nature portfolio

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# Reporting Summary

Nature Portfolio wishes to improve the reproducibility of the work that we publish. This form provides structure for consistency and transparency in reporting. For further information on Nature Portfolio policies, see our Editorial Policies and the Editorial Policy Checklist.

## Statistics

For all statistical analyses, confirm that the following items are present in the figure legend, table legend, main text, or Methods section.

| n/a | Confirmed | |
|---|---|---|
| ☐ | ☒ | The exact sample size (*n*) for each experimental group/condition, given as a discrete number and unit of measurement |
| ☐ | ☒ | A statement on whether measurements were taken from distinct samples or whether the same sample was measured repeatedly |
| ☐ | ☒ | The statistical test(s) used AND whether they are one- or two-sided<br>*Only common tests should be described solely by name; describe more complex techniques in the Methods section.* |
| ☐ | ☒ | A description of all covariates tested |
| ☐ | ☒ | A description of any assumptions or corrections, such as tests of normality and adjustment for multiple comparisons |
| ☐ | ☒ | A full description of the statistical parameters including central tendency (e.g. means) or other basic estimates (e.g. regression coefficient) AND variation (e.g. standard deviation) or associated estimates of uncertainty (e.g. confidence intervals) |
| ☐ | ☒ | For null hypothesis testing, the test statistic (e.g. *F*, *t*, *r*) with confidence intervals, effect sizes, degrees of freedom and *P* value noted<br>*Give P values as exact values whenever suitable.* |
| ☒ | ☐ | For Bayesian analysis, information on the choice of priors and Markov chain Monte Carlo settings |
| ☒ | ☐ | For hierarchical and complex designs, identification of the appropriate level for tests and full reporting of outcomes |
| ☒ | ☐ | Estimates of effect sizes (e.g. Cohen's *d*, Pearson's *r*), indicating how they were calculated |

*Our web collection on statistics for biologists contains articles on many of the points above.*

## Software and code

Policy information about availability of computer code

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| Data collection | Data were collected using Research Electronic Data Capture (REDCap), a secure web-based application for building and managing online surveys and databases. The REDCap platform was hosted by the Oregon Clinical & Translational Research Institute and maintained compliance with US Health Insurance Portability and Accountability Act (HIPAA) regulations. All data were entered by collaborators at participating hospitals into a standardized, electronic case report form developed specifically for this study. The REDCap data collection form was generated and iteratively refined through workshops and discussions with Global Neurosurgical Collaborative members from diverse countries differing by human development status and geographic region. No commercial software was used for primary data collection. |
| Data analysis | All statistical analyses were performed using open-source software: R version 4.6.0 (R Foundation for Statistical Computing, Vienna, Austria). Analyses included mixed-effects logistic regression models with inverse probability weighting, implemented using standard R packages. Results were independently verified using Stata version 19.5 (StataCorp, College Station, Texas). Specific analytical methods included: extreme gradient boosting (xgboost) with nested cross-validation for variable selection; Shapley Additive Explanations (SHAP) values for variable importance assessment; and bootstrap resampling (1,000 replicates) for median odds ratio confidence interval estimation. De-identified data and code has been uploaded to GitHub. |

For manuscripts utilizing custom algorithms or software that are central to the research but not yet described in published literature, software must be made available to editors and reviewers. We strongly encourage code deposition in a community repository (e.g. GitHub). See the Nature Portfolio guidelines for submitting code & software for further information.

# Data

Policy information about availability of data

All manuscripts must include a data availability statement. This statement should provide the following information, where applicable:

- Accession codes, unique identifiers, or web links for publicly available datasets
- A description of any restrictions on data availability
- For clinical datasets or third party data, please ensure that the statement adheres to our policy

A de-identified, individual patient-level version of the analytic dataset, as well as a data dictionary, is available for download on GitHub at: https://github.com/jgnugent/GNS-I-Analysis and has also been archived on Zenodo at: https://doi.org/10.5281/zenodo.20694959. These data will remain publicly available without an end date. Formal requests for the full dataset or for identifying metrics should be sent to the study's data guarantor (nugentj@ohsu.edu) and principal investigator (raslana@ohsu.edu) accompanied by proof of ethical approval from the applicant's home institution. Each request will be evaluated by the data guarantor and principal investigator on the basis of the proposed use and the adequacy of ethical approval, and applicants will receive a response within 30 days. Following approval of each individual request, the data will be shared directly with the interested party via a secure file-sharing system, including all raw data collected, the processing code used to generate the final analytic sample from the raw data, the final analytic dataset, as well as a codebook for both datasets within 30 days of approval. Additionally, the original study protocol and details regarding the collaborative are available online at https://globalneurosurg.org.

