SYSTEMATIC REVIEW
Alpha Psychiatry 2024;25(3):290-303
DOI: 10.5152/alphapsychiatry.2024.231443

A Meta-analysis of Predicting Disorders of Consciousness After Traumatic Brain Injury by Machine Learning Models

ABSTRACT

Objective: This study pursued a meta-analysis to evaluate the predictive accuracy of machine learning (ML) models in determining disorders of consciousness (DOC) among patients with traumatic brain injury (TBI).

Methods: A comprehensive literature search was conducted to identify ML applications in the establishment of a predictive model of DOC after TBI as of August 6, 2023. Two independent reviewers assessed publication eligibility based on predefined criteria. The predictive accuracy was measured using areas under the receiver operating characteristic curves (AUCs). Subsequently, a random-effects model was employed to estimate the overall effect size, and statistical heterogeneity was determined based on I^2 statistic. Additionally, funnel plot asymmetry was employed to examine publication bias. Finally, subgroup analyses were performed based on age, ML type, and relevant clinical outcomes.

Results: Final analyses incorporated a total of 46 studies. Both the overall and subgroup analyses exhibited considerable statistical heterogeneity. Machine learning predictions for DOC in TBI yielded an overall pooled AUC of 0.83 (95% CI: 0.82-0.84). Subgroup analysis based on age revealed that the ML model in pediatric patients yielded an overall combined AUC of 0.88 (95% CI: 0.80-0.95); among the model subgroups, logistic regression was the most frequently employed, with an overall pooled AUC of 0.85 (95% CI: 0.83-0.87). In the clinical outcome subgroup analysis, the overall pooled AUC for distinguishing between consciousness recovery and consciousness disorders was 0.84 (95% CI: 0.82-0.85).

Conclusion: The findings of this meta-analysis demonstrated outstanding accuracy of ML models in predicting DOC among patients with brain injuries, which presented substantial research value and potential of ML application in this domain.

Keywords: Brain injury, disorders of consciousness, cognitive neuroscience, machine learning, meta-analysis

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Received: November 23, 2023
Revision Requested: January 2, 2024
Last Revision Received: January 18, 2024
Accepted: February 19, 2024
Publication Date: July 26, 2024

Cite this article as: Zhu X, Gao L, Luo J. A meta-analysis of predicting disorders of consciousness after traumatic brain injury by machine learning models. *Alpha Psychiatry.* 2024;25(3):290-303.

Introduction

Traumatic brain injury (TBI) is a condition characterized by cranial and cerebral damage resulting from blunt force, penetrating injuries, or the influence of acceleration or deceleration forces.[1,2] This condition can lead to a diminished level of consciousness, memory loss, amnesia, and neurological abnormalities, with severe cases potentially resulting in fatality. Traumatic brain injury has raised widespread global concerns and ranked among the prevalent causes of disability and mortality. According to statistics, its global incidence rate stands at 295 per 100 000 individuals.[3] The aftermath of TBI can produce profound repercussions on patients' lives, with notable cognitive and motor function impairment. These sequelae represent some of the most frequent consequences, exerting a serious adverse impact on the affected individuals' overall quality of life.[4]

After severe TBI, a significant proportion of patients may not achieve full recovery and may experience coma followed by long-term disorders of consciousness (DOC), characterized by recovery of consciousness, limited awareness of oneself or the environment. Several studies have shown that a considerable number of patients with DOC will achieve the recovery of consciousness and functional independence in the initial year following TBI.[5,6] These patients exhibit substantial heterogeneity in various aspects, including age, comorbidity, cognitive function, injury mechanisms, and underlying pathology. The heterogeneity of this condition and differences in social environments and medical interventions contribute to substantial disparities in the prognostic outcomes among TBI patients. Consequently, accurately predicting the recovery of consciousness in TBI patients becomes challenging, with some individuals experiencing rapid improvement within a few weeks, while others may not recover consciousness at all. Accurately assessing the rehabilitation potential and predicting possible clinical outcomes of DOC patients is crucial as they enables healthcare professionals to identify rehabilitation needs and tailor personalized rehabilitation plans. While there exist standard clinical evaluation scales and neurophysiological methods for diagnosing and predicting clinical outcomes in these patients, these are also challenging tasks for clinical doctors.[7] Currently, an increasing number of researchers are dedicated to exploring methods aimed at enhancing the prognosis and quality of life assessment for TBI patients. These approaches encompass comprehensive evaluation models integrating clinical characteristics, medical imaging presentations, and biological markers. These models aim to provide a more precise assessment of TBI severity and anticipated outcomes of patients, allowing for early interventions targeting pathophysiological changes. Despite the development and validation of numerous prediction models for post-TBI functional outcomes, systematic reviews conducted between 2006 and 2008 revealed suboptimal methodological quality in these models.[8,9]

With the advent of big data era, the acquisition and storage of vast datasets have become relatively effortless, leading to heightened demands on the logic, efficiency, and depth of data processing. Machine learning (ML) technique is a pivotal player in the development of intricate clinical prediction models, not only contributing to enhanced model reproducibility but also driving the broader adoption of ML within the clinical medical domain.[10] ML methodologies exhibit proficiency in handling multidimensional variables and discerning nonlinear relationships between clinical pathological features and outcomes. The application of such methodologies has led to the emergence of research efforts across domains such as oncology and cardiovascular diseases, aiming at constructing more accurate prognostic models, offering dependable underpinnings for clinical disease prevention and treatment decision-making.[11]

MAIN POINTS

- *Significant heterogeneity was observed in the meta-analysis of prognostic models for traumatic brain injury (TBI) patients.*
- *The overall pooled area under the receiver operating characteristic curve (AUC) of machine learning (ML) models for DOC prediction in patients with TBI was high.*
- *The comprehensive AUC for distinguishing consciousness recovery vs. consciousness disorders was high.*
- *Among various models, lightGBM demonstrated the highest overall combined AUC, while the logistic regression (LR) model was the most extensively employed model.*

Innovative ML methodologies have recently emerged, yielding high precision when applied to medical datasets associated with TBIs.[12] While numerous investigations have addressed the prognosis of TBI patients by using ML models, some researchers have also conducted comprehensive systematic assessments and meta-analyses to evaluate the prognostic capacity of ML in the context of TBI.[13] Nevertheless, this research aspired to aggregate the most recent literature, updated existing meta-analysis findings, and encompassed a broader spectrum of ML algorithms. Moreover, we have noticed a gap in the previous meta-analysis, as it did not comprehensively assess the predictive capability of ML in forecasting DOC after TBI. Furthermore, our intention aimed to encompass studies on DOC prediction in TBI patients of all age groups, thereby expanding the scope of ML applicability in prognostic research for TBI to assess the precision and disparities across distinct ML algorithms in predicting TBI patient with DOC through extensive data modeling. Consequently, this study was to employ a meta-analysis approach to scrutinize the predictive accuracy of modeling DOC following TBI models, investigating the potential value of ML in the prognosis of brain injury patients, with the ultimate objective of furnishing more scientifically grounded medical evidence to guide the management and treatment of such patient cohorts.

Material and Methods

Inclusion and Exclusion Criteria

Inclusion Criteria: (a) Study participants encompassed individuals across all age groups who had suffered severe TBI; (b) primary focus of the research was on the development of prognostic models (including DOC) for severe TBI; and (c) the study design included cohort studies.

Exclusion Criteria: (a) Duplicate publications; (b) literature such as reviews, case reports, and conference abstracts; (c) publications with only abstracts or inaccessible full texts; (d) literature that did not construct a prognostic model but solely analyzed risk factors; (e) literature with an incomplete or insufficiently described model construction process; and (f) literature that developed risk prediction models based on systematic reviews.

Literature Retrieval Strategy

We retrieved studies to construct prognostic model (including DOC) for patients with brain injury published in PubMed and Web of Science, and the period for publication search ranged from the establishment of the database to August 6, 2023. This study used search terms in PubMed as follows: ("Brain injury"[All Fields] OR "Brain injuries"[All Fields] OR "Brain injuries"[MeSH Terms] OR "Head injury"[All Fields] OR "Severe brain injury"[All Fields] OR "Severe head injury"[All Fields] OR "Severe traumatic brain injury"[All Fields]) AND ("Prognostic calculator"[All Fields] OR "Prognostic models"[All Fields] OR "Prediction models"[All Fields] OR "Mathematical model"[All Fields]) AND ("Cognitive Impairment"[All Fields] OR "Consciousness Disorders"[All Fields] OR "Delirium"[All Fields] OR "Dementia"[All Fields] OR "Coma"[All Fields]) AND ("mortality"[MeSH Terms] OR "mortality"[All Fields] OR "mortalities"[All Fields] OR "mortality"[MeSH Subheading] OR "mortality"[MeSH Terms] OR ("death"[MeSH Terms] OR "death"[All Fields] OR "deaths"[All Fields]) OR "death"[MeSH Terms] OR ("outcome"[All Fields] OR "outcomes"[All Fields]) OR "mortal"[All Fields] OR "Outcome assessment"[All Fields] OR "Outcome prediction"[All Fields] OR "Outcome measure"[All Fields] OR

"Unfavorable outcome"[All Fields]). For the Web of Science database, the search terms were set as follows: TS= (("Brain injury" OR "Brain injuries" OR "Head injury" OR "Severe brain injury" OR "Severe head injury" OR "Severe traumatic brain injury") AND ("Cognitive Impairment" OR "Consciousness Disorders" OR "Delirium" OR "Dementia" OR "Coma") AND ("Prognostic calculator" OR "Prognostic models" OR "Prediction models" OR "Mathematical model") AND (Mortality OR Death OR Mortal* OR Outcome OR "Outcome Assessment" OR "Outcome prediction" OR "Outcome measure" OR "Unfavorable outcome")).

Literature Screening and Data Extraction

Tasks in this section were carried out independently by two researchers. They conducted literature screening and data extraction based on inclusion and exclusion criteria established in the literature. Cross-verification was performed to ensure consistency. In cases of disagreement, a third researcher was consulted to reach a final consensus. Information extracted encompassed details such as first authors, publication year, predictive models (ML algorithms), areas under the receiver operating characteristic curve (AUC) values, and clinical outcomes.

Statistical Method

In this section, we conducted heterogeneity tests using Stata software version 12.0 (StataCorp., LLC, College Station and Texas, USA). A fixed-effects model was employed for meta-analysis where heterogeneity test showed $I^2 < 50\%$, while a random-effects model was used when heterogeneity test indicated $I^2 > 50\%$. We calculated the combined AUC along with 95% CI as the effect size. When evident heterogeneity was noticed, subgroup analyses were employed, taking into account factors such as model type and age. Sensitivity analyses were also conducted to identify the sources of heterogeneity. Additionally, Egger's test was utilized to detect evidence of publication bias. A significance threshold of $P < .05$ was established to denote statistically significant differences.

Results

Literature Screening Results

In the initial stage, a preliminary literature search yielded a total of 310 relevant articles. Out of these articles, 70 duplicates were excluded, along with an additional 19 papers, such as reviews and conference proceedings, that did not meet the specific research criteria. Furthermore, six papers that were primarily focused on constructing risk prediction models on account of systematic reviews or meta-analyses were also excluded. Following the preliminary screening according to the titles and abstracts of the remaining articles, 135 papers that did not meet our predefined research standards were removed from this research. Consequently, a total of 46 articles were included in the meta-analysis. A comprehensive overview of the literature selection process is presented in Figure 1.

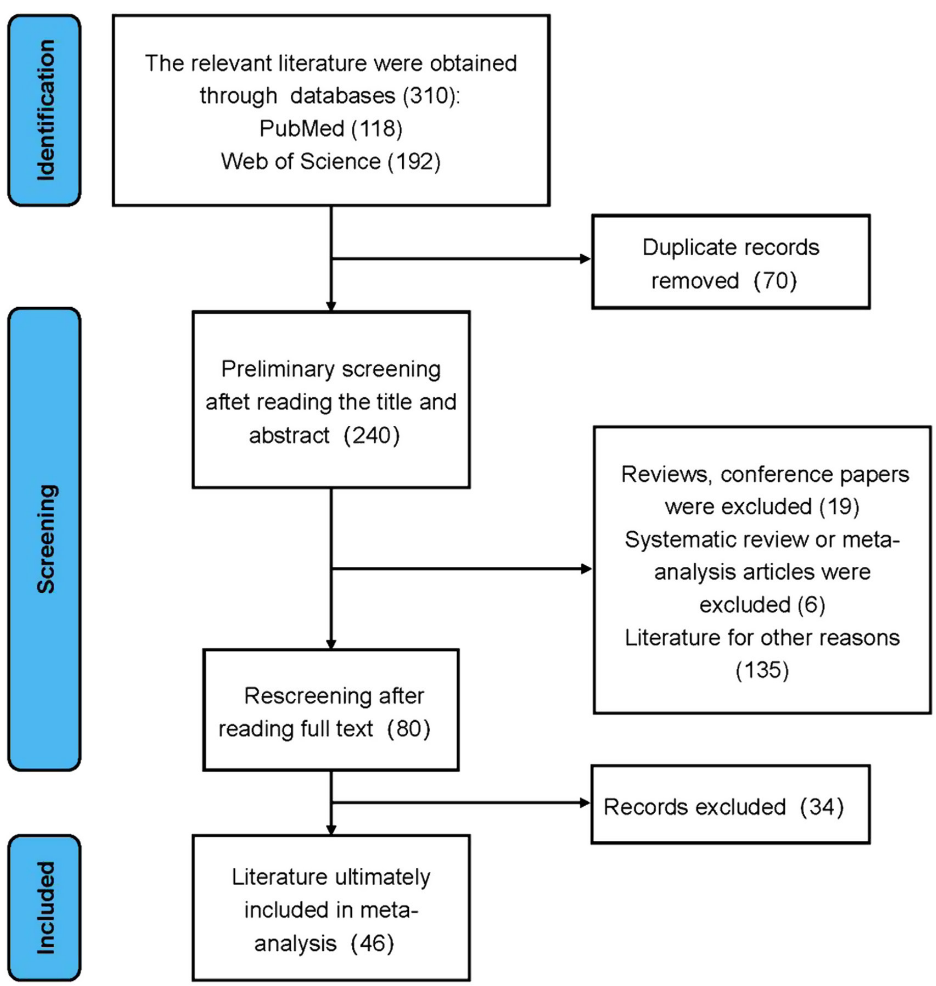

Figure 1. Flowchart of Literature Screening.

