

PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	Incidence of post-traumatic epilepsy following pediatric traumatic brain injury: protocol for systematic review and meta-analysis
AUTHORS	Mariajoseph, Frederick P.; Rewell, Sarah S.; O'Brien, Terence; Semple, Bridgette; Antonia-Baker, Ana

VERSION 1 – REVIEW

REVIEWER	Litofsky , Scott University of Missouri, Division of Neurological Surgery , University of Missouri School of Medicine , Columbia , MO , USA.
REVIEW RETURNED	02-Aug-2021

GENERAL COMMENTS	The authors have written a protocol to determine the incidence of pediatric post-traumatic epilepsy by a systematic review and meta-analysis. They should be able to accomplish their goals.
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REVIEWER	Baxendale, Sallie University College London, Department of Clinical and Experimental Epilepsy
REVIEW RETURNED	17-Sep-2021

GENERAL COMMENTS	<p>This paper describes a a protocol for a systematic review and analyses of the literature reporting the incidence of post traumatic epilepsy in paediatric populations.</p> <p>The authors are part of a group who are world renowned for their expertise in epilepsy. They identify a legitimate and important gap in our knowledge with respect to the paediatric population and describe a sound protocol to make sense of the literature to date. I have no doubt that, when complete, this study will make an important contribution to the clinical literature and will probably also become the go-to reference in medico-legal practice world wide.</p> <p>I have just two minor queries. How will the authors deal with papers that have reported outcomes in mixed adult and paediatric populations and ensure that these are captured in the search? It may not be possible to extract the paediatric data from such studies, but if it is, it would be a shame to exclude this data from the analysis. Secondly, could the authors give a little more detail about how they will be classifying and coding the pathology reported on the CT scans? We know in adults that long term consequences of TBI are often just as dependent on the mechanism of traumatic brain injury (DAI, bleeds, oedema etc) in addition to the severity and I suspect the same is true for post</p>
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traumatic epilepsy in paediatric populations. It would be good to have a look at this if the data is there, particularly with respect to signposting to future research on these mechanisms.

VERSION 1 – AUTHOR RESPONSE

RESPONSE TO REVIEWER #1

*Please consider revising the article title to include the secondary aims, if appropriate – eg, “Incidence of post-traumatic epilepsy following pediatric traumatic brain injury and associated risk factors: protocol for systematic review and meta-analysis”

- Thank you for your suggestion. However, given the observed heterogeneity in data included in publications in this field to date, we are still unsure of the extent to which we will be able to evaluate associated risk factors. We would therefore prefer to limit the scope of the title of our protocol, although we will certainly include the risk factors in the subsequent systematic review publication if robust statistical analysis of these factors is indeed possible with the dataset.

*Please update the “Methods and analysis” section of the abstract to include adequate description of the search strategy, including the databases to be searched, the date ranges to be covered by the searches, language restrictions, and main inclusion/exclusion criteria. The date range and language restrictions also need to be added to the description of the search strategy in the main text. If the final search date is not yet known (because not yet done or specified), you should still include the start date of the search (or, if no start date, state “from database inception”).

- We have updated the “methods and analysis section”, both in text (pages 7-8) and in the abstract (page 2), including date ranges and language restrictions. The abstract also has a more comprehensive description of the eligibility criteria.

*Please revise the “Ethics and dissemination” section of the abstract to (i) indicate that the planned publishing of the findings will be in a peer-reviewed journal; and (ii) delete the final sentence, as this is a Discussion point and is not appropriate for a protocol paper as it pre-empted the findings of the study.

- We have updated this section of the abstract to reflect your suggestion.

*Please revise the ‘Strengths and limitations’ section of your manuscript (after the abstract). This section should contain up to five short bullet points, no longer than one sentence each, that relate specifically to the methods. The aims and assumed relevance of the study should not be summarised here.

- Bullet points have been revised to more appropriately meet the requirements of this section.

*Please ensure that you have fully described the methodological limitations of the study in the ‘Strengths and limitations’ section, as well as in the main text Discussion section.

- We have more extensively outlined the limitations of the study in the discussion section (page 13).

*The “Ethics and dissemination” section in the main text should be moved out of the “Methods and analysis” section – this should be a main section and should be placed after the “Methods and analysis” section (ie, after the “Data analysis” subsection and before the Discussion).

- We have relocated this section as a main section in text (page 10).

*Please include, as a supplementary file, the precise, full search strategies for all databases, registers and websites, including any filters and limits used. This should be included as an appendix file for publication and should be cited in the main text where the search strategy is described.

- We have attached our search strategy as a supplementary file.

RESPONSE TO REVIEWER #2

*How will the authors deal with papers that have reported outcomes in mixed adult and paediatric populations and ensure that these are captured in the search? It may not be possible to extract the paediatric data from such studies, but if it is, it would be a shame to exclude this data from the analysis.

- We intend on including mixed adult-paediatric publications, as long as it is possible to differentiate and ascertain the paediatric cohort. We have now clarified this in our selection criteria (page 8). We believe our search strategy is broad enough to maximise publications with a discernable paediatric cohort, including mixed adult-paediatric studies. However, we have now noted the potential issue of extracting paediatric-specific data from such papers in our limitations section (page 11).

*Secondly, could the authors give a little more detail about how they will be classifying and coding the pathology reported on the CT scans? We know in adults that long term consequences of TBI are often just as dependent on the mechanism of traumatic brain injury (DAI, bleeds, oedema etc) in addition to the severity and I suspect the same is true for post traumatic epilepsy in paediatric populations. It would be good to have a look at this if the data is there, particularly with respect to signposting to future research on these mechanisms.

- We have included a proposed classification system (page 9). However, due to heterogeneity in studies, this may be subject to change when we have