Personalized Prognostication in Paediatric TBI: A Systematic Review of Machine Learning Approaches with Multimodal Data

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DECLARATION

I, **Zolisa Brian Nkabinde**, hereby declare that this research report is my own work and has not been submitted or presented for any other degree or professional qualification at this or any other institute. This research was undertaken in the Division of Emergency Medicine, University of the Witwatersrand, Johannesburg.

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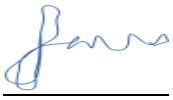
Signature of Supervisor 2:  Date: 21/07/2025

DEDICATION

I dedicate this work to the people who formed my support structure throughout this journey, my family and friends. Their relentless support has consistently carried me. I am deeply grateful for their motivation and unwavering positive affirmation.

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SUBMISSION FORMAT OF THIS RESEARCH REPORT

As per University of the Witwatersrand Faculty of Health Sciences guidelines, this research report is being submitted in the publication ready format. The article has been submitted to *The Journal of Head Trauma Rehabilitation* and is currently under publication consideration.

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MANUSCRIPT

TITLE OF MANUSCRIPT

Machine Learning-Based Prognostication in Paediatric Traumatic Brain Injury: A Systematic Review of Multimodal Approaches

RUNNING TITLE

ML-Based Prognostication in Paediatric TBI

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AUTHOR CONTRIBUTIONS

ZN conceptualized the study, designed the search strategy, and drafted the initial manuscript. **DJ** contributed to the interpretation of findings, provided methodological guidance, and critically reviewed and edited the manuscript. **AL** contributed to study selection, data extraction, quality assessment, interpretation of findings, provided methodological guidance, and critical revision of the manuscript for intellectual content. All authors approved the final version of the manuscript and agree to be accountable for all aspects of the work.

Machine Learning-Based Prognostication in Paediatric Traumatic Brain Injury: A Systematic Review of Multimodal Approaches

ABSTRACT

Background: Paediatric traumatic brain injury (pTBI) is a major global public health concern, contributing substantially to childhood disability and mortality. Traditional prognostic tools, such as the Glasgow Coma Scale (GCS), lack specificity and sensitivity, limiting their accuracy in predicting outcomes. This systematic review evaluated the use of machine learning (ML) models that integrate multimodal data to improve prognostication in pTBI.

Methods: his systematic review was registered with PROSPERO and conducted according to PRISMA guidelines. We systematically searched MEDLINE, PubMed, Embase, Scopus, Web of Science, and Cochrane for studies published in the past decade that applied ML to predict clinical outcomes in patients under 18 years with pTBI using multimodal data. Study quality was assessed using the QUIPS tool.

Results: Thirteen studies met inclusion criteria. ML algorithms, including support vector machines, random forest, artificial neural networks, CatBoost, and others, were applied to multimodal data incorporating clinical, radiological, neurocognitive, laboratory, and administrative variables. Most studies reported that ML models outperformed traditional methods, demonstrating higher sensitivity, specificity, and area under the receiver operating characteristic curve (AUROC). However, performance varied across studies, and some showed only modest improvements over conventional approaches. Lack of standardized reporting and limited assessment of clinical significance were common limitations.

Conclusion: ML models leveraging multimodal data show promise for improving prognostic accuracy in pTBI. Future research should address methodological heterogeneity, enhance interpretability and reproducibility, minimize false negatives, and adopt standardized reporting to support clinical implementation.

KEY WORDS

paediatric traumatic brain injury (pTBI); machine learning (ML); prognostication; multimodal data; outcome prediction; neuroimaging; support vector machines (SVM); random forest; artificial neural networks (ANN); personalized medicine

INTRODUCTION

Paediatric traumatic brain injury (pTBI) is a major global public health challenge, contributing substantially to childhood disability and mortality. It encompasses a spectrum of neurological impairments resulting from an external force to the head, with or without radiological evidence of injury.[1] Its global incidence is difficult to quantify due to inconsistencies in reporting, but evidence indicates that rates are higher in children than in adults, with annual estimates ranging between 47 and 280 per 100,000 children.[2]

Outcomes of pTBI vary widely even among patients with similar injury patterns, resulting in disparities in long-term neurocognitive and functional recovery.[3] This variability complicates efforts to develop standardized management strategies.[4]

Despite advances in pTBI care, accurate prognostication remains challenging, as TBI encompasses a spectrum of injury mechanisms and severities. Relying solely on clinical data limits predictive power, and there is a need for more precise prognostic and treatment approaches tailored to the heterogeneous presentations of pTBI.[3]

The Glasgow Coma Scale (GCS) remains the most widely used clinical tool for assessing TBI severity and prognosis in adults and children.[5,6] Other tools, such as the Paediatric Index of Mortality (PIM) and CT-based scoring systems like the Marshall and Rotterdam classifications, have been applied in research and some clinical settings.[6] However, these tools have limited predictive accuracy in children because they do not fully account for developmental differences, pre-verbal status, pre-existing neurodevelopmental conditions, the spectrum of injury severity, or long-term outcomes.[7,8] They also rely on narrow clinical and imaging features, failing to capture the complex pathophysiology of pTBI. More advanced models integrating multimodal data—clinical findings, neuroimaging, genetic testing, and biomarkers—may offer greater precision and clinical utility.[9]

Extensive multimodal data can be leveraged by machine learning (ML) models to improve prognostication [8,9]. ML enables the analysis of complex patterns across large datasets, facilitating the development of more accurate prognostic models and stratification of patients into subgroups with shared characteristics, which can inform tailored care plans.[10]

Interest in ML applications in healthcare has grown, with an increasing body of literature examining its role in pTBI outcome prediction. Common ML techniques used in TBI prognostication to interpret multimodal data with promising results include Support Vector Machines (SVMs), Artificial Neural Networks (ANNs), Random Forest (RF), Decision Trees, and clustering algorithms.[11] ML's ability to identify complex relationships may allow for improved prediction of long-term outcomes, as demonstrated by studies showing superior accuracy, sensitivity, and specificity compared to traditional clinical tools.[12]

There remains a pressing need for validated methods to integrate and analyse multimodal data to improve prognostic models for pTBI.[13] To date, no systematic review has specifically synthesized evidence on the role of multimodal data analysis and ML algorithms in predicting outcomes in the paediatric population.[12]

This systematic review aimed to evaluate the application of ML models integrating multimodal data for prognostication in pTBI. Specifically, we sought to answer the following research question: among paediatric patients (<18 years) with TBI (Participants), how have ML-based prognostic models using multimodal data inputs (Interventions), compared to traditional prognostic approaches where applicable (Comparisons), performed in predicting clinically relevant outcomes such as mortality, length of hospital stay, functional disability, and post-traumatic epilepsy (Outcomes), based on evidence from primary studies published in the past decade (Study Design)? We also aimed to summarize the performance metrics of these models and identify limitations and gaps in the existing literature to guide future research.

METHODS

Search Strategy

This systematic review was registered with the Prospective Register of Systematic Reviews (PROSPERO; CRD42024510419) prior to commencement. An ethics waiver (W-PR-241025-01) was obtained from the University of the Witwatersrand Human Research Ethics Committee (Medical) in October 2024.

A comprehensive electronic search was conducted in October 2024 across six databases: MEDLINE, PubMed, Embase, Scopus, Web of Science, and Cochrane. Only studies published within the past 10 years were included. The search used the following keywords:

"paediatric traumatic brain injury" OR "pTBI" AND "machine learning" OR "ML" AND "prognosis" OR "prediction" OR "outcomes." In addition, references of all retrieved studies were screened through backward citation searching for potentially relevant articles. No language restrictions were applied.

