

## A systematic review of paediatric traumatic brain injury as a risk factor for psychotic experiences

### Citation

King-Chi Yau, Grace Revill, Vaughan Bell. A systematic review of paediatric traumatic brain injury as a risk factor for psychotic experiences. PROSPERO 2022 CRD42022360772 Available from: [https://www.crd.york.ac.uk/prospero/display\\_record.php?ID=CRD42022360772](https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42022360772)

### Review question

This systematic review aims to determine the association between preceding paediatric traumatic brain injury (pTBI) and subsequent presence of psychotic experiences.

### Searches

The databases of PsycINFO (Ovid) (from 1806 onwards) and MEDLINE (Ovid) (from 1946 onwards) will be searched based on the main terms of (i) traumatic brain injury, (ii) psychotic experiences, and (iii) child. We will include all peer-reviewed primary studies published in English language with no publication date restrictions applied. The search will last from 1/10/2022 to 1/12/2022, to be carried out by reviewers (KCY, GR). Prior to the final analysis searches will be re-run to identify any further studies that can be included in the review.

### Types of study to be included

The following types of design will be included: randomised or non-randomised controlled trials, retrospective or prospective cohort studies, and case-control studies (including nested case-control and family studies). We will exclude meta-analyses, systematic reviews, literature reviews, cross-sectional studies, case reports or case series, qualitative studies, opinion pieces, editorials, comments, newsletters, book chapters, and congress papers.

### Condition or domain being studied

Paediatric traumatic brain injury. Psychotic experiences.

### Participants/population

We will include participants of any age or gender with a diagnosis of paediatric traumatic brain injury.

### Intervention(s), exposure(s)

Paediatric traumatic brain injury (pTBI) will be defined as an onset of traumatic brain injury (TBI) before adulthood (i.e., < 18 years old). pTBI can be determined by the age of the study population (e.g., children or adolescents with TBIs) or the time of the onset of TBI (e.g., adults with a history of pTBI). We will include participants with a diagnosis of pTBI based on screening tools, structured clinical interviews, medical records reviews, or clinical diagnosis. TBIs with severity ranging from mild (including concussion) to severe will be included. For exclusion, we will not select studies when the occurrence of pTBI cannot be determined and psychotic experiences have not been measured. In addition, we will not include studies when exposure to TBI cannot be differentiated from other non-TBI conditions within a single group.

### Comparator(s)/control

Studies with and without comparison groups will be included, with no exclusion criteria to be applied.

## Context

There will be no restrictions by country or care setting.

## Main outcome(s)

The main outcome of interest will be presence of psychotic experiences based on screening tools, psychometric measures, structured clinical interviews, medical records review, or clinical diagnosis. Psychotic experiences will include schizophrenia, psychosis, hallucination, paranoia, psychosis-risk syndromes, and psychotic-like experiences. We will only include studies indicating that the onset of psychotic experiences was after, instead of before, TBI. We will exclude studies reporting only the more general neuropsychiatric outcomes.

## Measures of effect

Odds ratio (OR) or standardised mean difference (SMD) as appropriate with 95% confidence interval (CI).

## Additional outcome(s)

Not applicable.

## Data extraction (selection and coding)

### Study Selection Process

Two reviewers (KCY, GR) will independently screen the titles and abstracts of all the records retrieved after removal of duplicates by Ovid's automatic de-duplication feature. In case of disagreement, discussion will be held. A third reviewer (VB) will be consulted if a consensus cannot be reached. Then, the two reviewers will independently screen the full-text reports, and similar processes of discussion between the two reviewers and consultation with the third reviewer, in the case of disagreement, will be held.

### Data Extraction Process

A data extraction excel sheet will be developed. Two reviewers (KCY, GR) will use it to independently extract study characteristics and outcomes, and data will be compared. In cases of conflicts, discussion will be held or the third reviewer (VB) will be consulted.

