 mins; (ii) confusion/disorientation, (iii) PTA <24-hours, and/or (iv) CT-detected intracranial injuries not requiring neurosurgery, respectively. Table 1 has been modified accordingly.

2) Further confusion on the diagnostic criteria can stem from the inclusion of more than four mTBI WHO criteria in the tables. Please link each assessment in the Introduction to the WHO criterion it fulfills, and in the Tables, list them in the order of the four WHO criteria.

Author response: Please see above reply to this reviewer's query #1.

Minor

1) The abstract Conclusion is that mTBI is prevalent in the ED. Is <2% considered prevalent?

Author response: The word 'prevalent' has now been changed to 'common' in the abstract Conclusion (pp 3).

2) Edit the third strength and limitation bullet to be a complete sentence.

Author response: This suggestion has been adopted. The third bullet point now reads (pp 4): 'This study provides novel data on proportions of rapid post-traumatic amnesia screening in NSW, Australia, where there is written recommendation around PTA screening in all Emergency Departments'.

3) As part of the final strength and limitation bullet, consider adding that this limitation of information about mTBI means that mTBI is in fact more prevalent than is possible to confirm here – that mTBI may be underreported.

Author response: The following information has been added to the fifth bullet point: '…with mTBI occurrence possibly being underestimated'. (pp 4).

4) In the second paragraph of the Discussion, consider pointing out that although confirmed mTBI diagnosis rate was low, your work confirms the single most effective assessment for increasing accuracy of mTBI diagnosis is of PTA.

Author response: Agreed. The following sentence has been added in the second paragraph of the Discussion (pp 13, first para): 'This study contributes to the existing knowledge-base, by providing unique Australian data and suggests that adopting standard criteria and assessment of PTA provide the best approach to improve accuracy of mTBI diagnosis'.

5) In the second paragraph of the Discussion, line 49, consider clarifying "(i.e., meeting 2 of the 4 WHO criteria)."

Author response: Agreed. This sentence in the Discussion (pp 14, last para) has been changed as suggested.

6) In Table S1, is Backache a disorder, finding, or neither?

Author response: We are unsure about the answer to this query. 'Backache' reflects the documented ED discharge code (SNOWMED code) in one of the analysed mTBI cases. SNOMED codes often refer to the injury type or symptoms reported by individuals presenting to the emergency department. Further information on this is unavailable.

Reviewer #3:

This is a valuable piece of work and I apologise for the delay in providing a review.

I do have the following queries.

1) You do raise in the limitations section that your population and site may not be generalisable. Is it possible to provide a description of the study setting and provide some insight into whether the findings are likely to be applicable to the rest of Australia.

Author response: Thank you for this comment. Detailed information of the study setting was included in our study protocol published in BMJ Open (and referenced in the Methods [25]), which states the following about the study site: 'Royal North Shore Hospital (RNSH) is a large hospital in metropolitan Sydney, New South Wales NSW, Australia, serving a population of 213 000 inhabitants in 2016, across four local government areas. The overall number of RNSH ED attendances in the study year was approximately 80 000, and of these, 30 000 were aged 18–65 years old.,

Therefore, findings from this study are likely to be applicable to other major trauma hospitals in Australia.

2) You highlight the proportion of all attendances which should have been diagnosed with TBI by the WHO criteria. Do you have any percentage of attendances which presented with head trauma?

Author response: This is a very interesting point, but unfortunately our study cannot provide this information, as collection of these data would have been too onerous and not feasible with the available resources and time.

3) You rightly highlight that post-traumatic amnesia is a particularly hard marker of TBI to record and measure. I personally feel that any retrospective chart review is likely to under-estimate this symptom and bias your estimate of the point prevalence of TBI over the 9 month period. Have you any prospective studies you can reference to compare your findings to?

Author response: Agreed, and this has been further acknowledged as a limitation of this study in the last bullet point (pp 4). Unfortunately, we are not aware of any prospective studies that have used standardised PTA assessment for TBI diagnosis in ED settings. This is what makes our study unique, albeit with some limitations, highlighting the need for further research in this area.

4) Do you have any insight into what TBI is being diagnostically coded as instead?

Author response: The top 25 and the full list of diagnosis code descriptors allocated to the identified mTBI cohort (confirmed and indeterminate mTBI) are illustrated in Table 4 and Table S3 respectively.

5) I think this is an interesting and well written study, but the implications or so what could be brought out better. I struggled to really find an implication for future practice or research other than highlighting that TBI is poorly coded, but as you reference this has already been demonstrated previously.

Author response: Thank you for this comment. We believe that major clinical implications of this study are that implementation of standard diagnostic criteria and PTA screening in ED settings can lead to substantial improvement in the accuracy of mTBI identification, and possibly the coding of these injuries, so that a reliable surveillance system can be established. These implications have now been more clearly outlined in the second paragraph of the Discussion (pp 13, first para)

VERSION 2 – REVIEW

REVIEWER	Fiona Lecky University of Sheffield, and Salford Royal Hospital, UK
REVIEW RETURNED	17-Dec-2019

GENERAL COMMENTS	Thank you for the revisions and acknowledging the challenges of applying the WHO criteria and PTA assessment in intoxicated patients, at the botton of page 15 "confound" should be changed to "confounding" for grammatical reasons

REVIEWER	Cameron Jeter The University of Texas Health Science Center at Houston
REVIEW RETURNED	10-Dec-2019

GENERAL COMMENTS	Thank you for addressing my suggestions.

REVIEWER	Carl Marincowitz Hull York Medical School UK
REVIEW RETURNED	18-Dec-2019

GENERAL COMMENTS	I am happy that the authors have addressed the majority of the points I raised. I suggest that the first sentence of the conclusion is reworded: MTBI may have higher impacts on emergency care settings than previously anticipated. Do you mean the MTBI is under diagnosed in an Emergency care setting?

VERSION 2 – AUTHOR RESPONSE

Reviewer #1:

Thank you for the revisions and acknowledging the challenges of applying the WHO criteria and PTA assessment in intoxicated patients, at the botton of page 15 "confound" should be changed to "confounding" for grammatical reasons

Author response: Thank you. As suggested this has been changed to ‘confounding.’

Reviewer #3:

I suggest that the first sentence of the conclusion is reworded:

MTBI may have higher impacts on emergency care settings than previously anticipated.

Do you mean the MTBI is under diagnosed in an Emergency care setting?

Author response: Yes, this is correct we have now reworded the first sentence in the conclusion - ‘The findings from this study indicate that mTBI is likely to be under-diagnosed in an emergency care setting.’