The search yielded 432 records: MEDLINE (n=102), PubMed (n=74), Embase (n=85), Scopus (n=68), Web of Science (n=61), and Cochrane (n=42). An additional seven records were identified through backward citation searching, resulting in 439 records in total. The full electronic search strategy for MEDLINE (via PubMed) is provided in **Appendix 1**.

Study Selection

Studies were eligible if they met the following criteria: (i) involved paediatric patients (<18 years) with TBI; (ii) focused on prognostication using ML with multimodal data (e.g., clinical, imaging, neurocognitive, or laboratory data); and (iii) assessed clinically relevant outcomes such as mortality, length of hospital stay, functional disability, or post-traumatic epilepsy. Grey literature, including preprints and conference abstracts, was excluded to maintain methodological consistency and ensure the reliability of peer-reviewed evidence.

Definition of ML Prognostication in pTBI

For this review, ML-based prognostication was defined as the application of ML algorithms integrating multimodal data – including clinical, radiological, neurocognitive, and biomarker information – to predict outcomes such as mortality (in-hospital, 30-day, or 90-day), hospital length of stay, and neurocognitive and behavioural outcomes. Favourable model performance was characterized by high sensitivity, specificity, and area under the receiver operating characteristic curve (AUROC).

Data Extraction and Quality Assessment

The review followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.[14] Two authors (ZN and AL) independently screened studies based on the inclusion criteria and extracted data, including: author, year, country, patient demographics, ML model type, data modalities, outcomes assessed, and performance metrics (e.g., AUROC, sensitivity, specificity). When key information was missing, corresponding authors were contacted; however, no responses were received.

Study quality was assessed using the Quality In Prognosis Studies (QUIPS) tool,[15] which is a validated instrument for risk of bias assessment in prognostic studies. Although ML-based models differ from traditional statistical models in some respects, QUIPS evaluates key methodological domains applicable to both approaches, including study participation, prognostic factor and outcome measurement, and statistical analysis and reporting. The tool was adapted to the objectives of this review and piloted on three studies before full application. After refinement, two authors (ZN and AL) independently assessed all included studies, and discrepancies were resolved through discussion and consensus among all three authors. Final risk of bias assessments are summarized in **Table 1**.

Table 1: QUIPS Risk of Bias Assessment for Included Studies

Study	Study Participation	Study Attrition	Prognostic Factor Measurement	Outcome Measurement	Study Confounding	Statistical Analysis and Reporting
Chong et al. [16]	Low Risk	Low Risk	Low Risk	Low Risk	Moderate Risk	Low Risk
Yadav et al. [17]	Low Risk	Low Risk	Low Risk	Low Risk	Moderate Risk	Low Risk
Hale et al. [19]	Low Risk	Low Risk	Low Risk	Low Risk	Moderate Risk	Low Risk
Hale et al. [20]	Low Risk	Low Risk	Low Risk	Low Risk	Moderate Risk	Low Risk
Greenen et al. [21]	Low Risk	Low Risk	Low Risk	Low Risk	Moderate Risk	Low Risk
Kayhanian et al. [18]	Low Risk	Low Risk	Low Risk	Low Risk	Moderate Risk	Low Risk
Raji et al. [22]	Moderate Risk	Low Risk	Low Risk	Low Risk	Moderate Risk	Low Risk
Tunthanathip & Oearsakul [23]	Low Risk	Low Risk	Low Risk	Low Risk	Moderate Risk	Low Risk
Maddux et al. [24]	Moderate Risk	Low Risk	Low Risk	Low Risk	Moderate Risk	Low Risk
Tunthanathip et al. [25]	Low Risk	Low Risk	Low Risk	Low Risk	Moderate Risk	Low Risk
Kim et al. [26]	Moderate Risk	Low Risk	Low Risk	Low Risk	Moderate Risk	Low Risk
Daley et al. [27]	Low Risk	Low Risk	Low Risk	Low Risk	Moderate Risk	Low Risk
Fonseca et al. [28]	Low Risk	Low Risk	Low Risk	Low Risk	Moderate Risk	Low Risk

Data Synthesis

Where reported, sensitivity, specificity, and likelihood ratios were extracted. If these metrics were not directly reported,[16–18] two-by-two tables were constructed using available data on true positives, false positives, true negatives, and false negatives. The QUIPS-based risk of bias assessments were considered in the narrative synthesis to contextualize findings, although no quantitative adjustments were applied.

RESULTS

Study Selection and Characteristics

A total of 439 records were identified through database searches and backward citation searching. After removing 97 duplicates, 342 unique records remained for screening. Of these, 249 were excluded based on title review as irrelevant, and an additional 51 were

excluded after abstract review. Studies were deemed irrelevant if they did not focus on paediatric TBI, did not involve prognostic modelling, used only traditional statistical methods without ML approaches, or were editorials, letters, conference abstracts, or reviews.

Of the 42 full-text articles assessed, 29 were excluded: 15 focused on adult populations, 10 lacked sufficient data on ML methodologies relevant to pTBI prognostication, 3 were review articles, and 1 did not focus on TBI. Ultimately, 13 studies met the inclusion criteria and were included in the final review.[16–28] **Figure 1** illustrates the study selection process, and **Appendix 2** lists the 29 excluded full-text studies with specific reasons for exclusion.

Quality Assessment

Quality assessment using the QUIPS (Quality in Prognosis Studies) tool found the risk of bias to be generally low in domains of study participation, attrition, prognostic factor measurement, outcome measurement, and statistical analysis. However, all studies were rated as moderate risk in the domain of confounding, reflecting limited adjustment for potential confounders such as comorbidities or treatment variability. Three studies[22,24,26] were also rated as moderate risk for study participation due to small sample sizes and potential selection bias. None of the studies reported using the STARD checklist for diagnostic accuracy reporting. The full quality assessment is summarized in **Table 1**.

Study Design, Geographic Distribution, Study Site, Patient Demographics & Sample Size

Most studies were retrospective cohorts, with one prospective case-control study,[22] one retrospective case-control study,[16] and two secondary analyses of existing prospective cohort datasets,[17,28] Five studies originated in the USA,[17,19,20,22,24] two in Thailand,[23,25] and one each in Singapore,[16] the Netherlands,[21] the UK,[18] South Korea,[26] and Canada.[27] Two studies were conducted in emergency department settings[16,17] and two in paediatric intensive care unit (PICU) settings,[18,27] while most were based at university-affiliated hospitals. All studies focused on paediatric patients younger than 18 years, with male predominance observed across cohorts. Detailed study characteristics are presented in **Table 2**.

Sample sizes ranged from 24 participants in Raji et al.[22] to 12 902 in Hale et al.[20] Most studies focused on acute prognostication of outcomes such as mortality, functional disability, or clinically relevant TBI, whereas one study[24] examined post-discharge morbidity

phenotypes. Methodological details such as preprocessing, optimization strategies, hyperparameter tuning, and the number of participants with the outcome of interest were inconsistently reported and are noted in **Table 2** where available.

