

Global Mortality Outcomes in Traumatic Brain Injury: A Systematic Review and Meta-Analysis

1. Background

Traumatic brain injury (TBI) remains a major cause of mortality and disability worldwide, particularly among young adults and economically productive populations. Despite advances in neurocritical care, neurosurgery, and trauma systems, mortality rates vary substantially across countries, healthcare settings, and injury severity categories. Reported mortality ranges from less than 5% in mild TBI to over 50% in severe TBI.

A comprehensive synthesis of available evidence is needed to estimate pooled mortality rates and identify factors contributing to mortality variation across different populations and healthcare systems.

2. Review Question

What is the pooled mortality rate among patients with traumatic brain injury, and what factors influence mortality outcomes?

3. Objectives

Primary Objective

- To estimate the pooled mortality rate among patients diagnosed with traumatic brain injury.
- Secondary Objectives
- To compare mortality across TBI severity categories (mild, moderate, severe).
- To evaluate mortality according to geographical regions.
- To assess mortality by age groups.
- To compare mortality between high-income and low- and middle-income countries.

4. PICO Framework

Component	Description
Population	Patients of any age diagnosed with TBI
Intervention/Exposure	Traumatic brain injury
Comparator	Different severity levels, regions, age groups, or management strategies
Outcome	Mortality (in-hospital, 30-day, ICU, or long-term mortality)

5. Eligibility Criteria

Inclusion Criteria

Studies that:

- Include patients with TBI.
- Report mortality outcomes.
- Use observational or interventional study designs.
- Provide sufficient data to calculate mortality proportions.
- Are published in peer-reviewed journals.
- Are published in English.

Eligible Designs

- Cohort studies
- Cross-sectional studies
- Case-control studies
- Randomized controlled trials (baseline mortality data)

Exclusion Criteria

- Case reports.
- Case series with fewer than 10 participants.
- Conference abstracts without full text.
- Reviews, editorials, commentaries.
- Animal studies.
- Cadaveric studies.
- Studies without mortality data.

6. Outcomes

Primary Outcome

- All-cause mortality among TBI patients.
- Mortality Definitions
- In-hospital mortality
- ICU mortality
- 30-day mortality
- 6-month mortality
- 12-month mortality

Secondary Outcomes

- Mortality by GCS category
- Mortality by age

- Mortality by sex
- Mortality by mechanism of injury
- Mortality by continent
- Mortality by country income level

7. Information Sources

- Electronic databases:
- PubMed/MEDLINE
- Embase
- Scopus
- Web of Science
- Cochrane Library
- Google Scholar

Additional sources:

- Reference lists of included studies.
- Grey literature where appropriate.

8. Search Strategy

PubMed Search Strategy

("Traumatic Brain Injury"[Mesh]

OR "Brain Injuries, Traumatic"[Mesh]

OR TBI

OR traumatic brain injury

OR head injury

OR brain trauma)

AND

(mortality

OR death

OR fatality

OR survival)

AND

(humans[MeSH])

No date restrictions initially.

9. Study Selection

Two independent reviewers will:

Stage 1

Screen titles and abstracts.

Stage 2

Review full texts.

Disagreements will be resolved by a third reviewer.

Selection process will be presented using a PRISMA flow diagram.

10. Data Extraction

A standardized extraction sheet will collect:

Study Characteristics

- Author
- Year
- Country
- Region
- Journal

Methodological Characteristics

- Study design
- Study period
- Sample size

Participant Characteristics

- Mean age
- Sex distribution
- GCS
- Injury mechanism

Outcome Data

- Total TBI patients
- Number of deaths
- Mortality percentage
- Follow-up duration

11. Risk of Bias Assessment

For observational studies:

Use the Newcastle-Ottawa Scale.

Domains:

- Selection
- Comparability
- Outcome assessment

For randomized trials:

Use the Cochrane Risk of Bias Tool.

Two reviewers will independently assess quality.

