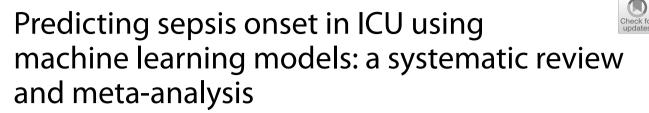
# RESEARCH





Zhenyu Yang<sup>1</sup>, Xiaoju Cui<sup>2</sup> and Zhe Song<sup>3\*</sup>

## Abstract

**Background** Sepsis is a life-threatening condition caused by an abnormal response of the body to infection and imposes a significant health and economic burden worldwide due to its high mortality rate. Early recognition of sepsis is crucial for effective treatment. This study aimed to systematically evaluate the performance of various machine learning models in predicting the onset of sepsis.

**Methods** We conducted a comprehensive search of the Cochrane Library, PubMed, Embase, and Web of Science databases, covering studies from database inception to November 14, 2022. We used the PROBAST tool to assess the risk of bias. We calculated the predictive performance for sepsis onset using the C-index and accuracy. We followed the PRISMA guidelines for this study.

**Results** We included 23 eligible studies with a total of 4,314,145 patients and 26 different machine learning models. The most frequently used models in the studies were random forest (n=9), extreme gradient boost (n=7), and logistic regression (n=6) models. The random forest (test set n=9, acc=0.911) and extreme gradient boost (test set n=7, acc=0.957) models were the most accurate based on our analysis of the predictive performance. In terms of the C-index outcome, the random forest (n=6, acc=0.79) and extreme gradient boost (n=7, acc=0.83) models showed the highest performance.

**Conclusion** Machine learning has proven to be an effective tool for predicting sepsis at an early stage. However, to obtain more accurate results, additional machine learning methods are needed. In our research, we discovered that the XGBoost and random forest models exhibited the best predictive performance and were most frequently utilized for predicting the onset of sepsis.

Trial registration CRD42022384015

Keywords Machine learning, Sepsis, Intensive care units, Meta-analysis

\*Correspondence:

Zhe Song

soongzhe@163.com

<sup>1</sup> Kunming Medical University, Kunming, Yunnan, China
<sup>2</sup> Chengyang District People's Hospital, Qingdao, Shandong, China

<sup>3</sup> Qinghai University, Xining, Qinghai, China

Qinghai University, Xining, Qinghai, China

### **Introduction** Sepsis is a sev

Sepsis is a severe and potentially life-threatening condition resulting from a dysregulated immune response to infection [1]. Early detection and prompt treatment are crucial for improving patient outcomes and reducing health care costs. In recent years, machine learning (ML) models have emerged as promising tools for detecting and managing sepsis in the intensive care unit (ICU) [2]. These models use complex algorithms and statistical



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methods to learn from large volumes of patient data, including vital signs, laboratory results, and electronic health records, and to predict the onset of sepsis before its clinical manifestations become apparent [3]. The early identification and treatment of sepsis are related to the improvement of patient prognosis. Machine learningbased warning systems may shorten recognition time. Adams R et al. [4] set up a system called the "Targeted Real-time Early Warning System", and they found that early warning systems have the potential to identify sepsis patients early and improve their prognosis and can identify and prioritize sepsis patients who would benefit the most from early treatment. By enabling early detection, ML models hold tremendous potential for enhancing patient care and reducing the burden of sepsis on health care systems worldwide.

The Sepsis-3 definitions suggest that patients with at least two of the following three clinical variables may be prone to the poor outcomes typical of sepsis: (1) a low blood pressure (SBP  $\leq$  100 mmHg), (2) a high respiratory rate ( $\geq$  22 breaths per min), or (3) altered mentation (Glasgow coma scale score <15). Machine learning can utilize computers to review a large number of clinical cases, and mature machine learning models can be used to make real-time evaluations of whether patients will develop sepsis, allowing for immediate intervention.

In this study, we aimed to explore the use of ML models for predicting the onset of sepsis in the ICU. Specifically, we reviewed the literature on ML models for sepsis prediction, highlighting their strengths and limitations. Additionally, in this article, we discuss the potential impact of these models on patient outcomes, clinical decision-making, and health care costs. Through this meta-analysis, we hope to shed light on the promise of ML models as tools for improving the management of sepsis in the ICU and beyond.

### Methods

#### Study design and literature search

This study retrieved relevant studies on the timing of sepsis diagnosis by machine learning from the Cochrane Library, Embase, PubMed, and Web of Science databases and extracted data from these studies. The Cochrane Library, Embase, PubMed and Web of Science databases were searched from inception to 14/11/2022. Search formulas were constructed based on combinations of MeSH headings and free words. We did not put any restriction on the language or region. The literature search was completed by Zhenyu Yang and Xiaoju Cui (the search detail is shown in Supplementary file 2). All selected studies were imported to EndNote 2020. We filtered studies according to the abstract. Duplicate articles were deleted. Literature screening was independently performed by

two reviewers (Zhenyu Yang and Xiaoju Cui). Any disagreement was settled by a third reviewer. The retrieval formular file is presented in Supplementary material 2.

### Inclusion and exclusion criteria

Inclusion criteria.

- (1) Randomized controlled trials (RCTs), prospective cohort studies, and nested case–control studies.
- (2) Studies in which the predictive model was completely established.

Exclusion criteria.

- (1) Studies unrelated to sepsis
- (2) Studies with incomplete data
- (3) Studies in which the outcome measures related to the effectiveness of predictive measures were not included.
- (4) Animal studies, reviews, conference abstracts, guidelines, letters, comments, and meta-analyses
- (5) Non-RCT research designs
- (6) Non-English articles
- (7) Basic articles on pathology, physiology, and biochemistry
- (8) Duplicate publications

## **Data extraction**

The data extraction form was detailed according to the Modified CHARMS checklist. The checklist included the name of the first author, publication date, nationality, duration of data collection, study design, type of validation (internal, external, random split and time split) and sample size (total number of participants, development and testing clusters).

## **Risk of bias assessment**

We used PROBAST and an external prognostic validity model to assess the risk of bias of the selected studies [5]. PROBAST is a checklist designed for systemic reviews of diagnostic or prognostic prediction models. The risk of bias was assessed independently by two reviewers (Zhe Song and Zhenyu Yang). PROBAST consists of two parts: A. an overall bias risk assessment (including research objects, predictors, results and statistical methods) and B. an overall applicability assessment (research objects, predictors and results).

### Statistical analysis

We performed descriptive statistics to summarize the characteristics of the models. For prediction models that were evaluated in more than two independent datasets, a random effect meta-analysis was conducted to estimate

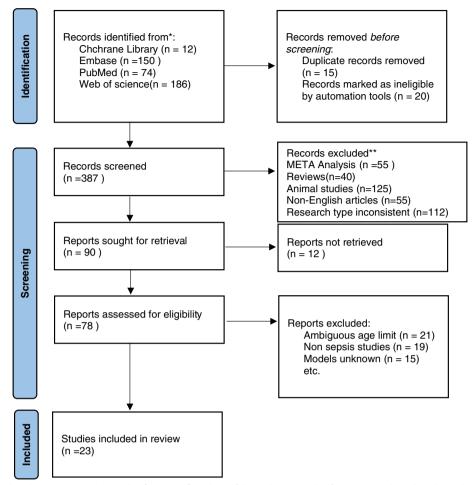


Fig. 1 PRISMA Study Selection Flowing Chart. This figure is a flowchart of the inclusion article after screening based on the inclusion and exclusion criteria in this study

their performance and accuracy. If a measure of uncertainty, such as the standard error or 95% confidence interval, was unavailable for the mean C-index, we computed it based on the number of events and participants. All data analyses were carried out using R software version 4.1.1.