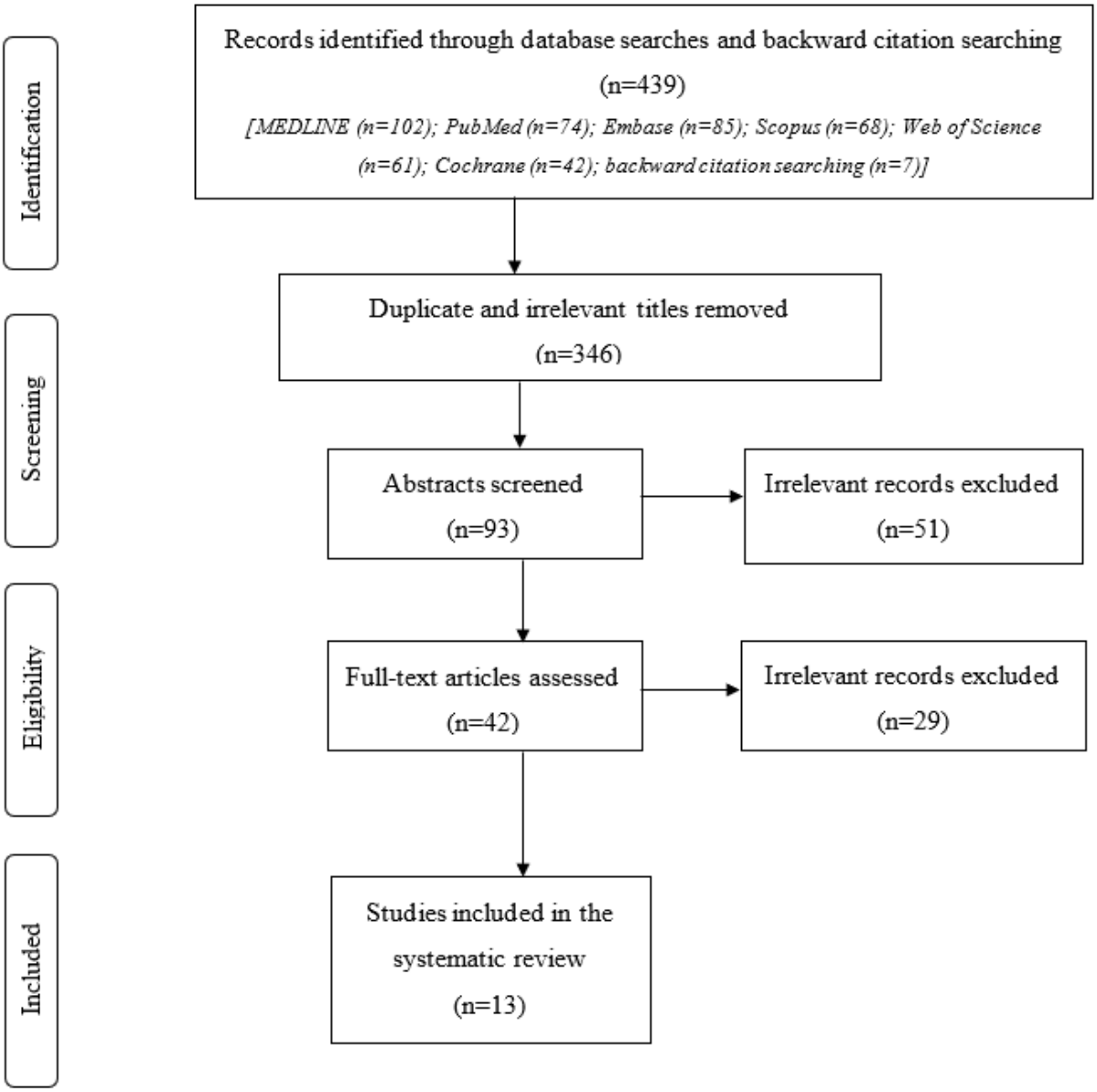

Figure 1. PRISMA flow diagram of study selection process

Table 2: Summary of studies included in the systematic review

Author / Year / Study Design	Geographic Distribution and Study Site	Study Aim	Population (Age, Sex, TBI Factors)	Sample Size & Reference Standard	Data Categories in ML Model	Predictors (Candidate / Final)	Internal Validation & Test Size	ML Methods & Implementation / Software Platform	Models Developed	Performance Metrics (Sens., Spec., AUROC)	Key Findings / Conclusions	Code Availability & Model Interpretability
Chong et al. [16] / 2015 / Retrospective case-control	Singapore; KK Women's and Children's Hospital, single-centre ED	To identify predictors of moderate-to-severe TBI in children <16 presenting to ED and compare ML vs logistic regression	<16 years; 70% male; moderate-to-severe TBI defined as GCS ≤13 or deterioration + abnormal CT	39 cases / 156 controls; reference: CT scan	Demographics, mechanism of injury, clinical (symptoms, physical findings)	Candidate: ≥11; Final (LR): 4; Final (ML): 7	Not explicitly reported; entire dataset used	Ensemble of 100 feed-forward neural networks (extreme learning machine); MATLAB v2009a	2 (Logistic regression and ML model)	ML: Sens 94.9%, Spec 97.4%, AUROC 0.98; LR: Sens 82.1%, Spec 92.3%, AUROC 0.93	ML outperformed LR and may guide CT use and monitoring decisions	Code not shared; interpretability: low (black box)
Yadav et al. [17] / 2016 / Retrospective secondary analysis	USA; PECARN multicentre database, 25 EDs	To validate automated outcome classification of paediatric head CT reports using hybrid NLP and ML	<18 years; Sex NR; CT findings per PECARN definitions; TBI severity per PECARN criteria	2121 CT reports; manual coding by trained abstractors as reference	Text features from CT reports: findings, modifiers, UMLS codes	Structured MedLEE output → word vectors; number of final predictors NR	50/50 random train-test split; test set 1061	Hybrid NLP (MedLEE) + Decision tree (CART); WEKA, Salford Predictive Miner	1	Sens 89.7%, Spec 91.9%, AUROC NR	NLP+ML reliably identified negative CT reports; manual review needed for positives	Code not shared; interpretability: high (decision tree transparent)
Hale et al. [19] / 2018 / Retrospective cohort	USA; Monroe Carell Jr. Children's Hospital, Vanderbilt Univ.	To assess CT-based classification systems and develop ANN to predict 6-month outcomes	<18 years; Sex NR; GCS documented or estimated; exclusion: no CT within 24h, fatal on arrival	565; reference: GOS at 6 months	Clinical (GCS, pupils) and laboratory (glucose, haemoglobin) and CT findings	Candidate: 9; Final: same 9	70/15/15 train/validation/test split; test set 84	ANN: 2-layer feed-forward; MATLAB R2016b	≥100	Sens/Spec NR; AUROC 0.946 ±0.042	ANN outperformed CT scores for predicting 6-month outcomes	Code not shared; interpretability: low (black box)
Hale et al. [20] / 2018 / Retrospective cohort	USA; PECARN multicentre database	To develop an ANN model to predict clinically relevant TBI (CRTBI) in children	<18 years; mean age ~8; 63% male; CRTBI (neurosurgery, intubation >24h, hospitalization ≥48h + CT findings, or death)	12902; reference: CRTBI definition	Clinical (mechanism, LOC, GCS) and radiologist-interpreted CT variables	Candidate: 23; Final: same 23	Random 70/15/15 train/validation/test split; test set ~1,935	ANN with 2 hidden layers; MATLAB R2016b	1	Sens 99.7%, Spec 60%, AUROC 0.99, Accuracy 98%, NPV 91%	ANN model demonstrated excellent discrimination and predictive utility for CRTBI in paediatric TBI	Code not shared; interpretability: low (black box)
Greenen et al. [21] / 2019 / Retrospective cohort	Netherlands; two institutional TBI registries	To develop and validate ML-based prognostic models in paediatric ultra-severe TBI	<18 years; 65% male; ultra-severe TBI (GCS 3–4)	112; reference: GOS at 6 months	Clinical and imaging variables (CT findings)	Candidate: 15; Final: 5 (age, pupil reactivity, cisterns, midline shift, glucose)	Internal 10-fold cross-validation and external	Recursive partitioning decision tree; Rpart, R software	2 (previous model validated + new model developed)	New model: Sens 93%, Spec 76%, AUROC 0.81, Accuracy 79%	Decision tree model with 5 predictors showed good discrimination: useful for risk	Code not shared; interpretability: high (decision tree transparent)