# Research involving human participants, their data, or biological material

Policy information about studies with human participants or human data. See also policy information about sex, gender (identity/presentation), and sexual orientation and race, ethnicity and racism.

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| Reporting on sex and gender | Sex was determined based on patients' medical records at the time of hospital admission. Gender was not separately assessed in this study. Sex was considered in the study design as a potential covariate for outcome analyses. Sex data were collected from medical records by local site investigators and entered into the REDCap database. In our cohort of 2,165 patients, 1,625 (75.2%) were male and 535 (24.8%) were female, with male predominance observed across all HDI tiers ($p<0.001$). The proportion of male patients ranged from 56.2% in very-high-HDI countries to 85.6% in low-HDI countries. |
| Reporting on race, ethnicity, or other socially relevant groupings | This international study did not collect data on race or ethnicity. The variable used was the Human Development Index (HDI) tier of each patient's country, which served as a proxy for socioeconomic development and healthcare resource availability at the population level. Countries were classified into four HDI tiers (very-high, high, medium, and low) based on the 2021-2022 United Nations Human Development Index, a composite measure considering life expectancy, education, and income. HDI tier was determined by country of enrollment (assigned variable, not self-reported) and used as the primary exposure variable in all analyses. We explicitly note that HDI is a country-level measure and should not be interpreted as an individual-level socioeconomic indicator, as substantial within-country variation exists in all settings. We controlled for confounding by adjusting for patient-level covariates (age, sex, injury severity, mechanism of injury, pre-hospital care factors) in multivariable models and used mixed-effects regression with country and institution as random effects to account for clustering and between-country variation in baseline mortality risk. |
| Population characteristics | The study population consisted of adults (≥18 years) with traumatic brain injury presenting to 100 participating hospitals across 29 countries between June 2019 and December 2022. Key population characteristics included:<br><br>Median age: 37 years (IQR 24-58), ranging from median 32 years in high-HDI countries to median 63 years in very-high-HDI countries.<br>Sex: 75.2% male, 24.8% female<br>Pre-injury health status: 86.3% had ASA-PS score I-II (healthy or mild systemic disease)<br>Prior TBI history: 8.7%<br>TBI severity: 62.1% mild, 16.5% moderate, 21.4% severe<br>Mechanism of injury: 50.4% traffic collisions, 34.6% falls, with marked variation by HDI tier<br>Polytrauma: 39.3%<br><br>Full demographic and clinical characteristics are presented in Tables 1 and 2. |
| Recruitment | Participating institutions were recruited through open invitation at global and regional scientific society meetings and social media outreach conducted by the Global Neurosurgical Collaborative (GNC). Participation was voluntary, with no financial incentives provided. Any medical institution capable of admitting TBI patients for medical or surgical management was eligible to participate. Potential biases:<br><br>Selection bias: Voluntary participation likely favored institutions with existing research infrastructure and personnel, potentially underrepresenting settings with the most limited resources.<br><br>Geographic imbalance: Despite recruitment efforts targeting LMICs, high-HDI tier countries contributed 43.7% of records (with Egypt alone contributing 27.1%), while low-HDI countries contributed only 16.1% despite bearing 93% of the global TBI mortality burden.<br><br>Referral bias: Participating hospitals were primarily tertiary referral centers, which may not represent community-level TBI care in each country.Survival bias: Patients who died before hospital arrival were not captured, potentially underestimating mortality in settings with limited pre-hospital care infrastructure.<br><br>These biases are discussed in detail in the manuscript limitations section |

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| Ethics oversight | The study was approved by the Oregon Health & Science University (OHSU) Institutional Review Board (IRB #00021490), which served as the central coordinating site. Individual institutions obtained ethical approval from their local IRB or Ethics Committee prior to participation. Informed consent was waived at most sites under provisions for minimal-risk observational research. All data were de-identified at local sites prior to international transfer. This is further discussed is the Methods. |

Note that full information on the approval of the study protocol must also be provided in the manuscript.