### Data Items

### *Outcomes*

We will primarily extract the number of participants experiencing psychotic experiences after TBI. For a particular study, there may be a multiplicity of results, and we will follow a priori defined rules of decision to select data. (i) When both the raw number of participants experiencing psychotic experiences and the calculated statistics (e.g., odds ratios) are available, we will extract the raw number. (ii) When descriptive statistics of interval measures of psychotic experiences and the calculated statistics (e.g., p values or effect sizes) are available, we will extract the descriptive statistics. (iii) When both non-imputed and imputed data are reported, we will choose the imputed.

### *Exposures*

We will primarily extract the number of participants experiencing TBI. If there is a multiplicity of results, and we will follow a priori defined rules of decision similar to those listed for outcome data (i.e., extracting raw values).

### *Study Characteristics*

We will extract the (i) year and location of the study, (ii) study design, and (iii) participant characteristics (in the exposure and control groups [if any]).

### Risk of bias (quality) assessment

Two reviewers (KCY & GR) will independently assess the quality of included studies using a 14-item checklist (Kmet et al., 2004) on a 3-point scale (0 = criteria not met; 1 = partially met; 2 = fully met), generating a summary score (total sum / total possible sum) ranging from 0 to 100, to categorise the low (0-49), moderate (50-74), and high (75-100) study quality. All disagreements will be resolved by consensus.

### Strategy for data synthesis

We will estimate the meta-analytic odds ratio (OR) or meta-analytic standardised mean difference (SMD) as appropriate with 95% confidence interval (CI) of psychotic experiences associated with preceding pTBI among the included studies using the R package meta. We will use funnel plots and Egger's test to examine potential publication bias.

If there are enough studies providing data for calculation or extraction of ORs or SMDs, we will first use the metaviz package in R to visualise small study effects and publication bias by a funnel plot. Afterwards, we will use the R metaprop package to compute the  $I^2$  statistic to measure heterogeneity among the included studies and we will use a random-effects model if heterogeneity is sufficiently high. We will conduct a leave-one-out sensitivity analysis to examine if the exclusion of any particular study would change the conclusions.

We will make a post-hoc decision to decide whether to carry out subgroup analyses based on subgroups of study design (e.g., case-control, cohort studies), study location, and diagnosis (e.g., schizophrenia, psychosis, psychotic-like experiences). If there are insufficient data for any meta-analyses, we will conduct a narrative synthesis based on ESRC guidelines (Popay et al., 2006). The focus of the narrative synthesis will be the relationship between preceding pTBI and subsequent psychotic experiences.

### Analysis of subgroups or subsets

We will make a post-hoc decision to decide whether to carry out subgroup analyses based on subgroups of study design (e.g., case-control, cohort studies), study location, and diagnosis (e.g., schizophrenia, psychosis, psychotic-like experiences).

### Contact details for further information

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### Organisational affiliation of the review

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### Review team members and their organisational affiliations

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### Type and method of review

Meta-analysis, Narrative synthesis, Systematic review

Anticipated or actual start date

01 October 2022

Anticipated completion date

30 September 2023

Funding sources/sponsors

Not applicable.

Conflicts of interest

Language

English

Country

England

Stage of review

Review Ongoing

Subject index terms status

Subject indexing assigned by CRD

Subject index terms

Brain Injuries, Traumatic; Child; Humans; Risk Factors

Date of registration in PROSPERO

22 September 2022

Date of first submission

22 September 2022

Stage of review at time of this submission

The review has not started

| Stage   | Started | Completed |
|---|---------|-----------|
| Preliminary searches  | No      | No        |
| Piloting of the study selection process                         | No      | No        |
| Formal screening of search results against eligibility criteria | No      | No        |
| Data extraction   | No      | No        |
| Risk of bias (quality) assessment                               | No      | No        |
| Data analysis   | No      | No        |

*The record owner confirms that the information they have supplied for this submission is accurate and complete and they understand that deliberate provision of inaccurate information or omission of data may be construed as scientific misconduct.*

*The record owner confirms that they will update the status of the review when it is completed and will add publication details in due course.*

## Versions

22 September 2022