## Results

### **Study selection**

A total of 422 articles were identified through various databases, including the Cochrane Library (n=12), Embase (n=150), PubMed (n=74), and Web of Science (n=186) databases. After eliminating 15 duplicate articles and excluding ineligible records using automation tools, we browsed 387 articles. Ultimately, 23 articles met the inclusion criteria and were included in our study [2, 6–27]. Figure 1 displays the PRISMA flow diagram illustrating our study selection process. The selection was conducted independently by two reviewers (Zhenyu Yang

and Xiaoju Cui). Any discrepancies were resolved by a third reviewer.

### **Characteristics of included studies**

A total of 1,287,160 individuals were included in this study, with 167,338 individuals included in the validation set. All articles analysed were published within the past 5 years, indicating a growing interest in the use of machine learning for sepsis prediction. Our research identified 81 prognostic models, including 5 based on deep learning, 4 based on InSight, 10 based on logistic regression, 6 based on multilayer perceptron, 8 based on neural networks, 8 based on support vector machines, 14 based on XGBoost, 15 based on random forest, and 11 based on SOFA. Detailed characteristics of the included studies can be found in Table 1.

#### **Quality assessment**

The quality assessment was conducted independently by two reviewers (Zhenyu Yang and Xiaoju Cui), and

Studies	First Author	Nation	Study Type	Sample source	Disease background	Diagnosis of sepsis	Missing data	Model type
SSP: Early prediction of sepsis using fully connected LSTM- CNN model	Alireza Rafiei2020	lran	Retrospective Cohort	Retrospectively	≥ 14y patients and ICU LOS> 10d	Sepsis 3.0	Multiple imputation	SSP-LSTM, SSP-GRU, InSight, AISE
Evaluation of a machine learning algorithm for up to 48-h advance prediction of sepsis using six vital signs	Christopher Barton2019	U.S.A	Prospectively	Prospectively	≥ 18y patients	Sepsis 3.0	Multiple imputation	MLA • SIRS • MEWS • SOFA
Predicting 30-days mortal- ity for MIMIC-III patients with sepsis-3: a machine learning approach using Xgboost	Nianzong Hou2020	P.R.C	Prospectively	Prospectively	≥ 18y patients and ICU LOS> 24d	Sepsis 3.0	Delete	XGBoost, LR,SAPS-II
A machine learning-based model for 1-year mortality prediction in patients admit- ted to an Intensive Care Unit with a diagnosis of sepsis	J E García- Gallo2018	Colom- bia	Retrospectively	Retrospectively	≥ 16y patients	Sepsis 3.0	Multiple imputation	SGB、OASIS、SOFA、SAPS2
Interpretable Machine Learn- ing for Early Predic- tionofPrognosisinSepsis:ADis- covery and Validation Study	Chang Hu2022	P.R.C	Prospectively	Prospectively	≥ 18y patients and ICU LOS> 24d	Sepsis 3.0	Multiple imputation	SVM、KNN、XGBoost、DT、RF、NB、LR
Machine Learn- ing Model to Iden- tify Sepsis Patients in the Emergency Depart- ment: Algorithm Develop- ment and Validation	Lin PC2021	P.R.C	Retrospective Cohort	Retrospective Cohort	≥ 20y patients	Sepsis 3.0	Multiple imputation	XGBoost 、 SIRS 、 SOFA
Dynamic Sepsis Predic- tion for Intensive Care Unit Patients Using XGBoost-Based Model With Novel Time- Dependent Features	Shuhui Liu2017	P.R.C	Retrospective Cohort	Retrospective Cohort	≥ 18y patients	Sepsis 3.0	Multiple imputation	RF 、GRU 、CNNLSTM 、EASP
Effect of a machine learning- based severe sepsis predic- tion algorithm on patient survival and hospital length of stay: a randomised clinical trial	Shimabukuro DW2018	U.S.A	Retrospective Cohort	Retrospective Cohort	≥ 18y patients	Sepsis 3.0	Multiple imputation	MLA • SIRS • MEWS • SOFA
A Predictive Model Based on Machine Learning for the Early Detection of Late-Onset Neonatal Sep- sis: Development and Obser- vational Study	Wongeun Song2022	KOREA	Retrospective Cohort	Retrospective Cohort	≥ 18y patients	Sepsis 3.0	Multiple imputation	RF • LR • SVM • NB • XGBOOST

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Table 1 (continued)								
Studies	First Author	Nation	Study Type	Sample source	Disease background	Diagnosis of sepsis	Missing data	Model type
Machine learning approach for the prediction of 30-day mortality in patients with sep- sis-associated encephalopa- thy	Liwei Peng2022	P.R.C	Retrospective Cohort	Retrospective Cohort	≥ 18y patients	Sepsis 3.0	Multiple imputation	CS · MIG · LLI · ET · RF · GB
Development and validation of a novel blending machine learning model for hospital mortality prediction in ICU patients with Sepsis	Zhixuan Zeng2021	P.R.C	Retrospective Cohort	Retrospective Cohort	≥ 18y patients	Sepsis 3.0	Multiple imputation	SAPSII、SOFA、LR、LDA、CART、NB、K NN、MLP、SVM、RF、XGB
Machine learning predicts mortality in septic patients using only routinely available ABG variables: a multi-centre evaluation	Bernhard Wer- nly2021	Austria	Retrospective Cohort	Retrospective Cohort	≥ 18y patients	Sepsis 3.0	Multiple imputation	LR、LSTM、SOFA
A Machine Learning Model for Accurate Prediction of Sepsis in ICU Patients	Dong Wang2021	P.R.C	Retrospective Cohort	Retrospective Cohort	≥ 18y patients	Sepsis 3.0	Multiple imputation	RF
Early Prediction of Mortality, Severity, and Length of Stay in the Intensive Care Unit of Sepsis Patients Based on Sepsis 3.0 by Machine Learning Models	Longxiang Su2021	Ger- many	Retrospective Cohort	Retrospective Cohort	≥ 18y patients	Sepsis 3.0	Multiple imputation	LR 、 RF 、 XGBoost
Supervised classifica- tion techniques for pre- diction of mortal- ity in adult patients with sep- sis	Rodríguez A2021 Colom- bia	Colom- bia	Retrospective Cohort	Retrospective Cohort	≥ 18y patients	Sepsis 3.0	Multiple imputation	DT • RF • NN • SVM
A Machine Learning Sepsis Prediction Algorithm for Intended Intensive Care Unit Use (NAVOY Sepsis): Proof-of-Concept Study	Inger Pers- son 2021	Sweden	Retrospective Cohort	Retrospective Cohort	≥ 18y patients	Sepsis 3.0	Multiple imputation	NAVOY
Development of a Nomo- gram to Predict 28-Day Mortality of Patients With Sepsis-Induced Coagulopa- thy: An Analysis of the MIMIC- III Database	Zongqing Lu2021	P.R.C	Retrospective Cohort	Retrospective Cohort	≥ 18y patients	Sepsis 3.0	Multiple imputation	Nomogram 、SOFA、LODS、SAPS II、SIC score