# Field-specific reporting

Please select the one below that is the best fit for your research. If you are not sure, read the appropriate sections before making your selection.

☒ Life sciences ☐ Behavioural & social sciences ☐ Ecological, evolutionary & environmental sciences

For a reference copy of the document with all sections, see nature.com/documents/nr-reporting-summary-flat.pdf

# Life sciences study design

All studies must disclose on these points even when the disclosure is negative.

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| Sample size | A priori power analysis estimated that 1,092 patients were needed to detect a 5% mortality difference with 80% power and a 5% type I error rate. The final sample of 2,165 patients exceeded this requirement, providing adequate power for the primary mortality outcome analyses. No formal sample size calculation was performed for secondary outcomes. The achieved sample size was determined by the number of eligible patients enrolled during pre-designated 14-day collection periods across 100 participating hospitals, with no minimum enrollment requirement per site to maximize geographic diversity and enable participation from lower-volume centers. |
| Data exclusions | Data exclusions were pre-established. Of 2,504 patient records collected from 120 institutions, 339 records were excluded during validation: 1 duplicate record; 1 record outside the study period; 65 records with unspecified data collection periods; 17 records with improperly entered collection periods; 53 records failing outcome validation queries; 43 records failing covariate validation queries; and 140 records from sites that failed to meet data quality standards (≥5% of records or ≥5% of key variables flagged after three months of remediation opportunity), and 20 records from 2 sites unable to produce consent documentation. After exclusions, 2,165 records from 100 sites were analyzed. All exclusion criteria were defined in the protocol prior to data analysis. |
| Replication | This was an observational cohort study; experimental replication is not applicable. However, data validity was verified through a three-tiered quality assurance process: (1) REDCap functionality checks for critical variables; (2) central validation by the GNC Steering Committee with the study biostatistician; (3) iterative review with collaborating sites over three months to resolve flagged outliers. Final analyses were confirmed using two independent statistical software packages (R version 4.6.0 and Stata version 19.5), yielding consistent results. |
| Randomization | Not applicable. This was an observational cohort study with no experimental intervention. All consecutive TBI patients meeting eligibility criteria during each site's pre-designated 14-day collection period were enrolled; no randomization was performed. |
| Blinding | Not applicable. This was an observational study with no experimental intervention requiring blinding. Data collectors were aware of patient HDI tier (determined by country of enrollment), but HDI classification occurred at the country level and could not be concealed. Statistical analysts were not blinded to HDI tier as this was the primary exposure of interest in the study design. |

# Reporting for specific materials, systems and methods

We require information from authors about some types of materials, experimental systems and methods used in many studies. Here, indicate whether each material, system or method listed is relevant to your study. If you are not sure if a list item applies to your research, read the appropriate section before selecting a response.

## Materials & experimental systems

| n/a | Involved in the study |
|---|---|
| ☒ | ☐ Antibodies |
| ☒ | ☐ Eukaryotic cell lines |
| ☒ | ☐ Palaeontology and archaeology |
| ☒ | ☐ Animals and other organisms |
| ☒ | ☐ Clinical data |
| ☒ | ☐ Dual use research of concern |
| ☒ | ☐ Plants |

## Methods

| n/a | Involved in the study |
|---|---|
| ☒ | ☐ ChIP-seq |
| ☒ | ☐ Flow cytometry |
| ☒ | ☐ MRI-based neuroimaging |

## Plants

Seed stocks

*Report on the source of all seed stocks or other plant material used. If applicable, state the seed stock centre and catalogue number. If plant specimens were collected from the field, describe the collection location, date and sampling procedures.*

Novel plant genotypes

*Describe the methods by which all novel plant genotypes were produced. This includes those generated by transgenic approaches, gene editing, chemical/radiation-based mutagenesis and hybridization. For transgenic lines, describe the transformation method, the number of independent lines analyzed and the generation upon which experiments were performed. For gene-edited lines, describe the editor used, the endogenous sequence targeted for editing, the targeting guide RNA sequence (if applicable) and how the editor was applied.*

Authentication

*Describe any authentication procedures for each seed stock used or novel genotype generated. Describe any experiments used to assess the effect of a mutation and, where applicable, how potential secondary effects (e.g. second site T-DNA insertions, mosiacism, off-target gene editing) were examined.*