Table 1. Features of Models Included in this Literature Study

Author	Year	Outcome	Model	AUC	CI_low	CI_up
Abujaber, Ahmad[14]	2020	Death	SVM	0.9560	0.8415982	0.8784018
	2020	Death	ANN	0.9160	0.7638849	0.8161151
Bae, In-Suk[15]	2019	Death	LR	0.8400	0.7810000	0.8980000
	2019	Consciousness disorders	LR	0.7920	0.7330000	0.8510000
Bertotti, Melina More[16]	2023	Death	LR	0.7300	0.7000000	0.7700000
	2023	Death	LR	0.7400	0.7100000	0.7700000
	2023	Death	LR	0.8000	0.7700000	0.8300000
Bobeff, Ernest J.[17]	2019	Death	LR	0.8880	0.8340000	0.9430000
	2019	Consciousness disorders	LR	0.8990	0.8450000	0.9530000
Camarano, Joseph G.[18]	2021	Death	IMPACT	0.8630	0.8580000	0.8670000
	2021	Death	CRASH	0.8580	0.8540000	0.8760000
Charry, Jose D.[19]	2017	Death	CRASH	0.7060	0.5900000	0.8210000
	2017	Death	CRASH+CT	0.5850	0.4890000	0.6810000
	2017	Death	IMPACT	0.6700	0.5750000	0.7630000
Czeiter, Endre[20]	2012	Death	IMPACT	0.8510	0.8470000	0.8550000
Faried, Ahmad[21]	2018	Death	CRASH	0.9320	0.8950000	0.9570000
	2018	Consciousness disorders	CRASH	0.9980	0.9960000	0.9990000
Gradisek, Primoz[22]	2012	Death	IMPACT	0.8110	0.7140000	0.9080000
	2012	Death	LR	0.9200	0.8940000	0.9890000
	2012	Death	LR	0.9200	0.8940000	0.9760000
Gravesteijn, Benjamin Y.[23]	2020	Death	LR	0.8100	0.7900000	0.8400000
	2020	Death	SVM	0.8100	0.7800000	0.8300000
	2020	Death	RF	0.7900	0.7700000	0.8200000
	2020	Death	NN	0.8100	0.7900000	0.8400000
	2020	Death	GBM	0.8100	0.7900000	0.8400000
	2020	Death	Lasso	0.8100	0.7900000	0.8400000
	2020	Death	RR	0.8100	0.7900000	0.8400000
	2020	Consciousness disorders	LR	0.8100	0.7900000	0.8300000
	2020	Consciousness disorders	SVM	0.8000	0.7900000	0.8200000
	2020	Consciousness disorders	RF	0.7900	0.7600000	0.8100000
	2020	Consciousness disorders	NN	0.8000	0.7900000	0.8200000
	2020	Consciousness disorders	GBM	0.8000	0.7800000	0.8200000
	2020	Consciousness disorders	Lasso	0.8100	0.7900000	0.8300000
	2020	Consciousness disorders	RR	0.8100	0.7900000	0.8300000
Greenan, Krista[24]	2019	Consciousness disorders	DT	0.8200	0.6900000	0.9300000
Han, Julian[25]	2014	Death	CRASH	0.8000	0.7500000	0.8500000
	2014	Death	CRASH+CT	0.8300	0.7800000	0.8700000
	2014	Death	IMPACT	0.8000	0.7500000	0.8500000
	2014	Death	IMPACT extended	0.8100	0.7600000	0.8600000
	2014	Death	IMPACT lab	0.8000	0.7500000	0.8600000
	2014	Consciousness disorders	CRASH	0.8600	0.8100000	0.9000000
	2014	Consciousness disorders	CRASH+CT	0.8900	0.8400000	0.9300000
	2014	Consciousness disorders	IMPACT	0.8400	0.8000000	0.8900000
	2014	Consciousness disorders	IMPACT extended	0.8800	0.8300000	0.9200000
	2014	Consciousness disorders	IMPACT lab	0.8700	0.8200000	0.9200000
Hsu, Sheng-Der[26]	2021	Death	J48	0.8200	0.9109216	0.9480784
	2021	Death	RF	0.9210	0.9114524	0.9485476
	2021	Death	Random tree	0.7350	0.8993058	0.9376942
	2021	Death	REP tree	0.8460	0.9045720	0.9424280
	2021	Death	KNN	0.7160	0.8993058	0.9376942
	2021	Death	SVM	0.7100	0.9109216	0.9480784
	2021	Death	NB	0.9170	0.9040444	0.9419556

(*Continued*)

Table 1. Features of Models Included in this Literature Study (Continued)

Author	Year	Outcome	Model	AUC	CI_low	CI_up
Kamal, Vineet Kumar[27]	2016	Death	LR	0.8360	0.7950000	0.8770000
	2016	Consciousness disorders	LR	0.8670	0.8230000	0.9010000
	2016	Death	LR	0.8730	0.8370000	0.9090000
	2016	Consciousness disorders	LR	0.8800	0.8420000	0.9180000
	2016	Death	LR	0.8710	0.8330000	0.9090000
	2016	Consciousness disorders	LR	0.8650	0.8220000	0.9080000
Kennedy, Lori[28]	2022	Death	LR	0.9094	0.8646000	0.9543000
Kesmarky, Klara[29]	2017	Death	IMPACT	0.8520	0.8240000	0.8800000
	2017	Death	IMPACT	0.8260	0.7950000	0.8570000
Kim, Hakseung[30]	2018	Death	IMPACT	0.9460	0.8390000	1.0000000
	2018	Death	IMPACT	0.5380	0.4160000	0.6600000
	2018	Death	IMPACT	0.6320	0.5270000	0.7360000
	2018	Death	CRASH	0.7660	0.6160000	0.9170000
	2018	Death	CRASH	0.5870	0.4670000	0.7070000
	2018	Death	CRASH	0.7350	0.6420000	0.8280000
Kim, Sol Bi[31]	2022	Death	LR	0.9253	0.8784000	0.9722000
Lang, Lijian[32]	2023	Death	LR	0.8590	0.8370000	0.8800000
Lee, Soo Hoon[33]	2018	Death	LR	0.9700	0.9600000	0.9780000
Leto, Elio[34]	2021	Death	LR	0.9010	0.8660000	0.9390000
Lingsma, Hester[35]	2013	Death	IMPACT	0.7700	0.7500000	0.7800000
	2013	Death	IMPACT extended	0.8100	0.8000000	0.8200000
	2013	Death	IMPACT lab	0.7900	0.7700000	0.8100000
	2013	Consciousness disorders	IMPACT	0.7800	0.7700000	0.7900000
	2013	Consciousness disorders	IMPACT extended	0.8100	0.8000000	0.8200000
	2013	Consciousness disorders	IMPACT lab	0.8100	0.7900000	0.8200000
	2013	Death	IMPACT	0.8500	0.8100000	0.8800000
	2013	Death	IMPACT extended	0.8900	0.8800000	0.9300000
	2013	Death	IMPACT lab	0.9000	0.8900000	0.9400000
	2013	Consciousness disorders	IMPACT	0.8200	0.7900000	0.8600000
	2013	Consciousness disorders	IMPACT extended	0.8600	0.8400000	0.9100000
	2013	Consciousness disorders	IMPACT lab	0.8700	0.8500000	0.9100000
Lu, Hsueh-Yi[36]	2015	Consciousness disorders	ANN	0.9613	0.7742832	0.9580168
	2015	Consciousness disorders	NB	0.9445	0.8224138	0.9790862
	2015	Consciousness disorders	DT	0.9186	0.7671637	0.9532363
	2015	Consciousness disorders	LR	0.9247	0.7614789	0.9504211
	2015	Death	ANN	0.9014	0.7648052	0.9533948
	2015	Death	NB	0.8104	0.6500954	0.8632046
	2015	Death	DT	0.7785	0.7146373	0.9084627
	2015	Death	LR	0.8729	0.6959307	0.8983693
Maeda, Yukihiro[37]	2019	Death	TRISS	0.7500	0.7200000	0.7900000
	2019	Consciousness disorders	CRASH	0.8600	0.8200000	0.9000000
	2019	Consciousness disorders	CRASH+CT	0.8600	0.8200000	0.8900000
	2019	Consciousness disorders	IMPACT	0.8100	0.7700000	0.8500000
	2019	Consciousness disorders	IMPACT extended	0.8500	0.8000000	0.8900000
Mikkonen, Era D.[38]	2019	Consciousness disorders	IMPACT	0.8500	0.7800000	0.9100000
Oh, Hyun Soo[39]	2013	Consciousness disorders	DT	0.8530	0.7540000	0.9020000
Pourahmad, Saeedeh[40]	2016	Consciousness disorders	DT	0.6950	0.6359460	0.7510540
	2016	Consciousness disorders	ANN	0.7050	0.6903323	0.7966677
Rached, Mohamed A. K. B.[41]	2019	Death	IMPACT	0.8260	0.7950000	0.8570000
	2019	Death	IMPACT+HAIS	0.8390	0.8100000	0.8690000

(*Continued*)

Table 1. Features of Models Included in this Literature Study (Continued)

Author	Year	Outcome	Model	AUC	CI_low	CI_up
Raj, Rahul[42]	2014	Death	APACHE II	0.8000	0.7700000	0.8400000
	2014	Death	IMPACT	0.8000	0.7700000	0.8300000
	2014	Death	IMPACT extended	0.8000	0.7700000	0.8300000
	2014	Death	IMPACT lab	0.8100	0.7800000	0.8400000
	2014	Consciousness disorders	APACHE II	0.7600	0.7300000	0.7900000
	2014	Consciousness disorders	IMPACT	0.7800	0.7500000	0.8100000
	2014	Consciousness disorders	IMPACT extended	0.7900	0.7600000	0.8200000
	2014	Consciousness disorders	IMPACT lab	0.7900	0.7600000	0.8200000
Raj, Rahul[43]	2014	Death	APACHE II	0.8100	0.7800000	0.8400000
	2014	Death	SAPS II	0.8100	0.7700000	0.8400000
	2014	Death	SOFA	0.6800	0.6400000	0.7200000
Rocha, Thiago Augusto Hernandes[44]	2020	Consciousness disorders	NB	0.8650	0.8560000	0.8740000
	2020	Consciousness disorders	RF	0.8490	0.8460000	0.8530000
	2020	Consciousness disorders	RR	0.8480	0.8450000	0.8530000
	2020	Consciousness disorders	GBM	0.8510	0.8490000	0.8530000
	2020	Consciousness disorders	BART	0.8450	0.8430000	0.8480000
	2020	Consciousness disorders	BT	0.8360	0.8270000	0.8460000
	2020	Consciousness disorders	DT	0.7980	0.7880000	0.8090000
	2020	Consciousness disorders	NN	0.7880	0.7780000	0.8000000
	2020	Consciousness disorders	KNN	0.6620	0.6610000	0.6650000
Rodrigues de Souza, Matheus[45]	2022	Death	IMPACT	0.8020	0.7230000	0.8820000
	2022	Death	IMPACT+CT	0.8980	0.8440000	0.9530000
Rubin, M. Laura[46]	2019	Consciousness disorders	Lasso	0.8500	0.7900000	0.9100000
Song, Juhyun[47]	2023	Death	LR	0.9120	0.8970000	0.9270000
	2023	Death	lightGBM	0.9400	0.9290000	0.9520000
	2023	Death	MLP	0.9220	0.9080000	0.9350000
Strnad, Matej[48]	2017	Death	LR	0.8300	0.7100000	0.9400000
Wan, Xueyan[49]	2017	Death	IMPACT	0.7600	0.6003115	0.8096885
	2017	Consciousness disorders	IMPACT	0.8000	0.6584015	0.8615985
	2017	Death	IMPACT extended	0.7600	0.6321614	0.8378386
	2017	Consciousness disorders	IMPACT extended	0.7900	0.6698048	0.8801952
	2017	Death	IMPACT lab	0.7300	0.5891786	0.8008214
	2017	Consciousness disorders	IMPACT lab	0.7700	0.6135595	0.8364405
Wang, Jian[50]	2021	Consciousness disorders	LR	0.8820	0.7840000	0.9790000
Wang, Ruoran[51]	2021	Death	LR	0.8840	0.8260000	0.9430000
Wang, Ruoran[52]	2022	Death	LR	0.8570	0.8120000	0.9010000
Wang, Ruoran[53]	2023	Death	DT	0.7120	0.6470000	0.7770000
	2023	Death	RF	0.7950	0.7390000	0.8510000
	2023	Death	SVM	0.7850	0.7300000	0.8400000
	2023	Death	NB	0.6580	0.6020000	0.7150000
	2023	Death	LR	0.7920	0.7360000	0.8480000
	2023	Death	Adaboost	0.7990	0.7460000	0.8530000
	2023	Death	XGboost	0.7660	0.7090000	0.8230000
Wang, Yifei[54]	2023	Death	LR	0.9220	0.8750000	0.9700000
Yang, Bocheng[55]	2022	Consciousness disorders	LR	0.7770	0.6560000	0.8970000
Yuan, Fang[56]	2012	Death	LR	0.7090	0.6710000	0.7460000
	2012	Death	LR	0.7840	0.7500000	0.8170000
	2012	Death	LR	0.8790	0.8520000	0.9050000
	2012	Consciousness disorders	LR	0.7470	0.7170000	0.7780000
	2012	Consciousness disorders	LR	0.7980	0.7410000	0.8040000
	2012	Consciousness disorders	LR	0.8450	0.8170000	0.8720000