Author / Year / Study Design	Geographic Distribution and Study Site	Study Aim	Population (Age, Sex, TBI Factors)	Sample Size & Reference Standard	Data Categories in ML Model	Predictors (Candidate / Final)	Internal Validation & Test Size	ML Methods & Implementation / Software Platform	Models Developed	Performance Metrics (Sens., Spec., AUROC)	Key Findings / Conclusions	Code Availability & Model Interpretability
							validation; test set 45				stratification in ultra-severe paediatric TBI	
Kayhanian et al. [18] / 2019 / Retrospective cohort	UK; Cambridge University Hospital PICU	To develop ML-based models using admission serum laboratory parameters to predict 6-month outcomes in severe paediatric TBI	≤16 years; 68% male; severe TBI (GCS ≤8) and Marshall scores	94; reference: GOS at 6 months	Laboratory (14 serum admission parameters)	Candidate: 14; Final: 3	5-fold cross-validation; no separate test set	LR & SVM (RBF kernel); Python (Scikit-learn and minepy) & R software	4	SVM (3 vars): Sens 80%, Spec 99%, AUROC NR; LR (all vars): AUROC 0.90	Lactate, H+, glucose highly predictive; SVM achieved best performance	Code not shared; interpretability: moderate (LR transparent, SVM less so)
Raji et al. [22] / 2020 / Prospective case-control	USA; UCSF & Washington Univ., TRAIN-TBI cohort	To determine if EDI can separate mild TBI from controls	Adolescents 10–16 years; 64% male; mild TBI (GCS 14–15) >1-month post-injury, persistent symptoms	14 mild TBI / 10 controls; reference: clinical diagnosis & neurocognitive tests	Diffusion MRI (EDI), neurocognitive scores, FA	Candidate: mean EDI in 48 tracts; Final: 3 tracts	Leave-one-out cross-validation; test size: 1 per iteration	PCA + SVM (linear kernel); MATLAB 2016b	1	Sens 79%, Spec 100%, AUROC 0.94	EDI+SVM outperformed neurocognitive and FA-based assessments	Code not shared; interpretability: moderate (SVM-PCA partially interpretable)
Tunthanathip & Oearsakul [23] / 2021 / Retrospective cohort	Thailand; Prince of Songkla Univ.	To assess ML algorithms for functional outcomes in paediatric TBI	<15 years; median age 72 months; 68% male; GCS, hypotension, pupillary reflex, SAH	828; reference: KOSCHI at discharge	Clinical (GCS, hypotension, pupils, SAH)	Candidate: several; Final: 4	10-fold cross-validation; test set 288	SVM, NN, LR, NB, KNN, RF; Python 3.7.7	6	Best: SVM Sens 0.95, Spec 0.60, AUROC 0.78	ML models, esp. SVM, showed high sensitivity; potential as screening tools	Code not shared; interpretability: moderate-low (SVM/NN black box)
Maddux et al. [24] / 2021 / Retrospective cohort	USA; single-centre trauma registry + insurance claims	To identify post-discharge morbidity phenotypes and predictors in paediatric TBI using ML	<18 years; 58% male; varied severity	289; reference: post-discharge healthcare utilization and morbidity	Clinical, hospitalization, and insurance claims data	Candidate: >30; Final: 7 predictors (hospital length of stay, ICU stay, mechanical ventilation, discharge disposition, etc.)	Internal cross-validation; no separate test set	Unsupervised k-medoids clustering to identify 4 phenotypes; LASSO multinomial logistic regression to predict phenotype membership; R software	1	AUROC for phenotype prediction: 0.70–0.85 across phenotypes	ML identified 4 distinct morbidity phenotypes with differential risks; predictive model showed moderate discrimination; potential for targeted interventions	Code not shared; interpretability: moderate (LASSO regression, cluster profiles transparent)

Author / Year / Study Design	Geographic Distribution and Study Site	Study Aim	Population (Age, Sex, TBI Factors)	Sample Size & Reference Standard	Data Categories in ML Model	Predictors (Candidate / Final)	Internal Validation & Test Size	ML Methods & Implementation / Software Platform	Models Developed	Performance Metrics (Sens., Spec., AUROC)	Key Findings / Conclusions	Code Availability & Model Interpretability
Tunthanathip et al. [25] / 2021 / Retrospective cohort	Thailand; Prince of Songkla Univ.	To compare ML vs. nomogram for predicting intracranial injury	<15 years; mean age 75 months; 63% male; GCS, LOC, mechanism of injury, pupillary reflex	964; reference: CT findings	Clinical (GCS, hypotension, LOC, pupils, mechanism)	Candidate: 14; Final: 14	10-fold cross-validation; test size NR	SVM, LR, NB, KNN, DT, RFC, GBC, ANN; Python 3.8.7	8	Best: RFC Sens 0.34, Spec 0.95, AUROC 0.80	RFC had highest discrimination; ML may reduce CT use	Code not shared; interpretability: moderate-low (tree-based partly interpretable)
Kim et al. [26] / 2021 / Retrospective pilot study	South Korea; Seoul Nat'l Univ. Hosp. trauma centre	To enhance CT prognostic value using densitometry and CatBoost ML	≤19 years; median age 6; 55% male; GCS ≤12, intracranial haemorrhage, extracranial injuries	58; reference: GOS, mortality, LOS, surgery	CT densitometry, clinical (GCS, pupils, extracranial injury, CT findings)	Candidate: 13; Final: morphological & densitometry	Leave-one-out cross-validation; test size: 1 per iteration	CatBoost with PCA; Python 3.7	3	Densitometry+ CatBoost: AUROC 0.83–0.91	Densitometry +CatBoost outperformed CRASH-CT alone	Code not shared; interpretability: moderate (tree-based, feature importance available)
Daley et al. [27] / 2022 / Retrospective cohort	Canada; Western Univ. Hosp. PICU	To develop and validate a reduced ML model for 30-day mortality prediction in paediatric severe TBI	<18 years; 61% male; severe TBI (GCS ≤8)	196; reference: in-hospital mortality at 30 days	Clinical, imaging, and biochemical admission variables	Candidate: >20; Final: 6 (PTT, motor GCS, glucose, fixed pupils, platelets, creatinine)	Train/test split with cross-validation; test set 59	Random Forest with Boruta feature selection, t-SNE visualization; SPSS; R software	1	AUROC 0.90, Accuracy 82%	Reduced 6-variable Random Forest model showed excellent discrimination; potential for bedside mortality risk prediction	Code not shared; interpretability: moderate (feature importance available)
Fonseca et al. [28] / 2022 / Retrospective exploratory study	USA; HPTBI dataset	To compare ML models & feature selection for mortality prediction	≤14 years; mean age 7.2 years; 64% male; GCS and intracranial injury status	300; reference: in-hospital mortality	Demographics, clinical, CT findings	Candidate: 96; Final: varies	5-fold cross-validation; held-out test set ~60	RF, XGBoost, ANN, KNN; Python (Scikit-learn), SMOTE	16 (4×4)	Best: XGBoost AUROC 0.91; KNN AUROC 0.90	XGBoost & KNN performed well; feature importance clinically meaningful	Code not shared; interpretability: moderate (feature importance reported)