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Studies	First Author	Nation	Study Type	Sample source	Disease background	Diagnosis of sepsis	Missing data	Model type	
A Simple Weaning Model Based on Interpretable Machine Learning Algorithm for Patients With Sepsis: A Research of MIMIC-IV and eICU Databases	Wanjun Liu2022	P.R.C	Retrospective Cohort	Retrospective Cohort	≥ 18y patients	Sepsis 3.0	Multiple imputation	XGBOOST • MLP • RF • SVM • LR • KNN	· SVM · LR · KNN
The development an artificial intelligence algorithm for early sepsis diagnosis in the intensive care unit	Yuan KC2020	P.R.C	Retrospective Cohort	Retrospective Cohort	≥ 18y patients	Sepsis 3.0	Multiple imputation	XGBoost 、SOFA	
Early diagnosis of blood- stream infections in the inten- sive care unit using machine- learning algorithms	Michael Roimi2019	Israel	Retrospective Cohort	Retrospective Cohort	≥ 18y patients	Sepsis 3.0	Multiple imputation	Ч.	
Predicting sepsis with a recur- rent neural network using the MIMIC III database	Matthieu Scherpf2019	Ger- many	Retrospective Cohort	Retrospective Cohort	≥ 18y patients	Sepsis 3.0	Multiple imputation	RNN 、 InSight	
Predicting central line-associ- ated bloodstream infections and mortality using super- vised machine learning	Joshua P. Par- reco20182018	U.S.A	Retrospective Cohort	Retrospective Cohort	≥ 19y patients	Sepsis 3.1	Multiple imputation	LR、GBT、DL	
Multicentre validation of a sepsis prediction algorithm using only vital sign data in the emergency department, general ward and ICU	Qingqing Mao2018	U.S.A	Retrospective Cohort	Retrospective Cohort	≥ 18y patients	Sepsis 3.0	Multiple imputation	Insight、 MEWS 、 SOFA 、 SIRS	FA 、 SIRS
Studies	Train set sepsis number	Train set number	number Testing set	t Method of testing	sting Test set sepsis number		Test set number	Number of variables	Outcome indicators
SSP: Early prediction of sepsis using fully connected LSTM- CNN model	2542	20336	-	Multicenter	2500	20000		4	AUROC, Sensitivity Specificity
Evaluation of a machine learning algorithm for up to 48-h advance prediction of sepsis using six vital signs	2649	91445	-	Multicenter	1024	21507		4	AUROC Sensitivity Specificity
Predicting 30-days mortal- ity for MIMIC-III patients with sepsis-3: a machine learning approach using Xgboost	10704	46520	-	Multicenter	88	4559		12	AUROC

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Table 1 (continued)								
Studies	Train set sepsis number	Train set number	Testing set	Method of testing	Test set sepsis number	Test set number	Number of variables	Outcome indicators
A machine learning-based model for 1-year mortality prediction in patients admit- ted to an Intensive Care Unit with a diagnosis of sepsis	46520	58977	-	Multicenter	5650	15254	<u>8</u>	AUROC
Interpretable Machine Learn- ing for Early Predic- tionofPrognosisin Sepsis: ADis- covery and Validation Study	12292	76540	<del></del>	Multicenter	8817	12292	15	AUROC Sensitivity Specificity
Machine Learn- ing Model to Iden- tify Sepsis Patients in the Emergency Depart- ment: Algorithm Develop- ment and Validation	6637	8296	-	Random sampling	506	1744	26	AUROC Sensitivity Specificity
Dynamic Sepsis Predic- tion for Intensive Care Unit Patients Using XGBoost- Based Model With Novel Time-Dependent Features	3526	34472	-	Random sampling	4526	34472	30	AUROC Sensitivity Specificity
Effect of a machine learning- based severe sepsis predic- tion algorithm on patient survival and hospital length of stay: a randomised clinical trial	67	142	0	Single center			m	AUROC Sensitivity Specificity
A Predictive Model Based on Machine Learning for the Early Detection of Late-Onset Neonatal Sep- sis: Development and Obser- vational Study	1572	40366	-	Multicenter	315	1257	21	AUROC Sensitivity Specificity
Machine learning approach for the prediction of 30-day mortality in patients with sepsis-associated encephalopathy	4897	382278	-	Multicenter	2097	382278	15	AUROC Sensitivity Specificity
Development and validation of a novel blending machine learning model for hospital mortality prediction in ICU patients with Sepsis	12558	200859	_	Multicenter	12095	61532	Q	AUROC

Table 1 (continued)								
Studies	Train set sepsis number	Train set number	Testing set	Method of testing	Test set sepsis number	Test set number	Number of variables	Outcome indicators
Machine learning predicts mortality in septic patients using only routinely available ABG variables: a multi-centre evaluation	8061	61532	_	Multicenter	3853	200859	23	Sensitivity Specificity
A Machine Learning Model for Accurate Prediction of Sepsis in ICU Patients	3539	17005	_	Multicenter	910	17005	55	AUROC, Sensitivity Specificity
Early Prediction of Mortality, Severity, and Length of Stay in the Intensive Care Unit of Sepsis Patients Based on Sepsis 3.0 by Machine Learning Models	2436	11512	0	Single center			26	AUROC, Sensitivity Specificity
Supervised classifica- tion techniques for pre- diction of mortal- ity in adult patients with sep- sis	2510	5022	-	Multicenter	2510	5022	27	AUROC, Sensitivity Specificity
A Machine Learning Sepsis Prediction Algorithm for Intended Intensive Care Unit Use (NAVOY Sepsis): Proof-of-Concept Study	2893	61532	0	Single center			Q	AUROC Sensitivity Specificity
Development of a Nomo- gram to Predict 28-Day Mortality of Patients With Sepsis-Induced Coagulopa- thy: An Analysis of the MIMIC- III Database	3280	9432	-	Multicenter	286	3280	1	AUROC
A Simple Weaning Model Based on Interpretable Machine Learning Algorithm for Patients With Sepsis: A Research of MIMIC-IV and elCU Databases	5020	10832	-	Multicenter	7081	33790	20	AUROC Sensitivity Specificity
The development an artifi- cial intelligence algorithm for early sepsis diagnosis in the intensive care unit	319	1588	0	Single center			19	AUROC Sensitivity Specificity

lable 1 (continued)								
Studies	Train set sepsis number	Train set sepsis Train set number Testing set number	Testing set	Method of testing Test set sepsis number	Test set sepsis number	Test set number	Number of variables	Outcome indicators
Early diagnosis of blood- stream infections in the intrensive care unit using machine-learning algorithms	1021	1812	-	Multicenter	2351	7419	29	AUROC Sensitivity Specificity
Predicting sepsis with a recur-4278 rent neural network using the MIMIC III database	4278	58976	0	Single center			10	AUROC
Predicting central line-associ-22201 ated bloodstream infections and mortality using super- vised machine learning	22201	57786	0	Single center			37	AUROC Sensitivity Specificity
Multicentre validation of a sepsis prediction algorithm using only vital sign data in the emergency department, general ward and ICU	1179	21604	0	Single center			7	AUROC Sensitivity Specificity

any discrepancies were resolved by a third reviewer. The results of the quality assessment are presented in the risk of bias picture (Fig. 2). Two studies (8.6%) were deemed to have a high risk of bias in the participant domain, 13 studies (58.3%) were deemed to have a high risk of bias in the analysis domain, and two studies (8.6%) were deemed to have a high risk of bias in the outcome domain. No studies were deemed to have a high risk of bias in the predictor domain. A high risk of bias in the analysis domain may be attributed to an inadequate sample size, insufficient events per variable (EPV), improper handling of missing data, or failure to report how missing data were handled. The PRISMA checklist can be found in Supplementary file 1.