12. Statistical Analysis

Effect Size

Primary effect size:

Mortality proportion

Mortality Rate = $\frac{\text{Deaths}}{\text{Total TBI Patients}}$

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Meta-analysis Model

Because substantial heterogeneity is anticipated:

- Random-effects model
- DerSimonian–Laird estimator

Heterogeneity

Assessed using:

I^2

I^2

Interpretation:

- 0–25% = low
- 26–50% = moderate
- 51–75% = substantial
 - 75% = considerable

Publication Bias

- Funnel plots

- Egger's regression test
- Begg's test

When ≥ 10 studies are available.

13. Subgroup Analyses

If data permit:

Severity

- Mild TBI
- Moderate TBI
- Severe TBI

Age

- Pediatric
- Adult
- Elderly

Region

- Africa
- Asia
- Europe
- North America
- South America
- Oceania

Income Level

According to World Bank:

- Low income

- Lower-middle income
- Upper-middle income
- High income

Study Design

- Prospective
- Retrospective

14. Meta-Regression

Potential covariates:

- Mean age
- Percentage male
- Severe TBI proportion
- Publication year
- Sample size
- Country income level

15. Sensitivity Analysis

- Leave-one-out analysis.
- Excluding high-risk-of-bias studies.
- Fixed-effects versus random-effects comparison.

16. Certainty of Evidence

Use the GRADE Working Group framework to evaluate:

- Risk of bias
- Inconsistency
- Indirectness
- Imprecision

- Publication bias

17. Reporting

The review will be reported according to the PRISMA 2020 statement.

Expected Primary Meta-Analysis

The primary outcome will be the pooled mortality proportion among patients with traumatic brain injury (TBI), with corresponding 95% confidence intervals (CI) estimated using a random-effects meta-analysis model (DerSimonian–Laird method) to account for expected clinical and methodological heterogeneity across studies.

Mortality Time Point Hierarchy

Where multiple mortality time points are reported within a study, the following hierarchy will be applied to ensure consistency:

- In-hospital mortality (preferred primary time point)
- 30-day mortality
- ICU mortality (if in-hospital or 30-day data are not available)
- Long-term mortality (≥ 6 months or longest available follow-up)

Data Transformation

To stabilize variances in proportion data and address studies with extreme event rates (very low or very high mortality), proportions will be transformed prior to pooling using:

- **Freeman–Tukey double arcsine transformation (primary approach)**

A sensitivity analysis will be conducted using:

- **Logit transformation of proportions**

Back-transformed pooled estimates will be reported for interpretability.

Heterogeneity Assessment

Statistical heterogeneity will be assessed using:

- **I² statistic**
- **Cochran's Q test (χ^2 test)**

Interpretation of I²:

- 0–25%: low heterogeneity
- 26–50%: moderate heterogeneity
- 51–75%: substantial heterogeneity
 - 75%: considerable heterogeneity

Subgroup and Meta-Regression Analyses

Where sufficient data are available, subgroup analyses will be performed based on:

- TBI severity (mild, moderate, severe)
- Age group (pediatric, adult, elderly)
- Geographic region
- Country income level (World Bank classification)
- Study design (prospective vs retrospective)

Meta-regression will explore potential sources of heterogeneity using:

- Mean/median age
- Proportion of severe TBI
- Year of publication
- Sample size
- Country income level

Software

All statistical analyses will be conducted using:

- **R software (version 4.x or later)**
- R packages:

- meta
- metafor
- dmetar (for diagnostic and sensitivity analyses)

Sensitivity Analyses

Robustness of pooled estimates will be assessed through:

- Leave-one-out (influence) analysis
- Exclusion of high risk-of-bias studies
- Comparison of fixed-effect vs random-effects models
- Comparison of transformation methods (Freeman–Tukey vs logit)

Publication Bias

If ≥ 10 studies are included in a meta-analysis, publication bias will be assessed using:

- Funnel plot asymmetry
- Egger's regression test
- Begg's rank correlation test