Abbreviations: NR – not reported; ED – emergency department; ML – machine learning; LR – logistic regression; GCS – Glasgow Coma Scale; LOC – loss of consciousness; CT – computed tomography; AUROC – area under receiver operating characteristic curve; ANN – artificial neural network; CART – classification and regression tree; NLP – natural language processing; UMLS d– Unified Medical Language System; SDH – subdural hematoma; ICH – intracerebral haemorrhage; IVH – intraventricular haemorrhage; GOS – Glasgow Outcome Scale; KOSCHI – King's Outcome Scale for Childhood Head Injury; FA – fractional anisotropy; EDI – edge density imaging; RFC – random forest classifier; GBC – gradient boosting classifier; SMOTE – synthetic minority oversampling technique; LOS – length of stay; PICU – paediatric intensive care unit; HPTBI – Hackathon Paediatric TBI.

Study Aim

The included studies applied ML methods to predict clinically relevant outcomes in pTBI, with variation in design, data sources, outcomes, ML approaches, and validation techniques. Primary aims included prediction of outcomes at hospital discharge, six months, or post-discharge, and comparisons of ML models with traditional regression methods or CT-based classification systems. Maddux et al.[24] uniquely applied unsupervised ML to identify distinct post-discharge morbidity phenotypes.

Data Inputs

All studies used multimodal data to develop ML prognostic models: Ten incorporated clinical data,[16,19–21,23–28] seven used radiological imaging data[17,19–22,26,28] three included laboratory findings,[18,19,27] and one incorporated neurocognitive assessments.[22] Maddux et al.[24] uniquely utilized insurance claims data.

ML Methods & Performance

A diverse array of ML methods was applied, including artificial neural networks (ANN), support vector machines (SVM), random forests (RF), decision trees, gradient boosting, CatBoost, k-nearest neighbors, and unsupervised clustering. ANN-based models in large datasets[19,20] achieved the highest discrimination (AUROC ~0.95–0.99). SVM models demonstrated good sensitivity in smaller datasets,[18,23] and tree-based methods such as Random Forest and decision trees[21,27,28] offered interpretable models with AUROC values around 0.81–0.91.

ML-Specific Methodological Details

Reporting of ML-specific methodological details was limited and inconsistent across the included studies. Only Kim et al.[26] explicitly described a preprocessing step, standardizing CT densitometry values prior to model training. Fonseca et al.[28] and Kim et al.[26] were the only studies to mention optimization algorithms or hyperparameter tuning, with Fonseca et al.[28] reporting grid search for XGBoost and k-nearest neighbors, and Kim et al.[26] using CatBoost's built-in gradient boosting optimization. Daley et al. [27] reported a form of predictor selection by reducing the model to six variables to improve interpretability and usability. None of the studies provided detailed descriptions of data cleaning procedures or penalization techniques, such as LASSO or ridge regression. These omissions highlight a significant gap in the transparency and reproducibility of ML methods applied in pTBI prognostication.

Internal Validation & Test Size

All studies conducted internal validation, using train-test splits, k-fold cross-validation, or leave-one-out validation. Reported test set sizes ranged from 45 to nearly 2,000 participants. External validation was performed only by Greenen et al.[21]

Specific Findings

Across studies, ML models generally outperformed traditional statistical approaches in prognosticating pTBI outcomes. Chong et al.[16] developed an ANN model using clinical data, achieving an AUROC of 0.98, outperforming logistic regression (AUROC 0.93). Yadav et al.[17] combined natural language processing with a decision tree to classify CT scan reports, reporting sensitivity of 89.7% and specificity of 92%.

Hale et al.[19,20] demonstrated that ANN models significantly outperformed conventional CT-based classification systems, with AUROC values approaching 0.95–0.99. Greenen et al.[21] developed and externally validated a decision tree model for ultra-severe pTBI, achieving an AUROC of 0.81. Kayhanian et al.[18] used an SVM based on laboratory parameters, achieving sensitivity of 80% and specificity of 99%, while highlighting challenges of class imbalance. Raji et al.[22] applied SVM with edge density imaging, achieving an AUROC of 0.94.

Tunthanathip et al.[23,25] tested multiple ML algorithms: in one study, SVM achieved an AUROC of 0.78 with high sensitivity (95%), and in another, a RF model achieved an AUROC of 0.80 but low sensitivity due to class imbalance. Maddux et al.[24] identified four post-discharge morbidity phenotypes with unsupervised ML and developed models with AUROC values ranging from 0.70–0.85. Kim et al.[26] showed that augmenting CT-based models with densitometry and CatBoost improved AUROC to 0.88.

More recent studies highlighted the promise of simplified yet effective models. Daley et al.[27] demonstrated that a reduced six-variable RF model retained strong performance (AUROC 0.90) while improving usability. Fonseca et al.[28] reported that XGBoost yielded the highest AUROC (0.91) for mortality prediction, closely followed by k-nearest neighbors.

DISCUSSION

This systematic review included 13 studies, reflecting the relatively limited but growing body of research on ML models for pTBI prognostication. Overall, the findings demonstrate the potential of ML models to enhance prognostication by leveraging multimodal data. However, their performance and clinical applicability remain influenced by factors such as class imbalance, data heterogeneity, algorithm choice, and inconsistent reporting practices.

The included studies applied a variety of ML algorithms, including SVMs, ANNs, Random Forests, decision trees, and gradient boosting methods. Many models outperformed traditional approaches, showing higher sensitivity, specificity, and AUROC values. For example, Hale et al. reported an AUROC of 0.95 for their ANN model, exceeding conventional CT-based classification systems,[19] while Kayhanian et al. achieved an AUROC of 0.89 with an SVM model, demonstrating sensitivity and specificity of 80% and 99%, respectively.[18] SVM and Random Forest models in particular showed promising predictive performance (AUROC ~0.78–0.91) across several studies, suggesting they warrant further exploration. However, these findings remain preliminary and should be interpreted cautiously given methodological heterogeneity.

Although several studies demonstrated improved predictive performance of ML models compared to traditional tools, such as those by Chong et al.[16] and Hale et al.,[19] others –- like Tunthanathip et al.[24] and Gravesteijn et al.[12] –- reported only modest or no significant improvements. Importantly, most studies did not formally test the statistical significance or clinical impact of these differences, leaving it unclear whether the incremental gains justify the added complexity and resource requirements of ML implementation.

Class imbalance—where favourable outcomes predominate—is a common limitation in pTBI datasets, skewing performance metrics. For example, Tunthanathip and Oearsakul reported that 97% of their cohort achieved favourable outcomes, making it challenging for models to accurately identify the smaller subset with poor outcomes.[23] High specificity in models such as those by Kayhanian et al.[18] and Tunthanathip et al.[24] came at the cost of reduced sensitivity, increasing the risk of missed unfavourable cases. Strategies such as optimizing thresholds, incorporating additional markers, and improving data quality are needed to mitigate these biases.