### Predictors

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Age, creatinine levels, and sodium levels were the most frequently used predictors (n=12), followed by blood pressure and platelet levels (n=11) and heart rate (n=9). The remaining predictors were ranked in descending order of frequency as follows: lactate levels and temperature (n=9), the WBC count (n=8), the respiratory rate and SOFA score (n=7), glucose, haemoglobin, MCHC, and PaO2 levels (n=6), the GCS score, ICU LOS, lymphocyte count, and PaCO2 levels (n=5), and BUN levels, cancer, and sex (n=4). These results are presented in Fig. 3.

#### Training set and test set accuracy

In the training set, the random forest model was the most frequently applied machine learning model (n=9), with an accuracy of 0.911 (0.485, 0.991). The XGBoost model showed the best predictive performance (n=6), with an accuracy of 0.970 (0.487, 0.997). In the test set, the random forest model was also the most frequently applied machine learning model (n=7), with an accuracy of 0.795 (0.638, 0.895). The deep learning model showed the best predictive performance (n=3), with an accuracy of 0.830 (0.814, 0.845). These results are presented in Figs. 4, 5, 6, 7 and 8.

#### Training set and test set c-index

Regarding the c-index results, in the training set, the XGBoost model was the most frequently utilized machine learning model, with a c-index of 0.83 (0.83, 0.84) in 7 studies. The InSight model exhibited the best performance, with a c-index of 0.91 (0.90, 0.93) in 2 studies. On the other hand, in the test set, the random forest model was the most frequently employed machine learning model, with a c-index of 0.83 (0.82,0.83) in 5 studies. In terms of performance, the random forest model (n = 5, c-index = 0.83 (0.82,0.83)) and XGBoost model (n = 3, c-index = 0.83 (0.82,0.84)) exhibited similar performance.

Detailed datasets can be found in Figs. 9, 10, 11, 12 and 13, and the overall results are presented in Supplementary file 3.

#### Discussion

The present study investigated 68 prognostic prediction models across 23 studies to assess the potential of machine learning models for predicting sepsis in the ICU. However, the risk of bias assessment revealed a high risk of bias in the analysis domain, which may be attributed to the small sample size, the processing of missing data, and the interpretation of complex data. Therefore, the research findings may have some deviation due to the insufficient sample size.

Sepsis is a severe medical condition that can cause widespread inflammation and damage to vital organs.

Early detection and treatment of sepsis are critical for improving patient outcomes and reducing health care costs. ML models can analyse large amounts of patient data, including vital signs, laboratory results, and electronic health records, to detect early signs of sepsis. ML algorithms can provide physicians with real-time recommendations for patient treatment and management based on the latest medical knowledge and patient data. The use of ML models for predicting the onset of sepsis in the ICU has the potential to revolutionize the way in which sepsis is detected, treated, and managed, leading to better patient outcomes and reduced health care costs.

Several studies have explored the potential of machine learning algorithms for predicting sepsis. Heather M et al. [28] developed a machine learning algorithm to

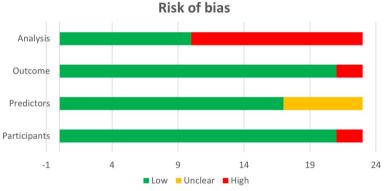


Fig. 2 Risk of Bias Assessment. This figure illustrates the risk bias included in this study

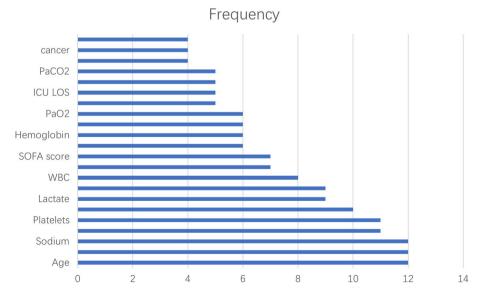
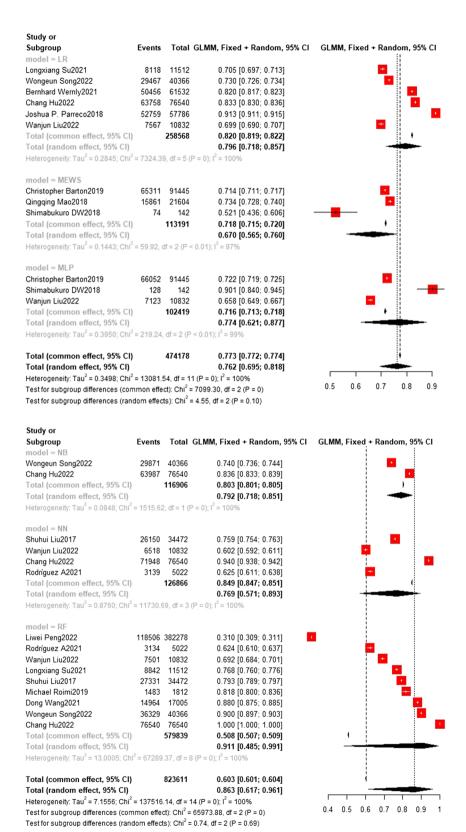


Fig. 3 Predictors Frequency Bar Chart. This figure indicates the number of times the items on the left side of the figure were used as indicators in the included literature

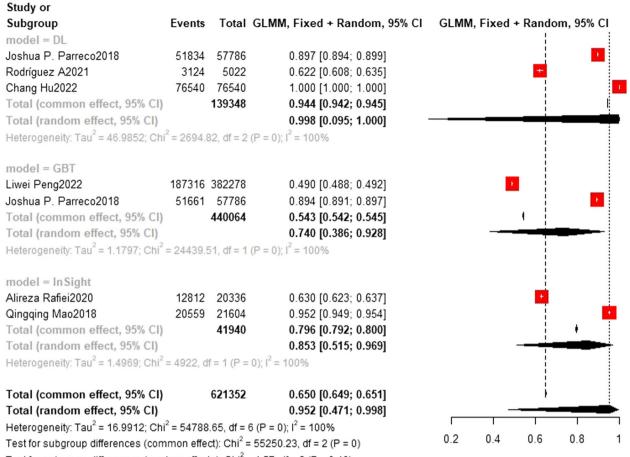
Study or Subgroup	Events	Total	GLMM, Fixed + Random, 95% Cl	GLMM, Fixed + Random, 95% CI
model = SOFA				
Qingqing Mao2018	7503	21604	0.347 [0.341; 0.354]	-
Yuan KC2020	790	1588	0.497 [0.473; 0.522]	<b></b>
Shimabukuro DW2018	75	142	0.528 [0.443; 0.612]	— <u>—</u>
Christopher Barton2019	54456	91445	0.596 [0.592; 0.599]	•
Bernhard Wernly2021	44303	61532	0.720 [0.716; 0.724]	•
Lin PC2021	6554	8296	0.790 [0.781; 0.799]	<b>•</b>
Total (common effect, 95% CI)		184607	0.616 [0.614; 0.618]	•
Total (random effect, 95% CI)			0.588 [0.460; 0.706]	
Heterogeneity: Tau <sup>2</sup> = 0.4117; Chi <sup>2</sup>	= 9979.76	6, df = 5 (	$(P = 0); I^2 = 100\%$	
model = SVM				
Rodríguez A2021	3099	5022	0.617 [0.603; 0.631]	<b>—</b>
Chang Hu2022	57175	76540		
Waniun Liu2022	8153	10832	0.753 [0.744; 0.761]	+
Wongeun Song2022	37540	40366	0.930 [0.927; 0.932]	•
Total (common effect, 95% CI)		132760		
Total (random effect, 95% CI)			0.788 [0.635; 0.889]	
Heterogeneity: Tau <sup>2</sup> = 0.6029; Chi <sup>2</sup>	= 5846.0	1, df = 3 (	(P = 0); I <sup>2</sup> = 100%	
model = XGBoost				
Wanjun Liu2022	7892	10832	0.729 [0.720; 0.737]	
Longxiang Su2021	8882	11512	0.772 [0.764; 0.779]	-
Lin PC2021	6471	8296	0.780 [0.771; 0.789]	+
Yuan KC2020	1302	1588	0.820 [0.800: 0.839]	
Wongeun Song2022	38348	40366	0.950 [0.948; 0.952]	•
Chang Hu2022	76540	76540	1.000 [1.000; 1.000]	
Total (common effect, 95% CI)		149134	0.935 [0.934; 0.936]	
Total (random effect, 95% CI)			0.970 [0.487; 0.999]	
Heterogeneity: Tau <sup>2</sup> = 18.6284; Ch	i <sup>2</sup> = 4711.3	37, df = 5	(P = 0); I <sup>2</sup> = 100%	
Total (common effect, 95% CI)		466501	0.770 [0.769; 0.771]	
Total (random effect, 95% CI)			0.841 [0.590; 0.951]	
Heterogeneity: $Tau^2 = 6.9488$ ; Chi <sup>2</sup> Test for subgroup differences (con				0.4 0.5 0.6 0.7 0.8 0.9 1
Test for subgroup differences (ran				