(*Continued*)

Table 1. Features of Models Included in this Literature Study (Continued)

Author	Year	Outcome	Model	AUC	CI_low	CI_up
Zhang, Zan[57]	2023	Death	LR	0.8130	0.6801644	0.8068356
	2023	Death	XGboost	0.9310	0.8699824	0.9560176
	2023	Death	lightGBM	0.9530	0.7311446	0.8378554
	2023	Death	FT-transformer	0.9240	0.7517249	0.8622751
	2023	Consciousness disorders	LR	0.8320	0.7295036	0.8484964
	2023	Consciousness disorders	XGboost	0.8930	0.7986695	0.9033305
	2023	Consciousness disorders	lightGBM	0.9130	0.7851645	0.8928355
	2023	Consciousness disorders	FT-transformer	0.8770	0.7797715	0.8882285
Zhao, Jian-Lan[58]	2019	Consciousness disorders	LR	0.9360	0.9230000	0.9490000
Zhou, Liang[59]	2023	Consciousness disorders	LR	0.9390	0.8990000	0.9790000

SVM, Support Vector Machine; ANN, Artificial Neural Network; LR, Logistic Regression; IMPACT, International Mission on Prognosis and Analysis on Clinical Trials in TBI; CRASH, Corticosteroid Randomization After Significant Head Injuryl; CRASH+CT, Corticosteroid Randomization After Significant Head Injury with Computed Tomography; RF, Random Forest; NN, Neural Network; GBM, Gradient Boosting Machine; Lasso, Least Absolute Shrinkage and Selection Operator; RR, Ridge Regression; DT, Decision Tree; IMPACT extended, International Mission on Prognosis and Analysis on Clinical Trials in TBI extended; IMPACT lab, International Mission on Prognosis and Analysis on Clinical Trials in TBI laboratory; J48, J48 decision tree algorithm; Random tree, Random Tree; REP tree, Reduced Error Pruning tree; KNN, K-Nearest Neighbors; NB, Naive Bayes; TRISS, Trauma and Injury Severity Score; IMPACT+HAIS, International Mission on Prognosis and Analysis on Clinical Trials in TBI with Abbreviated Injury Score; APACHE II, Acute Physiology and Chronic Health Evaluation II; SAPS II, Simplified Acute Physiology Score II; SOFA, Sequential Organ Failure Assessment; BART, Bayesian Additive Regression Trees; BT, Bootstrap aggregating; IMPACT+CT, International Mission on Prognosis and Analysis on Clinical Trials in TBI with Computed Tomography; lightGBM, Light Gradient Boosting Machine; MLP, Multilayer Perceptron; Adaboost, Adaptive Boosting; XGBoost, Extreme Gradient Boosting; FT-transformer, Feature Tokenizer-Transformer

Features of Models Included in Literature Studies

This study encompassed a total of 46 pieces of literature concerning the construction of predictive models for TBI. Features of the research models within the referenced literature are outlined in Table 1.

Meta-analysis Results

Our meta-analysis on the construction of DOC models for TBI patients revealed significant heterogeneity ($I^2 = 99.8\%$, $Q < 0.0001$). To determine this heterogeneity, we employed the meta-analysis using a random-effects model, as illustrated in Table 2. The findings indicated that in the context of DOC prediction in TBI patients, the overall pooled AUC of ML model was found to be 0.83, with a 95% CI ranging from 0.82 to 0.84.

Subgroup Analyses

We conducted a subgroup analysis across various age cohorts, as illustrated in Figure 2 and Supplementary Table 1. Overall, the pediatric cohort exhibited the highest aggregated AUC of 0.88 (95% CI [0.80; 0.95], $P = .09$), followed by the adult cohort with an overall aggregated AUC of 0.83 (95% CI [0.82; 0.85], $P < .001$). In contrast, the geriatric cohort had the lowest overall aggregated AUC of 0.77 (95% CI [0.74; 0.81], $P < .001$).

In Figure 3 and Supplementary Table 2, we presented our subgroup analysis results for various models. Notably, Light Gradient Boosting Machine (lightGBM) exhibited the highest overall combined AUC (AUC = 0.94, 95% CI [0.92; 0.96], $P = .55$). The logistic regression (LR) model emerged as the most extensively employed model within this study, yielding an overall combined AUC of 0.85 (95% CI [0.83; 0.87], $P < .001$).

Finally, another subgroup analysis was conducted for distinguishing various outcomes (consciousness recovery vs. consciousness disorders; consciousness recovery vs. death), as depicted in Figure 4 and Supplementary Table 3. Overall, the comprehensive AUC for consciousness recovery vs. consciousness disorders was 0.84 (95% CI [0.82; 0.85], $P < .001$), while the comprehensive AUC for consciousness recovery vs. death was 0.82 (95% CI [0.81; 0.84], $P < .001$).

Publication Bias Assessment and Sensitivity Analysis

On evaluation of the distribution of individual study data points, we observed a roughly symmetrical pattern, as depicted in Figure 5. Our Egger's test results ($P = .18472$) did not reveal any notable publication bias within the reviewed publications.

As illustrated in Figure 6, the outcomes of the sensitivity analysis demonstrate that the AUC values from each individual study fall within the combined interval. Most studies exhibit minimal deviations from the estimated values. Typically, impacts of any single study on the overall effect size appear to be negligible, indicating a level of stability in the combined effect estimate.

Discussion

Annual average number of TBI cases in China is reported to be approximately 3-4 million.[60] Traumatic brain injury is associated with the development of neurodegenerative disorders, including Alzheimer's disease, Parkinson's disease, and chronic traumatic encephalopathy and long-term neurological deficits, and patients are facing an increased risk of cognitive impairment and psychiatric complications over an extended duration. During the treatment phase of TBI, safe and effective neuroprotective therapy is beneficial for post-traumatic mental impairments. Meanwhile, the neuroinflammatory process also develops during the same period, and recent studies suggest that the evolving inflammatory process may present an opportunity for intervention.[61] However, administering anti-inflammatory drugs after injury is ineffective in treating TBI patients, and some components of the neuroinflammatory response seem to have a positive property in the recovery process.[62] In addition, survivors of severe brain injury may suffer from varying degrees of DOC, which as a type of serious brain function disorder, can leave up to 14% of patients in a coma or persistent vegetative state, with longer duration leading to higher mortality rates. Early intervention and treatment for DOC after TBI fundamentally impact the prognosis of such patients.[63]

Through the analysis of extensive clinical data and the application of state-of-the-art ML algorithms, researchers have attained more

Table 2. AUC value for Predicting DOC of Patients with Brain Injury

Author	AUC	Sensitivity	Weights	CI
Zhou, Liang	0.939	0.0204	0.60%	(0.899; 0.979)
Wang, Ruoran	0.884	0.0298	0.60%	(0.826; 0.943)
Rocha, Thiago Augusto Hernandes	0.865	0.0046	0.70%	(0.856; 0.874)
Rocha, Thiago Augusto Hernandes	0.849	0.0018	0.70%	(0.846; 0.853)
Rocha, Thiago Augusto Hernandes	0.848	0.002	0.70%	(0.845; 0.853)
Rocha, Thiago Augusto Hernandes	0.851	0.001	0.70%	(0.849; 0.853)
Rocha, Thiago Augusto Hernandes	0.845	0.0013	0.70%	(0.843; 0.848)
Rocha, Thiago Augusto Hernandes	0.836	0.0048	0.70%	(0.827; 0.846)
Rocha, Thiago Augusto Hernandes	0.798	0.0054	0.70%	(0.788; 0.809)
Rocha, Thiago Augusto Hernandes	0.788	0.0056	0.70%	(0.778; 0.800)
Rocha, Thiago Augusto Hernandes	0.662	0.001	0.70%	(0.661; 0.665)
Lang, Lijian	0.859	0.011	0.70%	(0.837; 0.880)
Czeiter, Endre	0.851	0.002	0.70%	(0.847; 0.855)
Wang, Yifei	0.922	0.0242	0.60%	(0.875; 0.970)
Kim, Hakseung	0.946	0.0411	0.50%	(0.839; 1.000)
Kim, Hakseung	0.538	0.0622	0.40%	(0.416; 0.660)
Kim, Hakseung	0.632	0.0533	0.40%	(0.527; 0.736)
Kim, Hakseung	0.766	0.0768	0.30%	(0.616; 0.917)
Kim, Hakseung	0.587	0.0612	0.40%	(0.467; 0.707)
Kim, Hakseung	0.735	0.0474	0.50%	(0.642; 0.828)
Kesmarky, Klara	0.852	0.0143	0.70%	(0.824; 0.880)
Kesmarky, Klara	0.826	0.0158	0.70%	(0.795; 0.857)
Rached, Mohamed A. K. B.	0.826	0.0158	0.70%	(0.795; 0.857)
Rached, Mohamed A. K. B.	0.839	0.0151	0.70%	(0.810; 0.869)
Oh, Hyun Soo	0.853	0.0378	0.50%	(0.754; 0.902)
Rodrigues de Souza, Matheus	0.802	0.0406	0.50%	(0.723; 0.882)
Rodrigues de Souza, Matheus	0.898	0.0278	0.60%	(0.844; 0.953)
Leto, Elio	0.901	0.0186	0.70%	(0.866; 0.939)
Han, Julian	0.8	0.0255	0.60%	(0.750; 0.850)
Han, Julian	0.83	0.023	0.60%	(0.780; 0.870)
Han, Julian	0.8	0.0255	0.60%	(0.750; 0.850)
Han, Julian	0.81	0.0255	0.60%	(0.760; 0.860)
Han, Julian	0.8	0.0281	0.60%	(0.750; 0.860)
Han, Julian	0.86	0.023	0.60%	(0.810; 0.900)
Han, Julian	0.89	0.023	0.60%	(0.840; 0.930)
Han, Julian	0.84	0.023	0.60%	(0.800; 0.890)
Han, Julian	0.88	0.023	0.60%	(0.830; 0.920)
Han, Julian	0.87	0.0255	0.60%	(0.820; 0.920)
Maeda, Yukihiro	0.75	0.0179	0.70%	(0.720; 0.790)
Maeda, Yukihiro	0.86	0.0204	0.60%	(0.820; 0.900)
Maeda, Yukihiro	0.86	0.0179	0.70%	(0.820; 0.890)

(*Continued*)

Table 2. AUC value for Predicting DOC of Patients with Brain Injury (Continued)