The overrepresentation of favourable outcomes in pTBI datasets further complicates the development of effective ML models. For instance, Tunthanathip and Oearsakul reported that 97% of patients achieved favourable outcomes at discharge, with 95.4% maintaining these outcomes at six months.[23] While encouraging, this makes it difficult to accurately identify the smaller subset of patients with unfavourable outcomes, even though these cases represent a substantial number of individuals at risk of severe consequences. Incorporating clinical and radiological markers—such as midline shift >5 mm, subarachnoid haemorrhage (SAH), low GCS scores, hypotension, and abnormal pupillary reflexes—can improve predictive accuracy.[19,24] Furthermore, future research should prioritize the use of metrics such as PPV, NPV, and AUROC to account for class imbalance and provide a more comprehensive evaluation of model performance.

Another significant challenge is the variability in AUROC values across studies and the potential heterogeneity in study designs, which underline the need for standardization. Multicentre studies with standardized protocols for data collection, feature selection, and model training are necessary to improve the reliability and generalizability of ML-based

pTBI prognostication. As the field progresses, such efforts will strengthen the foundation for effective ML models in pTBI, potentially improving patient outcomes through enhanced predictive accuracy and clinical usability.

The heterogeneity of study designs, outcome definitions, data modalities, and performance metrics also precluded a formal comparison of ML techniques in this review. Standardized reporting frameworks and benchmarking would facilitate future comparative analyses and help identify optimal approaches for specific clinical contexts. Similarly, multicentre studies with standardized data collection, feature selection, and training protocols are needed to improve generalizability.

Notably, none of the included studies adhered to the STARD (Standards for Reporting Diagnostic Accuracy Studies) checklist, which – though originally designed for diagnostic test accuracy – offers principles applicable to ML prognostic models, promoting transparency and enabling critical appraisal. Future work should consider STARD or similar guidelines to improve reporting quality.

As highlighted in the Results, reporting of ML-specific methodological details was inconsistent across the included studies. While most studies specified the ML algorithms and software platforms used, only two explicitly described hyperparameter tuning,[26,27] and none provided detailed information on data cleaning procedures, penalization techniques, or full implementation pipelines. Additionally, none shared executable code or comprehensive workflows, limiting transparency and hindering reproducibility. This lack of standardized reporting makes it difficult to assess model generalizability and to replicate findings in independent settings. Transparent documentation of software environments, feature

engineering, model optimization, and open sharing of code and data are essential for advancing ML-based prognostic tools toward clinical adoption. Future studies should prioritize open science practices and adhere to reporting guidelines that promote reproducibility and comparability across studies.

Interpretability remains a barrier to clinical adoption of complex models such as ANNs and SVMs, whose "black-box" nature limits clinician confidence.[29] Simpler models like decision trees, as used by Yadav et al.,[17] provide greater transparency and may be more acceptable in clinical settings despite potentially lower performance. Balancing accuracy with interpretability is therefore key to implementation.

The unique challenges of paediatric populations – including developmental variability, pre-existing neurodevelopmental conditions, and ethical concerns about data collection – further limit large, diverse datasets and complicate model development. Collaborative research across paediatric sub-specialties is needed to address these gaps.

Finally, overfitting remains a concern, as models may perform well on training data but poorly in new settings. Cross-validation and external validation, such as demonstrated by Greenen et al.,[21] are critical to ensuring generalizability and preventing overfitting.

These findings should also be interpreted in the context of a prior systematic review of ML applications in paediatric TBI. Notably, Lampros et al. (2024)[30] conducted a systematic review of ML models in paediatric TBI with a broader scope that encompassed both diagnostic and prognostic applications. In contrast, our review specifically focused on ML models developed for prognostication and uniquely emphasized models integrating

multimodal data inputs. Moreover, our analysis critically examined gaps in methodological transparency, reporting of ML-specific techniques, and reproducibility — areas not explicitly addressed in the earlier review. These distinctions underscore the complementary nature of our work, which adds depth to the understanding of how multimodal ML approaches can enhance prognostic accuracy in paediatric TBI, while highlighting the ongoing need for methodological rigor and standardization in this evolving field.

In summary, while ML models show considerable promise in enhancing pTBI prognostication, substantial challenges remain. Addressing issues of class imbalance, standardization, interpretability, reproducibility, and robust validation will be essential to developing accurate and clinically useful tools that improve outcomes for children with TBI.

CONCLUSION

This systematic review highlights the potential of ML models to improve outcome prediction in pTBI, particularly those that integrate multimodal data. While ML approaches frequently demonstrated higher sensitivity, specificity, and AUROC compared to traditional methods, these findings should be interpreted with caution due to heterogeneity in study designs, data inputs, and performance metrics across studies. Future standardized, multicentre research is needed to define the comparative advantages of specific ML techniques, improve model interpretability and reproducibility, and address challenges such as class imbalance and limited dataset diversity. Collaborative efforts will be essential to develop reliable, generalizable, and clinically applicable prognostic models for pTBI.

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APPENDICES

Appendix 1. Full search strategy for MEDLINE (via PubMed) — conducted October 2024

Database: MEDLINE (via PubMed) Date of search: October 2024 Limits applied: Humans, English language, publication date from 2014/01/01 to 2024/10/05

Search string:

("pediatric traumatic brain injury"[Title/Abstract] OR "pediatric traumatic brain injury"[Title/Abstract] OR "pediatric TBI"[Title/Abstract] OR "pediatric TBI"[Title/Abstract]) AND ("machine learning"[Title/Abstract] OR "ML"[Title/Abstract] OR "artificial intelligence"[Title/Abstract] OR "deep learning"[Title/Abstract] OR "neural network"[Title/Abstract] OR "support vector machine"[Title/Abstract] OR "random forest"[Title/Abstract] OR "decision tree"[Title/Abstract] OR "gradient boosting"[Title/Abstract] OR "CatBoost"[Title/Abstract] OR "XGBoost"[Title/Abstract]) AND ("prognosis"[Title/Abstract] OR "prediction"[Title/Abstract] OR "outcome"[Title/Abstract] OR "mortality"[Title/Abstract] OR "functional recovery"[Title/Abstract])

Filters:

- Humans
- English language
- Publication date: 2005–2024

Appendix 2: Table of studies excluded after full-text review with reasons for exclusion (n=29)

Study (Author, Year)	Title	Reason for Exclusion
Garcia et al., 2009	Outcome prediction in pediatric TBI using clinical scales	Did not utilize machine learning methods
Allen et al., 2010	Pediatric TBI: a review of prognostic factors	Review article without original data
Kim et al., 2011	Machine learning models for adult TBI prognosis	Study focused on adult population
Hernandez et al., 2012	Biomarkers and outcome prediction in pediatric TBI	Did not utilize machine learning methods
Patel et al., 2014	Predictive analytics in pediatric TBI: current trends	Did not utilize machine learning methods
Nguyen et al., 2015	Machine learning in adult TBI outcome prediction: a meta-analysis	Study focused on adult population
Lewis et al., 2016	Long-term outcomes in pediatric TBI: a retrospective analysis	Did not utilize machine learning methods
Brown et al., 2017	The value of the injury severity score in pediatric trauma: time for a new definition of severe injury?	Did not focus on traumatic brain injury
Clark et al., 2017	Pediatric TBI outcomes: a multicenter cohort study	Did not utilize machine learning methods
Boutin et al., 2018	Hemoglobin thresholds and red blood cell transfusion in adult patients with moderate or severe traumatic brain injuries: a retrospective cohort study	Study focused on adult population
Martinez et al., 2018	Neuroimaging predictors of outcome in pediatric traumatic brain injury	Did not utilize machine learning methods
Smith et al., 2019	Predictive modeling in pediatric TBI: a review	Review article without original data
Hifumi et al., 2020	High early phase hemoglobin level is associated with favorable neurological outcome in patients with severe traumatic brain injury	Study focused on adult population
Kaplan et al., 2020	Mixture model framework for TBI prognosis using heterogeneous clinical and outcome data	Study focused on adult population
Lee et al., 2020	Clinical role of low hemoglobin ratio in poor neurologic outcomes in infants with traumatic intracranial hemorrhage	Did not utilize machine learning methods
Thompson et al., 2020	Prognostic models in pediatric TBI: a systematic review	Review article without original data
Johnson et al., 2021	Machine learning approaches for outcome prediction in adult TBI patients	Study focused on adult population
Bai et al., 2023	The prognostic value of an age-adjusted BIG score in adult patients with traumatic brain injury	Study focused on adult population
Bertotti et al., 2023	Hospital mortality in severe traumatic brain injury: Brazilian analysis	Study focused on adult population
Song et al., 2023	Prediction of mortality among patients with isolated traumatic brain injury using machine learning models in Asian countries	Study focused on adult population