Study	Events	Total	GLMM, Fixed + Random, 95% CI	GLMM, Fixed + Random, 95% Cl
Alireza Rafiei2020	11592	20336	0.570 [0.563; 0.577]	•
Liwei Peng2022	317291	382278	0.830 [0.829; 0.831]	
Shuhui Liu2017	26300	34472	0.763 [0.758; 0.767]	•
Liwei Peng2022	244658	382278	0.640 [0.638; 0.642]	<b>1</b>
Shuhui Liu2017	26248	34472	0.761 [0.757; 0.766]	•
Liwei Peng2022	103215	382278	0.270 [0.269; 0.271]	4
Bernhard Wernly2021	54148	61532	0.880 [0.877; 0.883]	•
Liwei Peng2022	57342	382278	0.150 [0.149; 0.151]	•
Inger Persson2021	52918	61532	0.860 [0.857; 0.863]	•
Christopher Barton2019	47140	91445	0.516 [0.512; 0.519]	•
Qingqing Mao2018	11384	21604	0.527 [0.520; 0.534]	
Shimabukuro DW2018	97	142	0.683 [0.600; 0.759]	— <b>—</b>
Lin PC2021	5724	8296	0.690 [0.680; 0.700]	
Alireza Rafiei2020	13422	20336	0.660 [0.653; 0.667]	
Alireza Rafiei2020	14032	20336	0.690 [0.684; 0.696]	•
Total (common effect, 95% CI)		1903615	0.518 [0.517; 0.518]	
Total (random effect, 95% CI)			0.646 [0.529; 0.748]	
Heterogeneity: Tau <sup>2</sup> = 0.9197; Chi <sup>2</sup>	= 457114	.11, df = 1	4 (P = 0); $I^2 = 100\%$	
				0.2 0.3 0.4 0.5 0.6 0.7 0.8

Fig. 4 Train set accuracy. In the train set, XGBoost showed the best predicting performance (n = 6), with an accuracy of 0.970 (0.487, 0.999) The accuracy of SOFA model (n = 6) is 0.588 (0.460,0.706). The accuracy of SVM model (n = 4) is 0.788 (0.635,0.889) The accuracy of XGBoost model (n = 6) is 0.970 (0.487,0.999)



**Fig. 5** Train set accuracy. In the train set, the Random Forest model was the most frequently applied machine learning model (n=9), with an accuracy of 0.911 (0.485, 0.991). The accuracy of LR model (n=6) is 0.796 (0.718,0.857) The accuracy of MEWS model (n=3) is 0.670 (0.565,0.760) The accuracy of MLP model (n=3) is 0.774 (0.695,0.818). The accuracy of NB model (n=2) is 0.792 (0.718,0.851) The accuracy of NN model (n=4) is 0.769 (0.571,0.893)



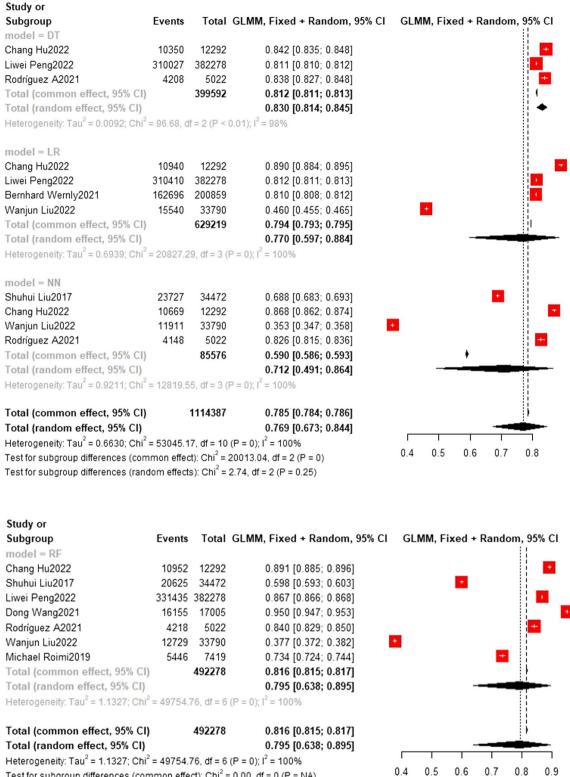
Test for subgroup differences (random effects): Chi<sup>2</sup> = 1.57, df = 2 (P = 0.46)

**Fig. 6** Train set accuracy. The accuracy of DL model (*n*=3) is 0.998 (0.095,1.000) GBT (*n*=2) and InSight model (*n*=2) are 0.740(0.386,0.928) and 0.853(0.515,0.969) respectively

predict severe sepsis and septic shock, which can predict, with high specificity, the impending occurrence of severe sepsis and septic shock. Lucas M Fleuren et al. designed a meta-analysis that found that individual machine learning models can accurately predict sepsis onset early, similar to the present study. Nianzong Hou et al. [29] developed an XGBoost model to predict 30-day mortality, which can assist clinicians in tailoring precise management and therapy for patients with sepsis. Dong Wang et al. [13] developed an artificial intelligence algorithm to predict sepsis early, which has shown good predictive ability in Chinese sepsis patients. However, external validation studies are necessary to confirm the universality of this method for the population and in treatment practice.

In this study, we concluded that two machine learning algorithms, the XGBoost and random forest, showed significant advantages in predicting sepsis incidence in ICU patients with higher ACC and c-index values compared to other models in this study, specifically the random forest (test set n=9, acc=0.911) and extreme gradient boost (test set n=7, acc=0.957) models. Compared to other studies, this study compared all previous machine learning models for predicting sepsis incidence in ICU patients, including 4,314,145 patients and 26 different machine learning models. This was a large, comprehensive study that strictly followed the PRISMA requirements for systematic evaluation and was methodologically rigorous and scientific. Based on this, we believe that our study is more accurate than previous studies.