Author	AUC	Sensitivity	Weights	CI
Maeda, Yukihiro	0.81	0.0204	0.60%	(0.770; 0.850)
Maeda, Yukihiro	0.85	0.023	0.60%	(0.800; 0.890)
Faried, Ahmad	0.932	0.0158	0.70%	(0.895; 0.957)
Faried, Ahmad	0.998	0.0008	0.70%	(0.996; 0.999)
Bertotti, Melina More	0.73	0.0179	0.70%	(0.700; 0.770)
Bertotti, Melina More	0.74	0.0153	0.70%	(0.710; 0.770)
Bertotti, Melina More	0.8	0.0153	0.70%	(0.770; 0.830)
Pourahmad, Saeedeh	0.695	0.0294	0.60%	(0.636; 0.751)
Pourahmad, Saeedeh	0.705	0.0271	0.60%	(0.690; 0.797)
Wan, Xueyan	0.76	0.0534	0.40%	(0.600; 0.810)
Wan, Xueyan	0.8	0.0518	0.40%	(0.658; 0.862)
Wan, Xueyan	0.76	0.0525	0.40%	(0.632; 0.838)
Wan, Xueyan	0.79	0.0537	0.40%	(0.670; 0.880)
Wan, Xueyan	0.73	0.054	0.40%	(0.589; 0.801)
Wan, Xueyan	0.77	0.0569	0.40%	(0.614; 0.836)
Wang, Ruoran	0.857	0.0227	0.60%	(0.812; 0.901)
Zhang, Zan	0.813	0.0323	0.60%	(0.680; 0.807)
Zhang, Zan	0.931	0.0219	0.60%	(0.870; 0.956)
Zhang, Zan	0.953	0.0272	0.60%	(0.731; 0.838)
Zhang, Zan	0.924	0.0282	0.60%	(0.752; 0.862)
Zhang, Zan	0.832	0.0304	0.60%	(0.730; 0.848)
Zhang, Zan	0.893	0.0267	0.60%	(0.799; 0.903)
Zhang, Zan	0.913	0.0275	0.60%	(0.785; 0.893)
Zhang, Zan	0.877	0.0277	0.60%	(0.780; 0.888)
Gravesteijn, Benjamin Y.	0.81	0.0128	0.70%	(0.790; 0.840)
Gravesteijn, Benjamin Y.	0.81	0.0128	0.70%	(0.780; 0.830)
Gravesteijn, Benjamin Y.	0.79	0.0128	0.70%	(0.770; 0.820)
Gravesteijn, Benjamin Y.	0.81	0.0128	0.70%	(0.790; 0.840)
Gravesteijn, Benjamin Y.	0.81	0.0128	0.70%	(0.790; 0.840)
Gravesteijn, Benjamin Y.	0.81	0.0128	0.70%	(0.790; 0.840)
Gravesteijn, Benjamin Y.	0.81	0.0128	0.70%	(0.790; 0.840)
Gravesteijn, Benjamin Y.	0.81	0.0102	0.70%	(0.790;0.830)
Gravesteijn, Benjamin Y.	0.8	0.0077	0.70%	(0.790; 0.820)
Gravesteijn, Benjamin Y.	0.79	0.0128	0.70%	(0.760; 0.810)
Gravesteijn, Benjamin Y.	0.8	0.0077	0.70%	(0.790; 0.820)
Gravesteijn, Benjamin Y.	0.8	0.0102	0.70%	(0.780; 0.820)
Gravesteijn, Benjamin Y.	0.81	0.0102	0.70%	(0.790; 0.830)
Gravesteijn, Benjamin Y.	0.81	0.0102	0.70%	(0.790; 0.830)
Hsu, Sheng-Der	0.82	0.0095	0.70%	(0.911; 0.948)
Hsu, Sheng-Der	0.921	0.0095	0.70%	(0.911; 0.949)
Hsu, Sheng-Der	0.735	0.0098	0.70%	(0.899; 0.938)
Hsu, Sheng-Der	0.846	0.0097	0.70%	(0.905; 0.942)
Hsu, Sheng-Der	0.716	0.0098	0.70%	(0.899; 0.938)
Hsu, Sheng-Der	0.71	0.0095	0.70%	(0.911; 0.948)
Hsu, Sheng-Der	0.917	0.0097	0.70%	(0.904; 0.942)
Kennedy, Lori	0.909	0.0229	0.60%	(0.865; 0.954)
Bae, In-Suk	0.84	0.0298	0.60%	(0.781; 0.898)
Bae, In-Suk	0.792	0.0301	0.60%	(0.733; 0.851)
Bobeff, Ernest J.	0.888	0.0278	0.60%	(0.834; 0.943)
Bobeff, Ernest J.	0.899	0.0276	0.60%	(0.845; 0.953)
Gradisek, Primoz	0.811	0.0495	0.50%	(0.714; 0.908)

(*Continued*)

Table 2. AUC value for Predicting DOC of Patients with Brain Injury (Continued)

Author	AUC	Sensitivity	Weights	CI
Gradisek, Primoz	0.92	0.0242	0.60%	(0.894; 0.989)
Gradisek, Primoz	0.92	0.0209	0.60%	(0.894; 0.976)
Kim, Sol Bi	0.925	0.0239	0.60%	(0.878; 0.972)
Charry, Jose D.	0.706	0.0589	0.40%	(0.590; 0.821)
Charry, Jose D.	0.585	0.049	0.50%	(0.489; 0.681)
Charry, Jose D.	0.67	0.048	0.50%	(0.575; 0.763)
Camarano, Joseph G.	0.863	0.0023	0.70%	(0.858; 0.867)
Camarano, Joseph G.	0.858	0.0056	0.70%	(0.854; 0.876)
Lu, Hsueh-Yi	0.961	0.0469	0.50%	(0.774; 0.958)
Lu, Hsueh-Yi	0.945	0.04	0.50%	(0.822; 0.979)
Lu, Hsueh-Yi	0.919	0.0475	0.50%	(0.767; 0.953)
Lu, Hsueh-Yi	0.925	0.0482	0.50%	(0.761; 0.950)
Lu, Hsueh-Yi	0.901	0.0481	0.50%	(0.765; 0.953)
Lu, Hsueh-Yi	0.81	0.0544	0.40%	(0.650; 0.863)
Lu, Hsueh-Yi	0.778	0.0494	0.50%	(0.715; 0.908)
Lu, Hsueh-Yi	0.873	0.0516	0.40%	(0.696; 0.898)
Raj, Rahul	0.8	0.0179	0.70%	(0.770; 0.840)
Raj, Rahul	0.8	0.0153	0.70%	(0.770; 0.830)
Raj, Rahul	0.8	0.0153	0.70%	(0.770; 0.830)
Raj, Rahul	0.81	0.0153	0.70%	(0.780; 0.840)
Raj, Rahul	0.76	0.0153	0.70%	(0.730; 0.790)
Raj, Rahul	0.78	0.0153	0.70%	(0.750; 0.810)
Raj, Rahul	0.79	0.0153	0.70%	(0.760; 0.820)
Raj, Rahul	0.79	0.0153	0.70%	(0.760; 0.820)
Yuan, Fang	0.709	0.0191	0.60%	(0.671; 0.746)
Yuan, Fang	0.784	0.0171	0.70%	(0.750; 0.817)
Yuan, Fang	0.879	0.0135	0.70%	(0.852; 0.905)
Yuan, Fang	0.747	0.0156	0.70%	(0.717; 0.778)
Yuan, Fang	0.798	0.0161	0.70%	(0.741; 0.804)
Yuan, Fang	0.845	0.014	0.70%	(0.817; 0.872)
Raj, Rahul	0.81	0.0153	0.70%	(0.780; 0.840)
Raj, Rahul	0.81	0.0179	0.70%	(0.770; 0.840)
Raj, Rahul	0.68	0.0204	0.60%	(0.640; 0.720)
Yang, Bocheng	0.777	0.0615	0.40%	(0.656; 0.897)
Abujaber, Ahmad	0.956	0.0094	0.70%	(0.842; 0.878)
Abujaber, Ahmad	0.916	0.0133	0.70%	(0.764; 0.816)
Song, Juhyun	0.912	0.0077	0.70%	(0.897; 0.927)
Song, Juhyun	0.94	0.0059	0.70%	(0.929; 0.952)
Song, Juhyun	0.922	0.0069	0.70%	(0.908; 0.935)
Wang, Ruoran	0.712	0.0332	0.60%	(0.647; 0.777)
Wang, Ruoran	0.795	0.0286	0.60%	(0.739; 0.851)
Wang, Ruoran	0.785	0.0281	0.60%	(0.730; 0.840)
Wang, Ruoran	0.658	0.0288	0.60%	(0.602; 0.715)
Wang, Ruoran	0.792	0.0286	0.60%	(0.736; 0.848)
Wang, Ruoran	0.799	0.0273	0.60%	(0.746; 0.853)
Wang, Ruoran	0.766	0.0291	0.60%	(0.709; 0.823)
Lee, Soo Hoon	0.97	0.0046	0.70%	(0.960; 0.978)
Strnad, Matej	0.83	0.0587	0.40%	(0.710; 0.940)
Lingsma, Hester	0.77	0.0077	0.70%	(0.750; 0.780)
Lingsma, Hester	0.81	0.0051	0.70%	(0.800; 0.820)
Lingsma, Hester	0.79	0.0102	0.70%	(0.770; 0.810)
Lingsma, Hester	0.78	0.0051	0.70%	(0.770; 0.790)
Lingsma, Hester	0.81	0.0051	0.70%	(0.800; 0.820)
Lingsma, Hester	0.81	0.0077	0.70%	(0.790; 0.820)
Lingsma, Hester	0.85	0.0179	0.70%	(0.810; 0.880)
Lingsma, Hester	0.89	0.0128	0.70%	(0.880; 0.930)
Lingsma, Hester	0.9	0.0128	0.70%	(0.890; 0.940)
Lingsma, Hester	0.82	0.0179	0.70%	(0.790; 0.860)
Lingsma, Hester	0.86	0.0179	0.70%	(0.840; 0.910)
Lingsma, Hester	0.87	0.0153	0.70%	(0.850; 0.910)
Rubin, M. Laura	0.85	0.0306	0.60%	(0.790; 0.910)
Kamal, Vineet Kumar	0.836	0.0209	0.60%	(0.795; 0.877)
Kamal, Vineet Kumar	0.867	0.0199	0.60%	(0.823; 0.901)
Kamal, Vineet Kumar	0.873	0.0184	0.70%	(0.837; 0.909)
Kamal, Vineet Kumar	0.88	0.0194	0.60%	(0.842; 0.918)
Kamal, Vineet Kumar	0.871	0.0194	0.60%	(0.833; 0.909)
Kamal, Vineet Kumar	0.865	0.0219	0.60%	(0.822; 0.908)
Zhao, Jian-Lan	0.936	0.0066	0.70%	(0.923; 0.949)
Wang, Jian	0.882	0.0497	0.50%	(0.784; 0.979)
Greenan, Krista	0.82	0.0612	0.40%	(0.690; 0.930)
Mikkonen, Era D.	0.85	0.0332	0.60%	(0.780; 0.910)
Total	0.829	NA	100%	(0.817; 0.840)

Heterogeneity: $tau^2 = 0.0045$; $\chi^2 = 74\,823.63$, $df = 162$ ($P = 0$); $I^2 = 100\%$.

accurate and individualized prognostic outcomes, thereby providing critical support for making treatment decisions and guiding rehabilitation planning in the context of DOC prediction in TBI. This underscores the extensive potential application prospects of ML in this domain. The study conducted by Abujaber et al in 2020 included adult patients with TBI who were admitted to hospital between 2014 and 2019 and utilized ML techniques to construct a predictive model for inpatient mortality rates among TBI patients. This research findings demonstrated that ML prognostic technology exhibited superior capabilities in predicting disease outcomes compared to traditional multivariate models. This investigation leveraged demographic data, injury characteristics, and computed tomography (CT) scan results from adult TBI patients as predictive factors and evaluated the predictive performance of both artificial neural networks (ANN) and support vector machines (SVM). The results indicated that both SVM and ANN models exhibited outstanding performance in terms of accuracy and AUC, with surpassing 91% and 93%, respectively. Notably, the SVM model outperformed others with an accuracy of 95.6% and an AUC of 96%. In the context of predicting mortality rates among TBI patients, the SVM model is superior than conventional multivariate LR analysis model.[14] A multicenter retrospective cohort study in South Korea delved into data from adult patients with severe trauma between 2014 and 2018 included 1169 subjects. This investigation employed a repertoire of five distinct ML algorithms, namely logistic regression analysis, extreme gradient boosting, Support Vector Machine, random forests, and elastic net (EN), to predict clinical outcomes. The study outcomes revealed that the EN model outperformed other models in terms of predictive accuracy, achieving an AUC of 0.799 and a predictive accuracy of 0.871 for in-hospital mortality outcomes.[64]

Age	AUC	95% CI	I²	χ²
Adult	0.83	[0.82;0.85]	99.81%	74663.24
Pediatric	0.88	[0.80;0.95]	49.62%	7.94
Geriatric	0.77	[0.74;0.81]	76.08%	66.90
Total	0.83	[0.82;0.84]	99.78%	74823.63

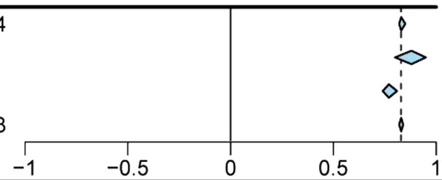

Figure 2. Impacts of Different Age Subgroups on the Accuracy of DOC Prediction in Patients with Brain Injury.