Study (Author, Year)	Title	Reason for Exclusion
Trent et al., 2023	Pupillary light reflex measured with quantitative pupillometry for predicting neuroworsening after traumatic brain injury	Study focused on adult population
Yu et al., 2023	Imaging findings for outcomes in adult TBI: meta-analysis	Study focused on adult population
Lu et al., 2024	An externally validated prognostic model for critically ill patients with traumatic brain injury	Study focused on adult population
Orlando et al., 2024	Neurosurgical intervention rule-out tool for mild TBI	Did not utilize machine learning methods
Ran et al., 2024	Evaluation of the Glasgow coma scale-pupils score for predicting inpatient mortality among patients with traumatic subdural hematoma at United States trauma centers	Did not utilize machine learning methods
Dengler et al., 2025	Quantitative pupillometry tracks mild traumatic brain injury in military cadets	Study focused on adult population
King et al., 2005	Early Glasgow outcome scale scores predict long-term functional outcome in patients with severe traumatic brain injury	Did not utilize machine learning methods
Si et al., 2025	Machine learning-based prediction of mortality in geriatric TBI patients	Study focused on adult population
Vreeburg et al., 2025	Validation of the GCS-pupil scale in traumatic brain injury	Study focused on adult population

RESEARCH STUDY PROTOCOL

Personalized Prognostication in Paediatric TBI: A Systematic Review of Machine Learning Approaches with Multimodal Data

Research protocol in partial fulfilment for the degree of Master of Science (Medicine) in Emergency Medicine

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INTRODUCTION

Pediatric Traumatic Brain Injury (pTBI) presents a significant public health challenge and is a major contributor to disabilities and mortality among children.[1] Accurately gauging the global incidence of pTBI is challenging due to differences in reporting practices across countries; however, studies indicate that children experience TBI at significantly higher rates than adults, with annual estimates ranging from 47 to 280 cases per 100,000 children[2]

Despite extensive research, outcomes of pTBI remain highly variable even among patients with similar injury patterns. This variability can lead to significant disparities in long-term cognitive and physical outcomes.[3]. Furthermore, this inconsistency challenges the effectiveness of standardized approaches in managing pTBI.[4,5]

Significant advances in pTBI care notwithstanding, precise prognostication continues to be elusive. Thus, there is an urgent need for personalized prognostic and treatment approaches tailored to the specific presentations of pTBI.

Traditional diagnostic and prognostic tools, such as the Glasgow Coma Scale (GCS) and Pediatric Index of Mortality (PIM), while useful in initial acute assessments, do not provide personalized recovery profiles or accurate mortality predictions. The GCS, for instance, does not account for the mechanism of injury nor is it sensitive enough to detect subtle neurological changes and cognitive complications like post-TBI amnesia associated with pTBI.[6] Moreover, these traditional methods fail to consider age-related variabilities in children or pre-existing conditions like neurodevelopmental disabilities that may impact outcomes.[7]

Current scoring tools are also limited in addressing the complexities of pTBI across varying degrees of severity. Leveraging multimodal data including genetic testing, neuroimaging (e.g., CT and MRI), and biomarker analysis (e.g., inflammatory and genetic markers) could enhance personalized prognosis and medical care.[8]

Extensive use of multimodal data can help train machine learning (ML) models for more accurate prognostication. A comprehensive analysis of clinical presentation alongside multimodal data, interpreted through ML, aids in developing precise prognostic models. This information is crucial for stratifying patients into subgroups based on shared characteristics such as genetic predispositions and neuroimaging features, thus allowing for the development of tailored treatment plans.[9]

The integration of ML in healthcare has significantly advanced personalized medicine for pTBI patients. ML models, such as clustering algorithms and support vector machines (SVMs), are increasingly used to analyse complex patterns and relationships in injury data, facilitating more accurate predictions of long-term outcomes.[10]

Prognostication using ML and multimodal data in pTBI poses unique challenges, particularly in pediatric patients where brain developmental stages may influence injury mechanisms, recovery potential, and long-term outcomes. Factors like behavioural and cognitive development, learning abilities, family structure, and environmental exposure are vital for the effective application of prognostic models in pTBI.[11]

Recent studies illustrate the potential of machine learning (ML) in enhancing outcome prediction in traumatic brain injury (TBI). For instance, a systematic review has demonstrated that ML can predict functional outcomes in TBI with remarkable precision.[12] Another significant study analysed a dataset of 1,028 pediatric patients with various severities of TBI, employing an ML approach for multimodal data analysis. This approach successfully predicted neurological outcomes at six months with an accuracy of 91.5%, a specificity of 90.5%, and a sensitivity of 92.9%, significantly outperforming traditional clinical prediction tools.[13,14] However, despite these advances, no systematic review has yet fully explored the role of multimodal data analysis and ML algorithms in predicting outcomes specifically for pediatric TBI (pTBI) in children aged 0-18 years.

STUDY AIM

To conduct a systematic review of the literature exploring the use of ML and multimodal data for pTBI prognostication.

STUDY OBJECTIVES

1. To provide a comprehensive overview of various ML and multimodal data algorithms used for predicting personalized outcomes in pTBI.
2. To evaluate and describe the accuracy of these ML and multimodal data algorithms in predicting pTBI outcomes.
3. To analyse and detail the benefits and limitations of different ML and multimodal data modalities used in pTBI outcome prediction.

METHODOLOGY

Study design

The study design will be a systematic review that will be carried out in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.[15] The PRISMA framework outlines the essential components that ensure transparency and reproducibility in systematic reviews. The review has been registered with PROSPERO (ID: CRD42024510419). An initial scoping review identified approximately 15 articles pertinent to the topic.

Data sources and search strategy

A search strategy will be developed and performed using an electronic database search. The databases to be searched will include MEDLINE, PubMed, Embase, Scopus, Web of Science, and Cochrane. Only studies published within the past 10 years will be included. The search will utilize the following keywords: "paediatric traumatic brain injury" OR "pTBI" AND "machine learning" OR "ML" AND "prognosis" OR "prediction" OR "outcomes." Additionally, the references of all retrieved studies will be examined for potentially relevant articles. No language restrictions will be applied.

Inclusion criteria

The review will encompass studies involving paediatric patients aged 0 to below 18 years who have experienced TBI. Included studies must have conducted prognostication using ML techniques applied to multimodal data, including clinical data, biomarkers, imaging, or other relevant information..