The XGBoost and random forest are two machine learning algorithms that showed significant advantages compared to other models in the present study. XGBoost is a popular open-source software library



Heterogeneity: Tau" = 1.1327; Chi" = 49754.76, df = 6 (P = 0); I" = 100% Test for subgroup differences (common effect):  $Chi^2 = 0.00$ , df = 0 (P = NA) Test for subgroup differences (random effects):  $Chi^2 = 0.00$ , df = 0 (P = NA)

**Fig. 7** Test set accuracy. In the test set, the Random Forest model was also the most frequently applied machine learning model (n = 7), with an accuracy of 0.795 (0.638, 0.895). The DT model showed the best predicting performance (n = 3), with an accuracy of 0.830 (0.814, 0.845). The accuracy of LR model (n = 4) and NN model (n = 4) are 0.770 (0.597, 0.884) and 0.712 (0.491, 0.864) respectively

Study or	
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Subgroup	Events	Total	GLMM, Fixed + Random, 95% C	GLMM, Fixed + Random, 95% CI			
model = SOFA							
Lin PC2021	1308	1744	0.750 [0.729; 0.770]				
Zhixuan Zeng2021	51256	61532	0.833 [0.830; 0.836]	•			
Bernhard Wernly2021	152653	200859	0.760 [0.758; 0.762]	•			
Fotal (common effect, 95% CI)		264135	0.777 [0.775; 0.779]				
Total (random effect, 95% CI)			0.784 [0.737; 0.825]				
Heterogeneity: Tau <sup>2</sup> = 0.0514; Chi <sup>2</sup>	= 1438.68	3, df = 2 (l	P < 0.01); I <sup>2</sup> = 100%				
model = SVM							
Chang Hu2022	10719	12292	0.872 [0.866; 0.878]	-			
Rodríguez A2021	4234	5022	0.843 [0.833; 0.853]				
Nanjun Liu2022	22132	33790	0.655 [0.650; 0.660]	+			
Total (common effect, 95% CI)		51104	0.726 [0.722; 0.730]	•			
Total (random effect, 95% CI)			0.804 [0.687; 0.885]				
Heterogeneity: Tau <sup>2</sup> = 0.3082; Chi <sup>2</sup>	= 2341.78	3, df = 2 (I	$P = 0$ ; $I^2 = 100\%$				
model = XGBoost							
Chang Hu2022	11001	12292	0.895 [0.889; 0.900]				
_in PC2021	1221	1744	0.700 [0.678; 0.722]				
Nanjun Liu2022	16412	33790	0.486 [0.480; 0.491]	<b>—</b>			
Total (common effect, 95% CI)		47826	0.599 [0.594; 0.603]	•			
Total (random effect, 95% CI)			0.727 [0.489; 0.881]				
Heterogeneity: Tau <sup>2</sup> = 0.8153; Chi <sup>2</sup>	= 5062.33	8, df = 2 (I	$P = 0$ ; $I^2 = 100\%$				
Fotal (common effect, 95% CI)		363065	0.746 [0.745; 0.748]	1			
Total (random effect, 95% CI)			0.773 [0.690; 0.839]				
Heterogeneity: Tau <sup>2</sup> = 0.4252; Chi <sup>2</sup>							
Test for subgroup differences (com	nmon effe	ct): Chi <sup>2</sup> =	= 6697.36, df = 2 (P = 0)	0.5 0.6 0.7 0.8 0			

Test for subgroup differences (common effects):  $Chi^2 = 0.51$ , df = 2 (P = 0.78)

Study	Events	Total	GLMM, Fixed + Random, 95% CI	GLMM, Fixed + Random, 95% CI
Liwei Peng2022	329906	382278	0.863 [0.862; 0.864]	
Shuhui Liu2017	24027	34472	0.697 [0.692; 0.702]	
Liwei Peng2022	331435	382278	0.867 [0.866; 0.868]	
Liwei Peng2022	323025	382278	0.845 [0.844; 0.846]	
Shuhui Liu2017	21352	34472	0.619 [0.614; 0.625]	+
Bernhard Wernly2021	170730	200859	0.850 [0.848; 0.852]	
Wanjun Liu2022	15398	33790	0.456 [0.450; 0.461]	•
Chang Hu2022	10596	12292	0.862 [0.856; 0.868]	
Liwei Peng2022	265301	382278	0.694 [0.693; 0.695]	
Zhixuan Zeng2021	49103	61532	0.798 [0.795; 0.801]	
Lin PC2021	593	1744	0.340 [0.318; 0.363]	<b>-</b>
Alireza Rafiei2020	15200	20000	0.760 [0.754; 0.766]	+
Alireza Rafiei2020	13400	20000	0.670 [0.663; 0.677]	+
Total (common effect, 95% CI)		1948273	0.806 [0.805; 0.806]	
Total (random effect, 95% CI)			0.739 [0.649; 0.812]	
Heterogeneity: Tau <sup>2</sup> = 0.6056; Chi <sup>2</sup>	= 87119.3	31, df = 12	$(P = 0); I^2 = 100\%$	
				0.4 0.5 0.6 0.7 0.8



Study or Subgroup	TE	SE	Weight (common)	-	Odds Ratio IV, Fixed + Random, 95% CI		ls Ratio Random, 95% CI
model = MLP			(,	(	,		1
Shimabukuro DW2018	-0.05	0.0032	21.8%	10.2%	0.95 [0.95; 0.96]		
Zhixuan Zeng2021		0.0036	17.3%	10.2%		•	
Wanjun Liu2022		0.0370	0.2%	9.6%			
Total (common effect, 95% CI)			39.2%			•	
Total (random effect, 95% CI)				30.0%			-
Heterogeneity: Tau <sup>2</sup> = 0.0304; Chi <sup>2</sup>	= 1835	08 df =	$2(P=0): ^2 =$				
			- (				
model = NN							
Zhixuan Zeng2021	-0.28	0.0037	16.3%	10.2%	0.75 [0.75; 0.76]		
Rodríguez A2021		0.0286	0.3%	9.9%			
Wanjun Liu2022	-0.53	0.0260	0.3%	9.9%	0.59 [0.56; 0.62]	-	
Matthieu Scherpf2019	-0.24	0.0194	0.6%	10.0%	0.79 [0.76; 0.82]	-+-	
Total (common effect, 95% CI)			17.5%		0.75 [0.74; 0.75]	+	
Total (random effect, 95% CI)				40.0%	0.68 [0.59; 0.79]		
Heterogeneity: Tau <sup>2</sup> = 0.0201; Chi <sup>2</sup>	= 138.	37. df = 3	(P < 0.01); I <sup>2</sup>	= 98%			
2							
model = SVM							
Zhixuan Zeng2021	-0.25	0.0023	42.6%	10.2%	0.78 [0.77; 0.78]	•	
Rodríguez A2021	-0.48	0.0291	0.3%	9.8%	0.62 [0.59; 0.66]	<b></b>	
Wanjun Liu2022	-0.49	0.0251	0.4%	9.9%	0.61 [0.58; 0.64]	- <b>-</b>	
Total (common effect, 95% CI)			43.3%		0.77 [0.77; 0.78]		
Total (random effect, 95% CI)				30.0%	0.67 [0.57; 0.78]		
Heterogeneity: Tau <sup>2</sup> = 0.0181; Chi <sup>2</sup>	= 149.3	3, df = 2 (	$P < 0.01$ ; $I^2 =$	99%			
Total (common effect, 95% CI)			100.0%		0.81 [0.80; 0.81]	1	
Total (random effect, 95% CI)				100.0%	0.71 [0.64; 0.78]	-	
Heterogeneity: Tau <sup>2</sup> = 0.0236; Chi <sup>2</sup>							
Test for subgroup differences (con	))	0.75	1 1.5				