Model	AUC	95% CI	I²	χ²
LR	0.85	[0.83;0.87]	95.91%	1002.50
NB	0.84	[0.70;0.98]	95.21%	83.54
RF	0.83	[0.76;0.90]	96.16%	104.25
RR	0.82	[0.77;0.88]	90.63%	21.34
GBM	0.82	[0.75;0.89]	94.24%	34.75
BART	0.84	[0.84;0.85]	–	0.00
BT	0.84	[0.83;0.85]	–	0.00
DT	0.79	[0.72;0.86]	78.25%	27.59
NN	0.80	[0.77;0.82]	39.93%	3.33
KNN	0.69	[0.35;1.03]	96.68%	30.08
IMPACT	0.81	[0.78;0.84]	94.90%	430.95
CRASH	0.82	[0.74;0.90]	98.97%	870.98
IMPACT+HAIS	0.84	[0.81;0.87]	–	0.00
IMPACT+CT	0.90	[0.84;0.95]	–	0.00
CRASH+CT	0.80	[0.58;1.01]	90.95%	33.15
IMPACT extended	0.83	[0.80;0.85]	82.69%	57.77
IMPACT lab	0.82	[0.79;0.86]	87.57%	72.40
TRISS	0.75	[0.72;0.78]	–	0.00
ANN	0.87	[0.69;1.05]	94.24%	52.11
XGboost	0.86	[0.65;1.08]	90.47%	20.98
lightGBM	0.94	[0.92;0.96]	0.00%	1.18
FT–transformer	0.90	[0.60;1.20]	29.34%	1.42
SVM	0.81	[0.70;0.92]	98.87%	353.15
Lasso	0.81	[0.78;0.84]	0.00%	1.60
J48	0.82	[0.80;0.84]	–	0.00
Random tree	0.74	[0.72;0.75]	–	0.00
REP tree	0.85	[0.83;0.86]	–	0.00
APACHE II	0.79	[0.72;0.86]	65.82%	5.85
SAPS II	0.81	[0.78;0.84]	–	0.00
SOFA	0.68	[0.64;0.72]	–	0.00
MLP	0.92	[0.91;0.94]	–	0.00
Adaboost	0.80	[0.75;0.85]	–	0.00
Total	0.83	[0.82;0.84]	99.78%	74823.63

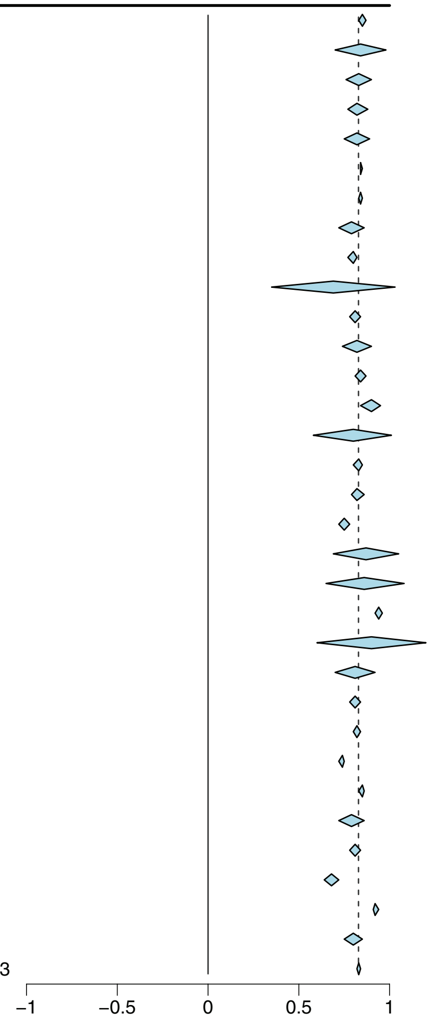

Figure 3. Impacts of different prediction models on the accuracy of DOC prediction in patients with brain injury. I^2 = "–" refers to the inclusion of a single literature in this subgroup, which is not applicable for the calculation of I^2.

Outcome	AUC	95% CI	I²	χ²
consciousness recovery vs. consciousness disorders	0.84	[0.82;0.85]	99.91%	71860.58
consciousness recovery vs. death	0.82	[0.81;0.84]	96.69%	2930.31
Total	0.83	[0.82;0.84]	99.78%	74823.63

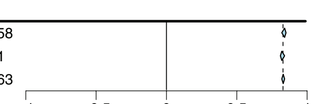

Figure 4. Impacts of different clinical outcomes on the accuracy of DOC prediction in patients with brain injury.

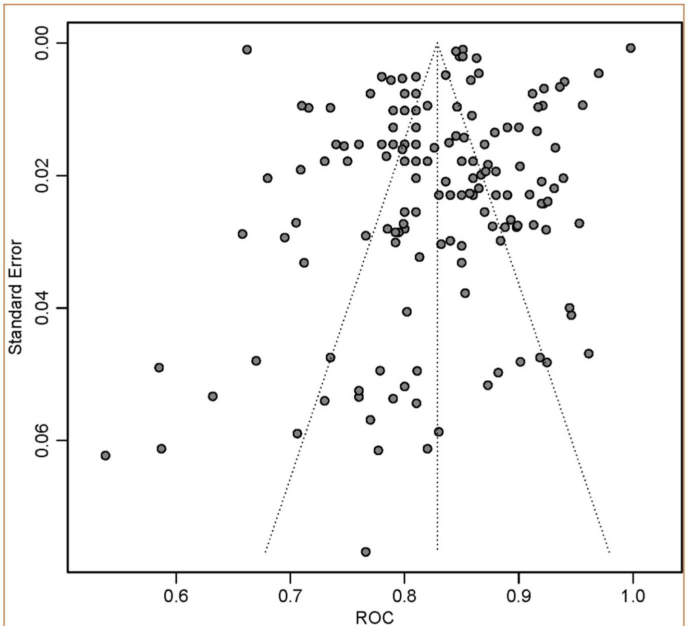

Figure 5. Funnel plot for publication bias assessment.

This study applied a systematic approach to retrieve cohort studies focusing on TBI patients across all age groups and the selection processes followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines, resulting in the inclusion of 46 publications. Through meta-analysis, our findings indicated that ML achieved a favorable predictive performance in predicting severe TBI, with an AUC of 0.83 and a 95% CI of (0.82; 0.84). The findings of this study offered valuable support to clinicians in making decisions regarding surgical interventions and non-surgical treatment options, with the potential impact on consciousness recovery and quality of life for patients. However, significant heterogeneity exists among the included studies due to variations in predictive factors, ML algorithms, sample sizes, diagnostic criteria, literature quality, gender distribution, and age demographics. To explore the potential sources of heterogeneity, we conducted subgroup analyses, Egger's tests, and sensitivity analyses, indicating that age distribution, the inclusion of specific ML algorithms, and clinical outcomes might be potential primary contributors to the heterogeneity. Our bias assessment indicated the absence of significant publication bias within the literature reviewed in this study. The combined effect sizes exhibited a degree of reliability and stability. Subgroup analyses on account of the model, age, and clinical outcomes revealed that the LightGBM model

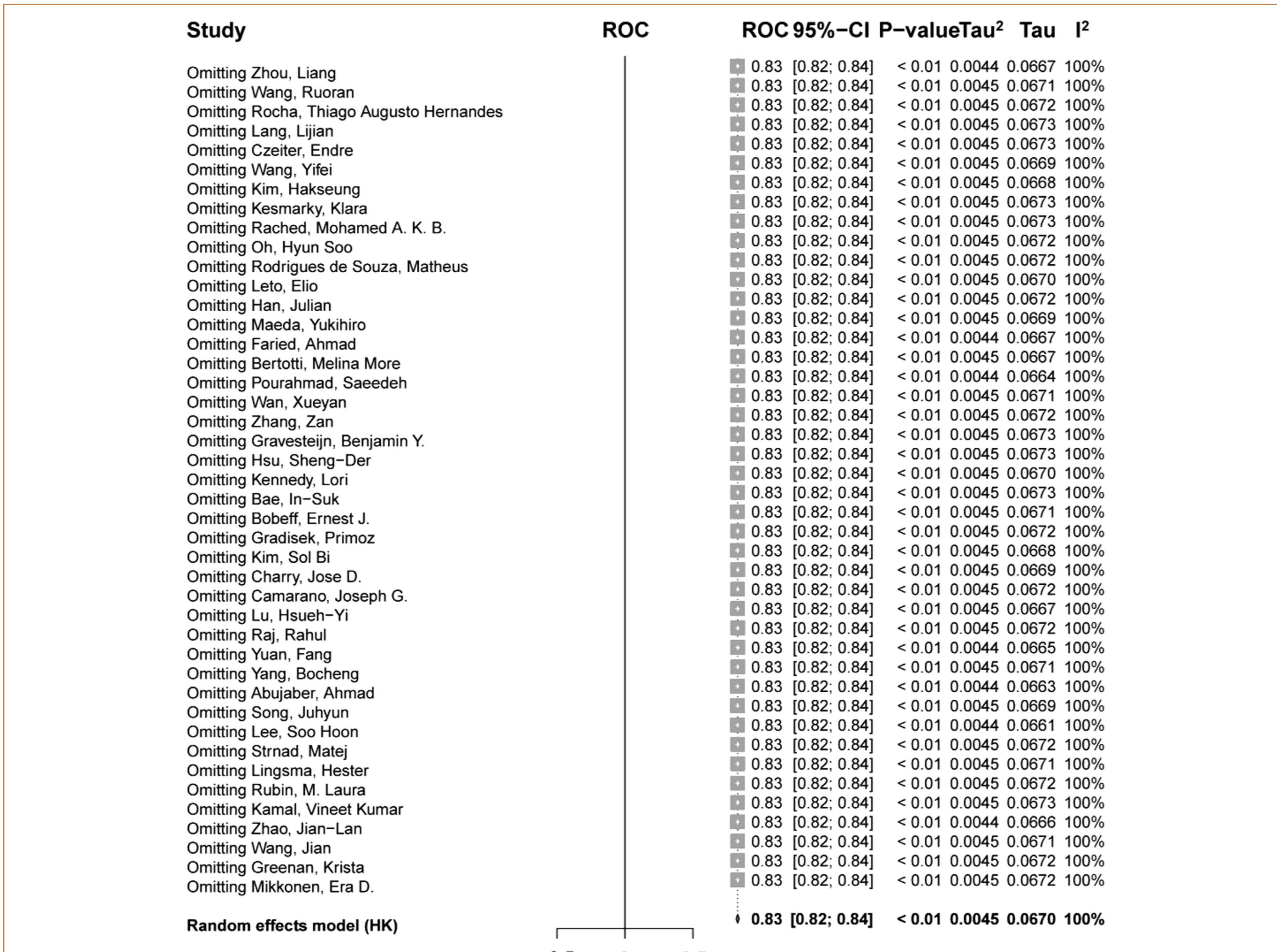

Figure 6. Sensitivity analysis.

outperformed other models in predictive accuracy, with an AUC of 0.94. Furthermore, ML algorithms such as Multilayer Perceptron (MLP), transformer: Feature Tokenizer-Transformer (FT-Transformer), and International Mission on Prognosis and Analysis on Clinical Trials in TBI with Computed Tomography (IMPACT+CT) have also demonstrated effectiveness in predicting consciousness recovery vs. consciousness disorders of TBI patients, with AUC values of 0.92, 0.90, and 0.90, respectively. Nevertheless, the literature using ML algorithms is relatively scarce, and further validation of the predictive accuracy in DOC of TBI patients are necessary. In the literature, the LR model has been the most widely utilized approach for modeling and predicting TBI patient outcomes. Overall, the LR model yields an AUC of 0.85, with a 95% CI [0.83; 0.87], surpassing some common ML models, including Naive Bayes (NB) (AUC = 0.84, 95% CI [0.70; 0.98]), Random Forest (RF) (AUC = 0.83, 95% CI [0.76; 0.90]), Gradient Boosting Machine (GBM) (AUC = 0.82, 95% CI [0.75; 0.89]), Decision Tree (DT) (AUC = 0.79, 95% CI [0.72; 0.86]), Neural Network (NN) (AUC = 0.80, 95% CI [0.77; 0.82]), K-Nearest Neighbors (KNN) (AUC = 0.69, 95% CI [0.35; 1.03]), and SVM (AUC = 0.81, 95% CI [0.70; 0.92]). In line with the present study, van der Ploeg et al[65] utilized modern modeling techniques to predict mortality rates among TBI patients. Their research revealed that the LR model exhibited the best performance, with a median AUC of 0.757, followed by the RF and SVM models, which achieved median AUC values of 0.735 and 0.732, respectively. Likewise, in the investigation of the ML predictive values for moderate-to-severe TBI, Gravesteijn et al[23] reported that ML algorithms did not demonstrate a significantly superior performance over traditional logistic regression models in predicting outcomes following moderate or severe TBI.