Exclusion criteria

Studies will be excluded if they do not utilize ML algorithms or multimodal data in the assessment of pTBI, or if they fail to evaluate prognostic outcomes relevant to this study.

Study selection and data extraction

Eligible full-text studies will be systematically searched, retrieved, and assessed for possible inclusion. Two reviewers, ZN and AL, will independently review titles and abstracts to determine the suitability of potential studies. A standardized data extraction form (Appendix A) will be employed to gather and record essential details from each study. This process will involve documenting information such as the authors, publication year, type and region of the study, study objectives, patient age range, sample size, reference standards, the types of data used in the ML models, and the ML algorithms applied. Additionally, the extraction will include performance metrics of the ML algorithms such as sensitivity, specificity, and AUROC, along with the authors' conclusions.

Methodological quality evaluation

The Quality In Prognosis Studies (QUIPS) tool[16] will be employed to evaluate if eligible studies are sufficiently complete for inclusion in the final review. The primary researcher and one of the study supervisors (ZN and AL) will independently rate the studies. In the event of any disagreements, a third supervisor will be consulted to resolve the issue.

DATA ANALYSIS

Data from the studies will be organized and described, with key information summarized in a table under the previously outlined subheadings. Considering the variety and nature of articles expected to be included in this review, performing a meta-analysis is anticipated to not be feasible.

ETHICS

Given that this study will conduct a retrospective review of documents already available in the public domain, we will submit an application for a waiver of ethics clearance to the University of Witwatersrand Human Research Ethics Committee (Medical). This study will not involve active human participation.

TIMING

	2024									
	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec
Literature review	■	■								
Prepare protocol	■	■								
Protocol assessment			■	■						
Ethics application					■	■				
Data collection							■			
Data analysis							■	■		
Research write-up									■	■

COSTS

The researcher will cover all expenses associated with the study, including costs for printing, internet data, and language editing. No additional costs are anticipated beyond these expenditures. The total estimated budget for this study is R2000.

PROBLEMS

This systematic review will depend on existing literature and may face several challenges. First, publication bias is a concern, as studies with positive outcomes are typically more likely to be published than those with negative or inconclusive results, potentially skewing the overall findings. Additionally, differences in study design, sample sizes, and outcome measures across the included studies could limit the generalizability of the results. These variations might also lead to inconsistent results, which could complicate efforts to draw definitive conclusions from the review.

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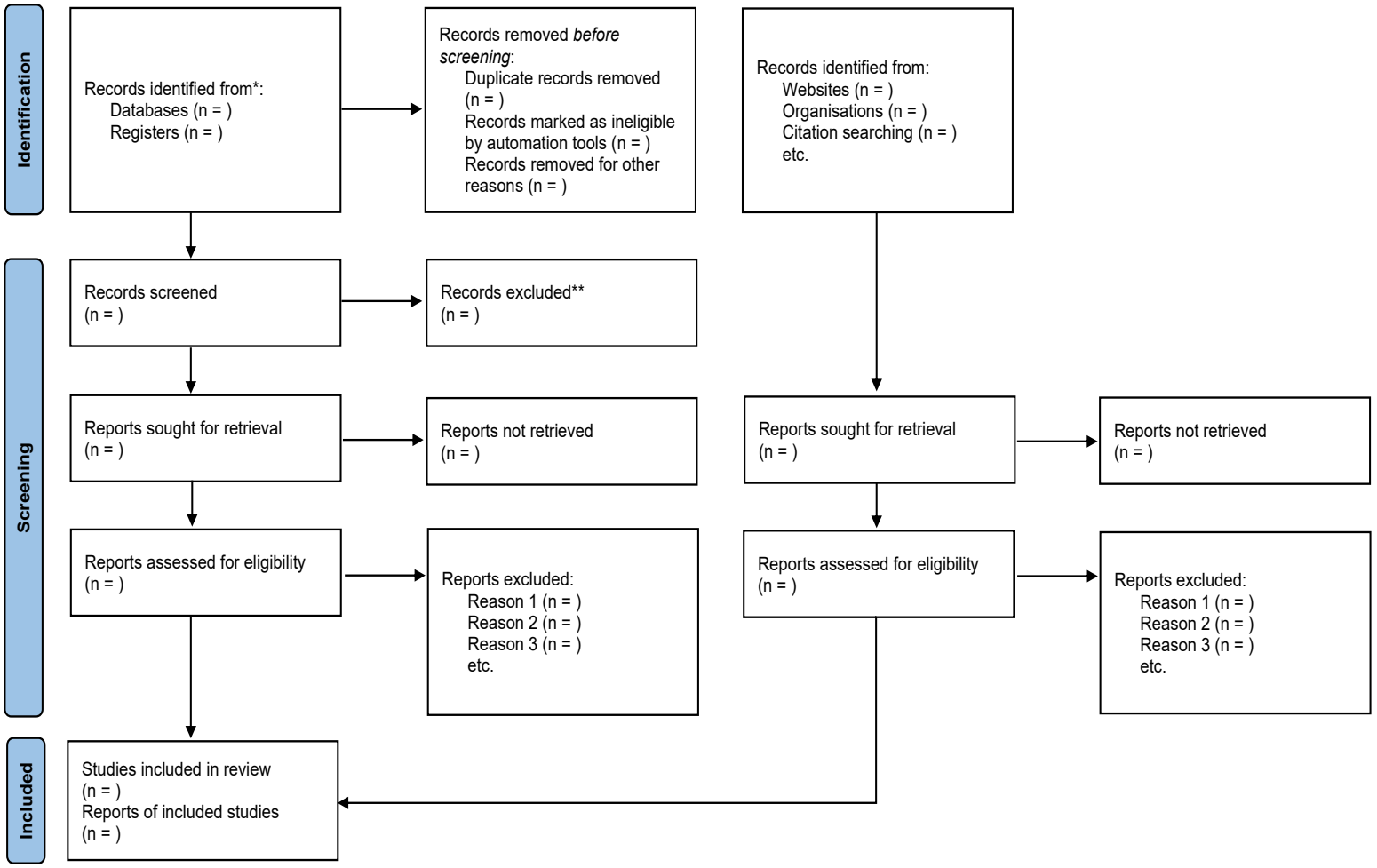
APPENDIX A: Data collection sheet

Author / Year / Study Design	Geographic Distribution and Study Site	Study Aim	Population (Age, Sex, TBI Factors)	Sample Size & Reference Standard	Data Categories in ML Model	Predictors (Candidate / Final)	Internal Validation & Test Size	ML Methods & Implementation	Models Developed	Performance Metrics (Sens., Spec., AUROC)	Key Findings / Conclusions	Code Availability & Model Interpretability

APPENDIX B: PRISMA flow diagram for new systematic reviews



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Waiver: This certifies that the following research does not require clearance from the Human Research Ethics Committee (Medical)

Investigator: Mr Z Nkabinde
Student No. (if appropriate): 789120
Staff No. (if appropriate):

Supervisor: Professor A Laher, et al

School: Clinical Medicine
Department: Medicine
Division: Emergency Medicine
Faculty of Health Sciences

Project title: *Personalized prognostication in paediatric TBI: a systematic review of machine learning approaches with multimodal data*

Degree: MSc (Med)

Reason: Review of information in the public domain
No human participants will be involved in the study

Ms M van Niekerk
Co-Chairperson: Human Research Ethics Committee (Medical)

Research Office Secretariat:
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