Test for subgroup differences (common effect):  $\text{Chi}^2$  = 1719.35, df = 2 (P = 0) Test for subgroup differences (random effects):  $\text{Chi}^2$  = 2.02, df = 2 (P = 0.37)

Study or Subgroup model = DL	TE	SE	Weight (common)		Odds Ratio IV, Fixed + Random, 95% CI	Odds Ratio IV, Fixed + Random, 95% Cl ∺¦
Rodríguez A2021	-0.48	0.0286	0.3%	12.2%	0.62 [0.59; 0.66]	II
Joshua P. Parreco2018	-0.12	0.0058	6.8%	12.8%		
Total (common effect, 95% CI	)		7.1%		0.87 [0.86; 0.88]	•
Total (random effect, 95% CI)				25.0%	0.74 [0.52; 1.05]	
Heterogeneity: Tau <sup>2</sup> = 0.0629; Chi	<sup>2</sup> = 148.	77, df = 1	(P < 0.01);   <sup>2</sup>	= 99%		
model = In Sight Matthieu Scherpf2019	-0.34	0.0472	0.1%	11.3%	0.71 [0.65; 0.78]	
Qingqing Mao2018	-0.08	0.0084	3.3%	12.8%	0.92 [0.91; 0.94]	•
Total (common effect, 95% Cl	)		3.4%		0.91 [0.90; 0.93]	-
Total (random effect, 95% CI)				24.1%	0.81 [0.63; 1.05]	
Heterogeneity: Tau <sup>2</sup> = 0.0324; Chi model = LR	<sup>2</sup> = 29.2	5, df = 1 (	(P < 0.01); l <sup>2</sup> =	97%		
Nianzong Hou2020	-0.20	0.0118	1.6%	12.7%		it l
Zhixuan Zeng2021	-0.24	0.0019	60.4%	12.8%	0.79 [0.79; 0.79]	<b>1</b>
Joshua P. Parreco2018	-0.13	0.0029	26.9%	12.8%	0.88 [0.87; 0.88]	
Wanjun Liu2022	-0.30	0.0207	0.5%	12.5%	0.74 [0.71; 0.77]	
Total (common effect, 95% Cl	)		89.5%		0.82 [0.81; 0.82]	K I
Total (random effect, 95% CI)				50.9%	0.81 [0.75; 0.86]	÷
Heterogeneity: Tau <sup>2</sup> = 0.0049; Chi	<sup>2</sup> = 957.	96, df = 3	: (P < 0.01); I <sup>2</sup>	= 100%		
Total (common effect, 95% Cl	)		100.0%		0.82 [0.82; 0.82]	1
Total (random effect, 95% CI)				100.0%	0.79 [0.72; 0.87]	<b></b>
Heterogeneity: Tau <sup>2</sup> = 0.0168; Chi Test for subgroup differences (co Test for subgroup differences (rar	mmon e	ffect): Ch	ni <sup>2</sup> = 302.77, d	lf = 2 (P < 0.		0.75 1 1.5

**Fig. 9** Train set c-index. In the train set, InSight exhibited the best performance with a c-index of 0.91 (0.90,0.93) in 2 studies. The rest are MLP(N=3), NN(n=4), SVM(n=3), DL(n=2) and LR(n=4). the C-index of them are 0.79 (0.65,0.97), 0.68(0.59,0.79), 0.67(0.57,0.78), 0.74(0.52,1.05) and 0.81(0.75,0.86)

Study or			Weight	Weight	Odds Ratio	Odds Ratio
Subgroup	TE	SE	(common)	(random)	IV, Fixed + Random, 95% C	I IV, Fixed + Random, 95% CI
model = RF						
Liwei Peng2022	-0.43	0.0277				-4-
Zhixuan Zeng2021	-0.24	0.0032	2.9%	8.0%	0.79 [0.79; 0.80]	**
Dong Wang2021	-0.13	0.0232	0.1%	7.8%	0.88 [0.84; 0.92]	+ +
Rodríguez A2021	-0.48	0.0286	0.0%	7.7%	0.62 [0.59; 0.66]	
Wanjun Liu2022	-0.37	0.0222	0.1%			
Michael Roimi2019	-0.14	0.0176			0.87 [0.84; 0.90]	+
Total (common effect, 95% CI			3.2%		0.79 [0.78; 0.79]	•
Total (random effect, 95% CI)				47.1%	0.74 [0.66; 0.84]	
Heterogeneity: Tau <sup>2</sup> = 0.0220; Chi <sup>2</sup>	= 209.3	22, df = 5	(P < 0.01); I <sup>2</sup>	= 98%		
model = SAPS II						
J E García-Gallo2018		0.0007				
Zongqing Lu2021		0.0136				+
Nianzong Hou2020		0.0102			• • •	+
Total (common effect, 95% CI)			57.0%			
Total (random effect, 95% CI)				24.0%	0.75 [0.70; 0.80]	•
Heterogeneity: Tau <sup>2</sup> = 0.0040; Chi <sup>2</sup>	= 175.	85, <mark>df</mark> = 2	? (P < 0.01); I <sup>2</sup>	= 99%		
model = SOFA						
J E García-Gallo2018		0.0009				
Zongqing Lu2021		0.0144				+
Lin PC2021		0.1082				
Yuan KC2020		0.0257		7.8%		
Total (common effect, 95% CI			39.9%			1
Total (random effect, 95% CI)				28.8%	0.62 [0.56; 0.69]	-
Heterogeneity: Tau <sup>2</sup> = 0.0097; Chi <sup>2</sup>	= 171.	84, df = 3	(P < 0.01); I <sup>2</sup>	= 98%		
Total (common effect, 95% CI			100.0%		0.66 [0.66; 0.66]	
Total (random effect, 95% CI)				100.0%	0.71 [0.65; 0.76]	
Heterogeneity: Tau <sup>2</sup> = 0.0194; Chi <sup>2</sup>						0.5 1 2
Test for subgroup differences (cor	nmon e	ffect): Ch	ni <sup>*</sup> = 28281.56	6, df = 2 (P =	0)	0.0 1 2

Test for subgroup differences (random effects): Chi<sup>2</sup> = 9.04, df = 2 (P = 0.01)

Study	TE SE	Weight	Weight (random)	Odds Ratio IV, Fixed + Random, 95% Cl	Odds Ratio IV, Fixed + Random, 95% Cl
Nianzong Hou2020	-0.15 0.0110	. ,	16.6%		
-				[····]	
Liwei Peng2022	-0.33 0.0176	1.1%	16.1%	0.72 [0.70; 0.75]	
Zhixuan Zeng2021	-0.22 0.0025	53.8%	17.0%	0.80 [0.80; 0.81]	• • • • • • • • • • • • • • • • • • •
Wanjun Liu2022	-0.22 0.0160	1.3%	16.3%	0.80 [0.78; 0.83]	+
Lin PC2021	-0.15 0.1768	0.0%	2.8%	0.86 [0.61; 1.22]	
Yuan KC2020	-0.33 0.0340	0.3%	14.3%	0.72 [0.68; 0.77]	_+_
Joshua P. Parreco2018	-0.13 0.0029	40.6%	17.0%	0.87 [0.87; 0.88]	•
Total (common effect, 95% Cl	)	100.0%		0.83 [0.83; 0.84]	i i i
Total (random effect, 95% CI)			100.0%	0.80 [0.75; 0.85]	<b>•</b>
Heterogeneity: Tau <sup>2</sup> = 0.0061; Chi	$^{2}$ = 552.09 df = 6	$(P < 0.01) \cdot I^2$	= 99%		
	002.00, 0.				0.75 1 1.5