A meta-analysis was conducted in 2023 to investigate the performance of ML in predicting the mortality risk of TBI patients, which represented the first systematic evaluation of ML models in forecasting mortality rates among TBI patients. This study included a total of 47 studies with C-index as the effect size. The findings unequivocally demonstrate the exceptional precision of ML models in predicting mortality rates among TBI patients. The majority of ML models, including SVM, DT, LR, RF, and NN, yielded C-indices exceeding 0.8.[66] Within the scope of this study, several ML models including SVM, DT, LR, RF, and NN demonstrated ROC AUC values exceeding 0.79, indicating their favorable performance in predicting clinical outcomes among TBI patients. Additionally, a subgroup analysis was conducted based on the age distribution of TBI patients. The findings revealed that the ML models exhibited the highest overall predictive accuracy in pediatric TBI patients, with an AUC value of 0.88, 95% CI [0.80; 0.95], while their predictive performance was less favorable in geriatric TBI patients, yielding an AUC value of 0.77 (95% CI [0.74; 0.81]). These disparities might be attributed to notable variations in patient injury characteristics and pathophysiological processes, potentially influenced by variations in the number of studies included. Subgroup analyses for different outcomes demonstrated that these ML models performed well in predicting clinical outcomes in TBI patients, including consciousness recovery vs. consciousness disorders and consciousness recovery vs. death (0.84 vs. 0.82). This study has several limitations. Due to objective constraints, literature from additional medical database sources was unavailable; the literature included in this study was not selectively distinguished by data type but rather subjected to an overall assessment of prognostic accuracy, resulting in significant heterogeneity.

In summary, this study underscores the significant potential of ML in the field of DOC prediction in TBI. Through the integration and analysis of large-scale clinical data, ML demonstrated outstanding performance in accurately forecasting DOC outcomes among TBI patients. Ongoing enhancements to ML algorithms contributes to the continuous refinement of clinical decision support systems, meeting the pressing demand within clinical practice for precise risk prediction models of the highest quality.

The present meta-analysis demonstrated that ML models yielded remarkable performance in predicting the DOC of TBI patients, particularly employed in case–control studies. However, in this study, the ML models did not consistently demonstrate a performance advantage over traditional LR models, and the assessment of clinical outcomes was limited by heterogeneity across studies. Therefore, it is imperative to formulate standardized reporting guidelines for ML in the context of TBI.

Availability of Data and Materials: The data are extracted from published studies and are available in the article, and the datasets are not subject to restrictions.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – X.Z., L.G., J.L.; Design – J.L.; Supervision – X.Z., L.G., J.L.; Resources – J.L.; Materials – X.Z., L.G., J.L.; Data collection and/or Processing – X.Z., L.G., J.L.; Analysis and/or linterpretation – X.Z., L.G., J.L.; Literature Search – J.L., X.Z.; Writing – X.Z., L.G., J.L.; Critical Review – J.L., X.Z.

Declaration of Interests: The authors have no conflicts of interest to declare.

Funding: This study was supported by Key Research Project of Sichuan Province Science and Technology Plan (2020YFS0489).

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Supplementary Table 1. The Inclusion of Literature Information in Age Subgroup Analysis

Author	AUC	CI	χ2	I^2
Zhou, Liang	0.939	[0.899;0.979]		
Wang, Ruoran	0.884	[0.826;0.942]		
Rocha, Thiago Augusto Hernandes	0.865	[0.856;0.874]		
Rocha, Thiago Augusto Hernandes	0.849	[0.846;0.852]		
Rocha, Thiago Augusto Hernandes	0.848	[0.844;0.852]		
Rocha, Thiago Augusto Hernandes	0.851	[0.849;0.853]		
Rocha, Thiago Augusto Hernandes	0.845	[0.843;0.847]		
Rocha, Thiago Augusto Hernandes	0.836	[0.827;0.845]		
Rocha, Thiago Augusto Hernandes	0.798	[0.788;0.808]		
Rocha, Thiago Augusto Hernandes	0.788	[0.777;0.799]		
Rocha, Thiago Augusto Hernandes	0.662	[0.660;0.664]		
Lang, Lijian	0.859	[0.838;0.880]		
Czeiter, Endre	0.851	[0.847;0.855]		
Wang, Yifei	0.922	[0.875;0.969]		
Kim, Hakseung	0.538	[0.416;0.660]		
Kim, Hakseung	0.587	[0.467;0.707]		
Kesmarky, Klara	0.852	[0.824;0.880]		
Kesmarky, Klara	0.826	[0.795;0.857]		
Rached, Mohamed A. K. B.	0.826	[0.795;0.857]		
Rached, Mohamed A. K. B.	0.839	[0.810;0.868]		
Oh, Hyun Soo	0.853	[0.779;0.927]		
Rodrigues de Souza, Matheus	0.802	[0.723;0.881]		
Rodrigues de Souza, Matheus	0.898	[0.844;0.952]		
Leto, Elio	0.901	[0.865;0.937]		
Han, Julian	0.8	[0.750;0.850]		
Han, Julian	0.83	[0.785;0.875]		
Han, Julian	0.8	[0.750;0.850]		
Han, Julian	0.81	[0.760;0.860]		
Han, Julian	0.8	[0.745;0.855]		
Han, Julian	0.86	[0.815;0.905]		
Han, Julian	0.89	[0.845;0.935]		
Han, Julian	0.84	[0.795;0.885]		
Han, Julian	0.88	[0.835;0.925]		
Han, Julian	0.87	[0.820;0.920]		
Maeda, Yukihiro	0.75	[0.715;0.785]		
Maeda, Yukihiro	0.86	[0.820;0.900]		
Maeda, Yukihiro	0.86	[0.825;0.895]		
Maeda, Yukihiro	0.81	[0.770;0.850]		
Maeda, Yukihiro	0.85	[0.805;0.895]		
Faried, Ahmad	0.932	[0.901;0.963]		
Faried, Ahmad	0.998	[0.997;0.999]		
Bertotti, Melina More	0.73	[0.695;0.765]		

(*Continued*)

Supplementary Table 1. The Inclusion of Literature Information in Age Subgroup Analysis (Continued)

Author	AUC	CI	χ2	I^2
Bertotti, Melina More	0.74	[0.710;0.770]		
Bertotti, Melina More	0.8	[0.770;0.830]		
Pourahmad, Saeedeh	0.695	[0.637;0.753]		
Pourahmad, Saeedeh	0.705	[0.652;0.758]		
Wang, Ruoran	0.857	[0.813;0.901]		
Zhang, Zan	0.813	[0.750;0.876]		
Zhang, Zan	0.931	[0.888;0.974]		
Zhang, Zan	0.953	[0.900;1.006]		
Zhang, Zan	0.924	[0.869;0.979]		
Zhang, Zan	0.832	[0.773;0.891]		
Zhang, Zan	0.893	[0.841;0.945]		
Zhang, Zan	0.913	[0.859;0.967]		
Zhang, Zan	0.877	[0.823;0.931]		
Gravesteijn, Benjamin Y.	0.81	[0.785;0.835]		
Gravesteijn, Benjamin Y.	0.81	[0.785;0.835]		
Gravesteijn, Benjamin Y.	0.79	[0.765;0.815]		
Gravesteijn, Benjamin Y.	0.81	[0.785;0.835]		
Gravesteijn, Benjamin Y.	0.81	[0.785;0.835]		
Gravesteijn, Benjamin Y.	0.81	[0.785;0.835]		
Gravesteijn, Benjamin Y.	0.81	[0.785;0.835]		
Gravesteijn, Benjamin Y.	0.81	[0.790;0.830]		
Gravesteijn, Benjamin Y.	0.8	[0.785;0.815]		
Gravesteijn, Benjamin Y.	0.79	[0.765;0.815]		
Gravesteijn, Benjamin Y.	0.8	[0.785;0.815]		
Gravesteijn, Benjamin Y.	0.8	[0.780;0.820]		
Gravesteijn, Benjamin Y.	0.81	[0.790;0.830]		
Gravesteijn, Benjamin Y.	0.81	[0.790;0.830]		
Hsu, Sheng-Der	0.82	[0.801;0.839]		
Hsu, Sheng-Der	0.921	[0.902;0.940]		
Hsu, Sheng-Der	0.735	[0.716;0.754]		
Hsu, Sheng-Der	0.846	[0.827;0.865]		
Hsu, Sheng-Der	0.716	[0.697;0.735]		
Hsu, Sheng-Der	0.71	[0.691;0.729]		
Hsu, Sheng-Der	0.917	[0.898;0.936]		
Bae, In-Suk	0.84	[0.782;0.898]		
Bae, In-Suk	0.792	[0.733;0.851]		
Gradisek, Primoz	0.811	[0.714;0.908]		
Gradisek, Primoz	0.92	[0.873;0.967]		
Gradisek, Primoz	0.92	[0.879;0.961]		
Kim, Sol Bi	0.925	[0.878;0.972]		
Charry, Jose D.	0.706	[0.591;0.821]		
Charry, Jose D.	0.585	[0.489;0.681]		
Charry, Jose D.	0.67	[0.576;0.764]		
Camarano, Joseph G.	0.863	[0.859;0.867]		
Camarano, Joseph G.	0.858	[0.847;0.869]		
Lu, Hsueh-Yi	0.961	[0.869;1.053]		
Lu, Hsueh-Yi	0.945	[0.866;1.023]		
Lu, Hsueh-Yi	0.919	[0.826;1.012]		
Lu, Hsueh-Yi	0.925	[0.830;1.019]		
Lu, Hsueh-Yi	0.901	[0.807;0.996]		
Lu, Hsueh-Yi	0.81	[0.704;0.917]		

(*Continued*)

Supplementary Table 1. The Inclusion of Literature Information in Age Subgroup Analysis (Continued)

Author	AUC	CI	χ2	I^2
Lu, Hsueh-Yi	0.778	[0.682;0.875]		
Lu, Hsueh-Yi	0.873	[0.772;0.974]		
Raj, Rahul	0.8	[0.765;0.835]		
Raj, Rahul	0.8	[0.770;0.830]		
Raj, Rahul	0.8	[0.770;0.830]		
Raj, Rahul	0.81	[0.780;0.840]		
Raj, Rahul	0.76	[0.730;0.790]		
Raj, Rahul	0.78	[0.750;0.810]		
Raj, Rahul	0.79	[0.760;0.820]		
Raj, Rahul	0.79	[0.760;0.820]		
Yuan, Fang	0.709	[0.672;0.746]		
Yuan, Fang	0.784	[0.751;0.817]		
Yuan, Fang	0.879	[0.853;0.905]		
Yuan, Fang	0.747	[0.717;0.777]		
Yuan, Fang	0.798	[0.767;0.829]		
Yuan, Fang	0.845	[0.818;0.872]		
Raj, Rahul	0.81	[0.780;0.840]		
Raj, Rahul	0.81	[0.775;0.845]		
Raj, Rahul	0.68	[0.640;0.720]		
Yang, Bocheng	0.777	[0.657;0.897]		
Abujaber, Ahmad	0.956	[0.938;0.974]		
Abujaber, Ahmad	0.916	[0.890;0.942]		
Song, Juhyun	0.912	[0.897;0.927]		
Song, Juhyun	0.94	[0.929;0.951]		
Song, Juhyun	0.922	[0.909;0.935]		
Lee, Soo Hoon	0.97	[0.961;0.979]		
Strnad, Matej	0.83	[0.715;0.945]		
Lingsma, Hester	0.77	[0.755;0.785]		
Lingsma, Hester	0.81	[0.800;0.820]		
Lingsma, Hester	0.79	[0.770;0.810]		
Lingsma, Hester	0.78	[0.770;0.790]		
Lingsma, Hester	0.81	[0.800;0.820]		
Lingsma, Hester	0.81	[0.795;0.825]		
Lingsma, Hester	0.85	[0.815;0.885]		
Lingsma, Hester	0.89	[0.865;0.915]		
Lingsma, Hester	0.9	[0.875;0.925]		
Lingsma, Hester	0.82	[0.785;0.855]		
Lingsma, Hester	0.86	[0.825;0.895]		
Lingsma, Hester	0.87	[0.840;0.900]		
Rubin, M. Laura	0.85	[0.790;0.910]		
Kamal, Vineet Kumar	0.836	[0.795;0.877]		
Kamal, Vineet Kumar	0.867	[0.828;0.906]		
Kamal, Vineet Kumar	0.873	[0.837;0.909]		
Kamal, Vineet Kumar	0.88	[0.842;0.918]		
Kamal, Vineet Kumar	0.871	[0.833;0.909]		
Kamal, Vineet Kumar	0.865	[0.822;0.908]		
Zhao, Jian-Lan	0.936	[0.923;0.949]		
Wang, Jian	0.882	[0.785;0.979]		
Age=Adult	**0.833**	**[0.821;0.845]**	**74663.24**	**99.81%**
Kim, Hakseung	0.946	[0.866;1.026]		
Kim, Hakseung	0.766	[0.616;0.916]		

(*Continued*)

Supplementary Table 1. The Inclusion of Literature Information in Age Subgroup Analysis (Continued)

Author	AUC	CI	χ2	I^2
Kennedy, Lori	0.909	[0.865;0.954]		
Greenan, Krista	0.82	[0.700;0.940]		
Mikkonen, Era D.	0.85	[0.785;0.915]		
Age=Pediatric	**0.878**	**[0.802;0.954]**	**7.94**	**49.62%**
Kim, Hakseung	0.632	[0.528;0.736]		
Kim, Hakseung	0.735	[0.642;0.828]		
Wan, Xueyan	0.76	[0.655;0.865]		
Wan, Xueyan	0.8	[0.698;0.902]		
Wan, Xueyan	0.76	[0.657;0.863]		
Wan, Xueyan	0.79	[0.685;0.895]		
Wan, Xueyan	0.73	[0.624;0.836]		
Wan, Xueyan	0.77	[0.659;0.881]		
Bobeff, Ernest J.	0.888	[0.834;0.942]		
Bobeff, Ernest J.	0.899	[0.845;0.953]		
Wang, Ruoran	0.712	[0.647;0.777]		
Wang, Ruoran	0.795	[0.739;0.851]		
Wang, Ruoran	0.785	[0.730;0.840]		
Wang, Ruoran	0.658	[0.602;0.714]		
Wang, Ruoran	0.792	[0.736;0.848]		
Wang, Ruoran	0.799	[0.746;0.852]		
Wang, Ruoran	0.766	[0.709;0.823]		
Age=Geriatric	**0.773**	**[0.738;0.808]**	**66.9**	**76.08%**

Supplementary Table 2. The Inclusion of Literature Information in Prediction Model Subgroup Analysis

Author	AUC	CI	χ^2	I^2
Zhou, Liang	0.939	[0.899;0.979]		
Wang, Ruoran	0.884	[0.826;0.942]		
Lang, Lijian	0.859	[0.838;0.880]		
Wang, Yifei	0.922	[0.875;0.969]		
Leto, Elio	0.901	[0.865;0.937]		
Bertotti, Melina More	0.73	[0.695;0.765]		
Bertotti, Melina More	0.74	[0.710;0.770]		
Bertotti, Melina More	0.8	[0.770;0.830]		
Wang, Ruoran	0.857	[0.813;0.901]		
Zhang, Zan	0.813	[0.750;0.876]		
Zhang, Zan	0.832	[0.773;0.891]		
Gravesteijn, Benjamin Y.	0.81	[0.785;0.835]		
Gravesteijn, Benjamin Y.	0.81	[0.790;0.830]		
Kennedy, Lori	0.909	[0.865;0.954]		
Bae, In-Suk	0.84	[0.782;0.898]		
Bae, In-Suk	0.792	[0.733;0.851]		
Bobeff, Ernest J.	0.888	[0.834;0.942]		
Bobeff, Ernest J.	0.899	[0.845;0.953]		
Gradisek, Primoz	0.92	[0.873;0.967]		
Gradisek, Primoz	0.92	[0.879;0.961]		
Kim, Sol Bi	0.925	[0.878;0.972]		
Lu, Hsueh-Yi	0.925	[0.830;1.019]		
Lu, Hsueh-Yi	0.873	[0.772;0.974]		
Yuan, Fang	0.709	[0.672;0.746]		
Yuan, Fang	0.784	[0.751;0.817]		
Yuan, Fang	0.879	[0.853;0.905]		
Yuan, Fang	0.747	[0.717;0.777]		
Yuan, Fang	0.798	[0.767;0.829]		
Yuan, Fang	0.845	[0.818;0.872]		
Yang, Bocheng	0.777	[0.657;0.897]		
Song, Juhyun	0.912	[0.897;0.927]		
Wang, Ruoran	0.792	[0.736;0.848]		
Lee, Soo Hoon	0.97	[0.961;0.979]		
Strnad, Matej	0.83	[0.715;0.945]		
Kamal, Vineet Kumar	0.836	[0.795;0.877]		
Kamal, Vineet Kumar	0.867	[0.828;0.906]		
Kamal, Vineet Kumar	0.873	[0.837;0.909]		
Kamal, Vineet Kumar	0.88	[0.842;0.918]		
Kamal, Vineet Kumar	0.871	[0.833;0.909]		
Kamal, Vineet Kumar	0.865	[0.822;0.908]		
Zhao, Jian-Lan	0.936	[0.923;0.949]		
Wang, Jian	0.882	[0.785;0.979]		
LR	**0.854**	**[0.834;0.873]**	**1002.5**	**95.91%**
Rocha, Thiago Augusto Hernandes	0.865	[0.856;0.874]		
Hsu, Sheng-Der	0.917	[0.898;0.936]		
Lu, Hsueh-Yi	0.945	[0.866;1.023]		
Lu, Hsueh-Yi	0.81	[0.704;0.917]		
Wang, Ruoran	0.658	[0.602;0.714]		
NB	**0.84**	**[0.699;0.981]**	**83.54**	**95.21%**
Rocha, Thiago Augusto Hernandes	0.849	[0.846;0.852]		

(*Continued*)

Supplementary Table 2. The Inclusion of Literature Information in Prediction Model Subgroup Analysis (Continued)

Author	AUC	CI	χ^2	I^2
Gravesteijn, Benjamin Y.	0.79	[0.765;0.815]		
Gravesteijn, Benjamin Y.	0.79	[0.765;0.815]		
Hsu, Sheng-Der	0.921	[0.902;0.940]		
Wang, Ruoran	0.795	[0.739;0.851]		
RF	**0.831**	**[0.759;0.902]**	**104.25**	**96.16%**
Rocha, Thiago Augusto Hernandes	0.848	[0.844;0.852]		
Gravesteijn, Benjamin Y.	0.81	[0.785;0.835]		
Gravesteijn, Benjamin Y.	0.81	[0.790;0.830]		
RR	**0.825**	**[0.768;0.881]**	**21.34**	**90.63%**
Rocha, Thiago Augusto Hernandes	0.851	[0.849;0.853]		
Gravesteijn, Benjamin Y.	0.81	[0.785;0.835]		
Gravesteijn, Benjamin Y.	0.8	[0.780;0.820]		
GBM	**0.822**	**[0.753;0.891]**	**34.75**	**94.24%**
Rocha, Thiago Augusto Hernandes	0.845	[0.843;0.847]		
BART	**0.845**	**[0.843;0.847]**	**0**	**-**
Rocha, Thiago Augusto Hernandes	0.836	[0.827;0.845]		
BT	**0.836**	**[0.827;0.845]**	**0**	**-**
Rocha, Thiago Augusto Hernandes	0.798	[0.788;0.808]		
Oh, Hyun Soo	0.853	[0.779;0.927]		
Pourahmad, Saeedeh	0.695	[0.637;0.753]		
Lu, Hsueh-Yi	0.919	[0.826;1.012]		
Lu, Hsueh-Yi	0.778	[0.682;0.875]		
Wang, Ruoran	0.712	[0.647;0.777]		
Greenan, Krista	0.82	[0.700;0.940]		
DT	**0.792**	**[0.720;0.863]**	**27.59**	**78.25%**
Rocha, Thiago Augusto Hernandes	0.788	[0.777;0.799]		
Gravesteijn, Benjamin Y.	0.81	[0.785;0.835]		
Gravesteijn, Benjamin Y.	0.8	[0.785;0.815]		
NN	**0.796**	**[0.771;0.822]**	**3.33**	**39.93%**
Rocha, Thiago Augusto Hernandes	0.662	[0.660;0.664]		
Hsu, Sheng-Der	0.716	[0.697;0.735]		
KNN	0.688	[0.345;1.031]	30.08	96.68%
Czeiter, Endre	0.851	[0.847;0.855]		
Kim, Hakseung	0.946	[0.866;1.026]		
Kim, Hakseung	0.538	[0.416;0.660]		
Kim, Hakseung	0.632	[0.528;0.736]		
Kesmarky, Klara	0.852	[0.824;0.880]		
Kesmarky, Klara	0.826	[0.795;0.857]		
Rached, Mohamed A. K. B.	0.826	[0.795;0.857]		
Rodrigues de Souza, Matheus	0.802	[0.723;0.881]		
Han, Julian	0.8	[0.750;0.850]		
Han, Julian	0.84	[0.795;0.885]		
Maeda, Yukihiro	0.81	[0.770;0.850]		
Wan, Xueyan	0.76	[0.655;0.865]		

(*Continued*)

Supplementary Table 2. The Inclusion of Literature Information in Prediction Model Subgroup Analysis (Continued)

Author	AUC	CI	χ^2	I^2
Wan, Xueyan	0.8	[0.698;0.902]		
Gradisek, Primoz	0.811	[0.714;0.908]		
Charry, Jose D.	0.67	[0.576;0.764]		
Camarano, Joseph G.	0.863	[0.859;0.867]		
Raj, Rahul	0.8	[0.770;0.830]		
Raj, Rahul	0.78	[0.750;0.810]		
Lingsma, Hester	0.77	[0.755;0.785]		
Lingsma, Hester	0.78	[0.770;0.790]		
Lingsma, Hester	0.85	[0.815;0.885]		
Lingsma, Hester	0.82	[0.785;0.855]		
Mikkonen, Era D.	0.85	[0.785;0.915]		
IMPACT	**0.805**	**[0.775;0.836]**	**430.95**	**94.90%**
Kim, Hakseung	0.766	[0.616;0.916]		
Kim, Hakseung	0.587	[0.467;0.707]		
Kim, Hakseung	0.735	[0.642;0.828]		
Han, Julian	0.8	[0.750;0.850]		
Han, Julian	0.86	[0.815;0.905]		
Maeda, Yukihiro	0.86	[0.820;0.900]		
Faried, Ahmad	0.932	[0.901;0.963]		
Faried, Ahmad	0.998	[0.997;0.999]		
Charry, Jose D.	0.706	[0.591;0.821]		
Camarano, Joseph G.	0.858	[0.847;0.869]		
CRASH	**0.821**	**[0.738;0.904]**	**870.98**	**98.97%**
Rached, Mohamed A. K. B.	0.839	[0.810;0.868]		
IMPACT+HAIS	**0.839**	**[0.810;0.868]**	**0**	**-**
Rodrigues de Souza, Matheus	0.898	[0.844;0.952]		
IMPACT+CT	**0.898**	**[0.844;0.952]**	**0**	**-**
Han, Julian	0.83	[0.785;0.875]		
Han, Julian	0.89	[0.845;0.935]		
Maeda, Yukihiro	0.86	[0.825;0.895]		
Charry, Jose D.	0.585	[0.489;0.681]		
CRASH+CT	**0.797**	**[0.580;1.013]**	**33.15**	**90.95%**
Han, Julian	0.81	[0.760;0.860]		
Han, Julian	0.88	[0.835;0.925]		
Maeda, Yukihiro	0.85	[0.805;0.895]		
Wan, Xueyan	0.76	[0.657;0.863]		
Wan, Xueyan	0.79	[0.685;0.895]		
Raj, Rahul	0.8	[0.770;0.830]		
Raj, Rahul	0.79	[0.760;0.820]		
Lingsma, Hester	0.81	[0.800;0.820]		
Lingsma, Hester	0.81	[0.800;0.820]		
Lingsma, Hester	0.89	[0.865;0.915]		
Lingsma, Hester	0.86	[0.825;0.895]		
IMPACT extended	**0.828**	**[0.802;0.854]**	**57.77**	**82.69%**
Han, Julian	0.8	[0.745;0.855]		
Han, Julian	0.87	[0.820;0.920]		
Wan, Xueyan	0.73	[0.624;0.836]		
Wan, Xueyan	0.77	[0.659;0.881]		
Raj, Rahul	0.81	[0.780;0.840]		
Raj, Rahul	0.79	[0.760;0.820]		

(*Continued*)

Supplementary Table 2. The Inclusion of Literature Information in Prediction Model Subgroup Analysis (Continued)

Author	AUC	CI	χ^2	I^2
Lingsma, Hester	0.79	[0.770;0.810]		
Lingsma, Hester	0.81	[0.795;0.825]		
Lingsma, Hester	0.9	[0.875;0.925]		
Lingsma, Hester	0.87	[0.840;0.900]		
IMPACT lab	**0.822**	**[0.788;0.856]**	**72.4**	**87.57%**
Maeda, Yukihiro	0.75	[0.715;0.785]		
TRISS	**0.75**	**[0.715;0.785]**	**0**	**-**
Pourahmad, Saeedeh	0.705	[0.652;0.758]		
Lu, Hsueh-Yi	0.961	[0.869;1.053]		
Lu, Hsueh-Yi	0.901	[0.807;0.996]		
Abujaber, Ahmad	0.916	[0.890;0.942]		
ANN	**0.868**	**[0.686;1.051]**	**52.11**	**94.24%**
Zhang, Zan	0.931	[0.888;0.974]		
Zhang, Zan	0.893	[0.841;0.945]		
Wang, Ruoran	0.766	[0.709;0.823]		
XGboost	**0.865**	**[0.651;1.079]**	**20.98**	**90.47%**
Zhang, Zan	0.953	[0.900;1.006]		
Zhang, Zan	0.913	[0.859;0.967]		
Song, Juhyun	0.94	[0.929;0.951]		
lightGBM	**0.939**	**[0.921;0.958]**	**1.18**	**0.00%**
Zhang, Zan	0.924	[0.869;0.979]		
Zhang, Zan	0.877	[0.823;0.931]		
FT-transformer	**0.9**	**[0.602;1.199]**	**1.42**	**29.34%**
Gravesteijn, Benjamin Y.	0.81	[0.785;0.835]		
Gravesteijn, Benjamin Y.	0.8	[0.785;0.815]		
Hsu, Sheng-Der	0.71	[0.691;0.729]		
Abujaber, Ahmad	0.956	[0.938;0.974]		
Wang, Ruoran	0.785	[0.730;0.840]		
SVM	**0.813**	**[0.701;0.925]**	**353.15**	**98.87%**
Gravesteijn, Benjamin Y.	0.81	[0.785;0.835]		
Gravesteijn, Benjamin Y.	0.81	[0.790;0.830]		
Rubin, M. Laura	0.85	[0.790;0.910]		
Lasso	**0.813**	**[0.783;0.842]**	**1.6**	**0.00%**
Hsu, Sheng-Der	0.82	[0.801;0.839]		
J48	**0.82**	**[0.801;0.839]**	**0**	**-**
Hsu, Sheng-Der	0.735	[0.716;0.754]		
Random tree	**0.735**	**[0.716;0.754]**	**0**	**-**
Hsu, Sheng-Der	0.846	[0.827;0.865]		
REP tree	**0.846**	**[0.827;0.865]**	**0**	**-**
Raj, Rahul	0.8	[0.765;0.835]		
Raj, Rahul	0.76	[0.730;0.790]		
Raj, Rahul	0.81	[0.780;0.840]		
APACHE II	**0.79**	**[0.723;0.856]**	**5.85**	**65.82%**
Raj, Rahul	0.81	[0.775;0.845]		
SAPS II	**0.81**	**[0.775;0.845]**	**0**	**-**
Raj, Rahul	0.68	[0.640;0.720]		
SOFA	**0.68**	**[0.640;0.720]**	**0**	**-**
Song, Juhyun	0.922	[0.909;0.935]		
MLP	**0.922**	**[0.909;0.935]**	**0**	**-**
Wang, Ruoran	0.799	[0.746;0.852]		
Adaboost	**0.799**	**[0.746;0.852]**	**0**	**-**

Supplementary Table 3. The Inclusion of Literature Information in Clinical Outcomes Subgroup Analysis

Author	AUC	CI	χ²	I^2
Zhou, Liang	0.939	[0.899;0.979]		
Rocha, Thiago Augusto Hernandes	0.865	[0.856;0.874]		
Rocha, Thiago Augusto Hernandes	0.849	[0.846;0.852]		
Rocha, Thiago Augusto Hernandes	0.848	[0.844;0.852]		
Rocha, Thiago Augusto Hernandes	0.851	[0.849;0.853]		
Rocha, Thiago Augusto Hernandes	0.845	[0.843;0.847]		
Rocha, Thiago Augusto Hernandes	0.836	[0.827;0.845]		
Rocha, Thiago Augusto Hernandes	0.798	[0.788;0.808]		
Rocha, Thiago Augusto Hernandes	0.788	[0.777;0.799]		
Rocha, Thiago Augusto Hernandes	0.662	[0.660;0.664]		
Oh, Hyun Soo	0.853	[0.779;0.927]		
Han, Julian	0.86	[0.815;0.905]		
Han, Julian	0.89	[0.845;0.935]		
Han, Julian	0.84	[0.795;0.885]		
Han, Julian	0.88	[0.835;0.925]		
Han, Julian	0.87	[0.820;0.920]		
Maeda, Yukihiro	0.86	[0.820;0.900]		
Maeda, Yukihiro	0.86	[0.825;0.895]		
Maeda, Yukihiro	0.81	[0.770;0.850]		
Maeda, Yukihiro	0.85	[0.805;0.895]		
Faried, Ahmad	0.998	[0.997;0.999]		
Pourahmad, Saeedeh	0.695	[0.637;0.753]		
Pourahmad, Saeedeh	0.705	[0.652;0.758]		
Wan, Xueyan	0.8	[0.698;0.902]		
Wan, Xueyan	0.79	[0.685;0.895]		
Wan, Xueyan	0.77	[0.659;0.881]		
Zhang, Zan	0.832	[0.773;0.891]		
Zhang, Zan	0.893	[0.841;0.945]		
Zhang, Zan	0.913	[0.859;0.967]		
Zhang, Zan	0.877	[0.823;0.931]		
Gravesteijn, Benjamin Y.	0.81	[0.790;0.830]		
Gravesteijn, Benjamin Y.	0.8	[0.785;0.815]		
Gravesteijn, Benjamin Y.	0.79	[0.765;0.815]		
Gravesteijn, Benjamin Y.	0.8	[0.785;0.815]		
Gravesteijn, Benjamin Y.	0.8	[0.780;0.820]		
Gravesteijn, Benjamin Y.	0.81	[0.790;0.830]		
Gravesteijn, Benjamin Y.	0.81	[0.790;0.830]		
Bae, In-Suk	0.792	[0.733;0.851]		
Bobeff, Ernest J.	0.899	[0.845;0.953]		
Lu, Hsueh-Yi	0.961	[0.869;1.053]		
Lu, Hsueh-Yi	0.945	[0.866;1.023]		
Lu, Hsueh-Yi	0.919	[0.826;1.012]		
Lu, Hsueh-Yi	0.925	[0.830;1.019]		
Raj, Rahul	0.76	[0.730;0.790]		
Raj, Rahul	0.78	[0.750;0.810]		
Raj, Rahul	0.79	[0.760;0.820]		
Raj, Rahul	0.79	[0.760;0.820]		
Yuan, Fang	0.747	[0.717;0.777]		
Yuan, Fang	0.798	[0.767;0.829]		
Yuan, Fang	0.845	[0.818;0.872]		
Yang, Bocheng	0.777	[0.657;0.897]		
Lingsma, Hester	0.78	[0.770;0.790]		
Lingsma, Hester	0.81	[0.800;0.820]		
Lingsma, Hester	0.81	[0.795;0.825]		
Lingsma, Hester	0.82	[0.785;0.855]		
Lingsma, Hester	0.86	[0.825;0.895]		
Lingsma, Hester	0.87	[0.840;0.900]		
Rubin, M. Laura	0.85	[0.790;0.910]		
Kamal, Vineet Kumar	0.867	[0.828;0.906]		
Kamal, Vineet Kumar	0.88	[0.842;0.918]		
Kamal, Vineet Kumar	0.865	[0.822;0.908]		
Zhao, Jian-Lan	0.936	[0.923;0.949]		
Wang, Jian	0.882	[0.785;0.979]		
Greenan, Krista	0.82	[0.700;0.940]		
Mikkonen, Era D.	0.85	[0.785;0.915]		
Consciousness disorders	**0.835**	**[0.820;0.850]**	**71860.58**	**99.91%**
Wang, Ruoran	0.884	[0.826;0.942]		
Lang, Lijian	0.859	[0.838;0.880]		
Czeiter, Endre	0.851	[0.847;0.855]		
Wang, Yifei	0.922	[0.875;0.969]		
Kim, Hakseung	0.946	[0.866;1.026]		
Kim, Hakseung	0.538	[0.416;0.660]		
Kim, Hakseung	0.632	[0.528;0.736]		
Kim, Hakseung	0.766	[0.616;0.916]		
Kim, Hakseung	0.587	[0.467;0.707]		
Kim, Hakseung	0.735	[0.642;0.828]		
Kesmarky, Klara	0.852	[0.824;0.880]		
Kesmarky, Klara	0.826	[0.795;0.857]		
Rached, Mohamed A. K. B.	0.826	[0.795;0.857]		
Rached, Mohamed A. K. B.	0.839	[0.810;0.868]		
Rodrigues de Souza, Matheus	0.802	[0.723;0.881]		
Rodrigues de Souza, Matheus	0.898	[0.844;0.952]		
Leto, Elio	0.901	[0.865;0.937]		
Han, Julian	0.8	[0.750;0.850]		
Han, Julian	0.83	[0.785;0.875]		
Han, Julian	0.8	[0.750;0.850]		
Han, Julian	0.81	[0.760;0.860]		
Han, Julian	0.8	[0.745;0.855]		
Maeda, Yukihiro	0.75	[0.715;0.785]		
Faried, Ahmad	0.932	[0.901;0.963]		
Bertotti, Melina More	0.73	[0.695;0.765]		
Bertotti, Melina More	0.74	[0.710;0.770]		
Bertotti, Melina More	0.8	[0.770;0.830]		
Wan, Xueyan	0.76	[0.655;0.865]		

(*Continued*)

Supplementary Table 3. The Inclusion of Literature Information in Clinical Outcomes Subgroup Analysis (Continued)

Author	AUC	CI	χ^2	I^2
Wan, Xueyan	0.76	[0.657;0.863]		
Wan, Xueyan	0.73	[0.624;0.836]		
Wang, Ruoran	0.857	[0.813;0.901]		
Zhang, Zan	0.813	[0.750;0.876]		
Zhang, Zan	0.931	[0.888;0.974]		
Zhang, Zan	0.953	[0.900;1.006]		
Zhang, Zan	0.924	[0.869;0.979]		
Gravesteijn, Benjamin Y.	0.81	[0.785;0.835]		
Gravesteijn, Benjamin Y.	0.81	[0.785;0.835]		
Gravesteijn, Benjamin Y.	0.79	[0.765;0.815]		
Gravesteijn, Benjamin Y.	0.81	[0.785;0.835]		
Gravesteijn, Benjamin Y.	0.81	[0.785;0.835]		
Gravesteijn, Benjamin Y.	0.81	[0.785;0.835]		
Gravesteijn, Benjamin Y.	0.81	[0.785;0.835]		
Hsu, Sheng-Der	0.82	[0.801;0.839]		
Hsu, Sheng-Der	0.921	[0.902;0.940]		
Hsu, Sheng-Der	0.735	[0.716;0.754]		
Hsu, Sheng-Der	0.846	[0.827;0.865]		
Hsu, Sheng-Der	0.716	[0.697;0.735]		
Hsu, Sheng-Der	0.71	[0.691;0.729]		
Hsu, Sheng-Der	0.917	[0.898;0.936]		
Kennedy, Lori	0.909	[0.865;0.954]		
Bae, In-Suk	0.84	[0.782;0.898]		
Bobeff, Ernest J.	0.888	[0.834;0.942]		
Gradisek, Primoz	0.811	[0.714;0.908]		
Gradisek, Primoz	0.92	[0.873;0.967]		
Gradisek, Primoz	0.92	[0.879;0.961]		
Kim, Sol Bi	0.925	[0.878;0.972]		
Charry, Jose D.	0.706	[0.591;0.821]		
Charry, Jose D.	0.585	[0.489;0.681]		
Charry, Jose D.	0.67	[0.576;0.764]		
Camarano, Joseph G.	0.863	[0.859;0.867]		
Camarano, Joseph G.	0.858	[0.847;0.869]		
Lu, Hsueh-Yi	0.901	[0.807;0.996]		
Lu, Hsueh-Yi	0.81	[0.704;0.917]		
Lu, Hsueh-Yi	0.778	[0.682;0.875]		
Lu, Hsueh-Yi	0.873	[0.772;0.974]		
Raj, Rahul	0.8	[0.765;0.835]		
Raj, Rahul	0.8	[0.770;0.830]		
Raj, Rahul	0.8	[0.770;0.830]		
Raj, Rahul	0.81	[0.780;0.840]		
Yuan, Fang	0.709	[0.672;0.746]		
Yuan, Fang	0.784	[0.751;0.817]		
Yuan, Fang	0.879	[0.853;0.905]		
Raj, Rahul	0.81	[0.780;0.840]		
Raj, Rahul	0.81	[0.775;0.845]		
Raj, Rahul	0.68	[0.640;0.720]		
Abujaber, Ahmad	0.956	[0.938;0.974]		
Abujaber, Ahmad	0.916	[0.890;0.942]		
Song, Juhyun	0.912	[0.897;0.927]		
Song, Juhyun	0.94	[0.929;0.951]		
Song, Juhyun	0.922	[0.909;0.935]		

(*Continued*)

Supplementary Table 3. The Inclusion of Literature Information in Clinical Outcomes Subgroup Analysis (Continued)

Author	AUC	CI	χ^2	I^2
Wang, Ruoran	0.712	[0.647;0.777]		
Wang, Ruoran	0.795	[0.739;0.851]		
Wang, Ruoran	0.785	[0.730;0.840]		
Wang, Ruoran	0.658	[0.602;0.714]		
Wang, Ruoran	0.792	[0.736;0.848]		
Wang, Ruoran	0.799	[0.746;0.852]		
Wang, Ruoran	0.766	[0.709;0.823]		
Lee, Soo Hoon	0.97	[0.961;0.979]		
Strnad, Matej	0.83	[0.715;0.945]		
Lingsma, Hester	0.77	[0.755;0.785]		
Lingsma, Hester	0.81	[0.800;0.820]		
Lingsma, Hester	0.79	[0.770;0.810]		
Lingsma, Hester	0.85	[0.815;0.885]		
Lingsma, Hester	0.89	[0.865;0.915]		
Lingsma, Hester	0.9	[0.875;0.925]		
Kamal, Vineet Kumar	0.836	[0.795;0.877]		
Kamal, Vineet Kumar	0.873	[0.837;0.909]		
Kamal, Vineet Kumar	0.871	[0.833;0.909]		
Death	**0.823**	**[0.807;0.840]**	**2930.31**	**96.69%**