**Fig. 10** Train set c-index. In the train set, XGBoost (bottom) was the most frequently utilized machine learning model with a c-index of 0.83 (0.83, 0.84) in 7 studies. The rest are RF(n=6) SAPS II(n=3) and SOFA(n=4), the C-index of them are 0.79 (0.78, 0.79) 0.70(0.70, 0.70) and 0.66(0.66, 0.66)

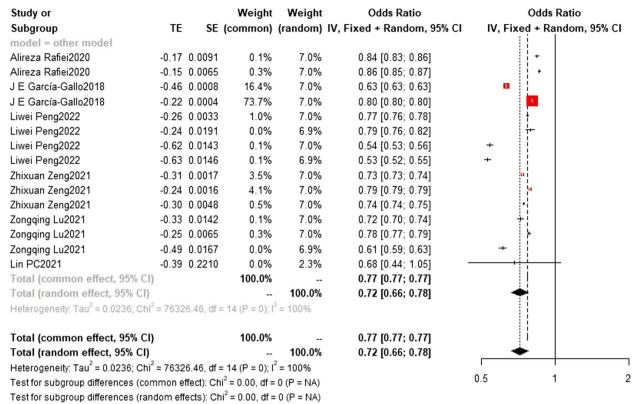


Fig. 11 Train set c-index. (Other models include GRU, LSTM, SIRS, SIC, SGB, OASIS, Nomogram, LODS, LDA, CART, MIG, LLI, ET, CS) In train set, the c-index of other models (*n* = 6) is 0.72 (0.66, 0.78)

for machine learning that is optimized for speed and scalability, making it one of the most efficient gradient boosting algorithms available. It can handle missing data and noisy data, making it a robust solution for real-world data problems. Random forest is a widely used ensemble machine learning algorithm that combines multiple trees to form a forest and produces a final prediction by aggregating the results from all the trees. These algorithms have been applied in various industries, including finance, health care, and marketing, and have won several machine learning competitions [30]. In our research, the random forest and XGBoost models showed significant advantages compared to other models. We also found other studies using machine learning to predict the incidence of sepsis. Bloch et al. [31] conducted a study using machine learning to predict the onset of sepsis. They found that the support vector machine (SVM) model had the best performance in predicting the onset of sepsis. Compared with this study, the study conducted by Bloch et al. focused on the data of a single medical centre and did not evaluate the data of other medical centres; therefore, the results can only reflect the situation of their single centre, lacking reference value for other regions.

### Conclusion

Machine learning has proven to be an effective tool for predicting sepsis at an early stage. However, to obtain more accurate results, additional machine learning methods are needed. In our research, we discovered that XGBoost and random forest models are the most commonly used models for predicting sepsis incidence in ICU patients, and they exhibit significant performance and accuracy compared to other models. The use of predictive models for early risk assessment has relatively ideal effects in preventing sepsis incidence in ICU patients; however, it still needs further improvement. Therefore, we look forward to more validated machine learning methods based on convenient, noninvasive, or minimally invasive predictive indicators, which may have significant performance and accuracy in predicting sepsis incidence in ICU patients.

Study or			Weight	Weight	Odds Ratio	Odds Ratio
Subgroup	TE	SE	(common)	(random)	IV, Fixed + Random, 95% CI	IV, Fixed + Random, 95% CI
model = SVM						
Zhixuan Zeng2021	-0.25	0.0049	31.9%	18.4%	0.78 [0.77; 0.78]	•
Rodríguez A2021	-0.54	0.0481	0.3%	16.8%	0.58 [0.53; 0.64]	
Wanjun Liu2022	-0.46	0.0121	5.3%	18.3%	0.63 [0.62; 0.65]	•
Total (common effect, 95% CI)			37.6%		0.75 [0.74; 0.76]	•
Total (random effect, 95% CI)				53.4%	0.66 [0.56; 0.78]	
Heterogeneity: Tau <sup>2</sup> = 0.0217; Chi <sup>2</sup>	= 285.4	4, df = 2 (	P < 0.01); I <sup>2</sup> =	99%		
model = XGBoost						
Zhixuan Zeng2021	-0.21	0.0044	40.3%	18.4%	0.81 [0.81; 0.82]	•
Wanjun Liu2022	-0.15	0.0059	22.0%	18.3%	0.86 [0.85; 0.87]	•
Lin PC2021	-0.29	0.1428	0.0%	9.9%	0.75 [0.57; 0.99]	
Total (common effect, 95% CI)			62.4%		0.83 [0.82; 0.84]	•
Total (random effect, 95% CI)				46.6%	0.83 [0.79; 0.88]	•
Heterogeneity: Tau <sup>2</sup> = 0.0014; Chi <sup>2</sup>	= 56, d	f=2(P <	: 0.01); I <sup>2</sup> = 96	1%		
Total (common effect, 95% CI)			100.0%		0.80 [0.80; 0.80]	•
Total (random effect, 95% CI)				100.0%	0.73 [0.64; 0.83]	
Heterogeneity: Tau <sup>2</sup> = 0.0240; Chi <sup>2</sup>	= 640.	01, df = 5	(P < 0.01); I <sup>2</sup>	= 99%	-	
Test for subgroup differences (cor					01)	0.75 1 1.5
			2			

Test for subgroup differences (random effects):  $\text{Chi}^2 = 6.67$ , df = 1 (P < 0.01)

Study or			Weight	Weight	Odds Ratio	Odds Ratio
Subgroup	TE	SE	(common)	(random)	IV, Fixed + Random, 95% CI	IV, Fixed + Random, 95% CI
model = RF						
Zhixuan Zeng2021		0.0045		10.5%		
Dong Wang2021		0.0053		10.5%	•	
Rodríguez A2021		0.0465		9.5%		
Wanjun Liu2022		0.0076				•
Michael Roimi2019		0.0165		10.4%		↓ +
Total (common effect, 95% CI)			59.1%			•
Total (random effect, 95% CI)				51.5%	0.78 [0.66; 0.93]	
Heterogeneity: Tau <sup>2</sup> = 0.0383; Chi <sup>2</sup>	= 1708	.54, df =	$4 (P = 0); I^2 =$	100%		
model = SAPS II						
Zongqing Lu2021	-0.30	0.0240	1.0%	10.3%		
Zhixuan Zeng2021		0.0050		10.5%		<u>a</u>
Total (common effect, 95% CI)			23.5%		0.77 [0.76; 0.78]	*
Total (random effect, 95% CI)				20.8%	0.76 [0.73; 0.79]	♠
Heterogeneity: Tau <sup>2</sup> = 0.0005; Chi <sup>2</sup>	= 2.81,	df = 1 (P	$P = 0.09$ ; $I^2 = 0$	54%		
model = SOFA						
Zhixuan Zeng2021	-0.35	0.0058	16.6%	10.5%	0.71 [0.70; 0.71]	•
Zongqing Lu2021	-0.34	0.0254	0.9%	10.2%	0.71 [0.68; 0.75]	
Lin PC2021	-0.42	0.1018	0.1%	7.0%	0.66 [0.54; 0.81]	
Total (common effect, 95% CI)			17.5%		0.71 [0.70; 0.71]	•
Total (random effect, 95% CI)				27.7%	0.71 [0.70; 0.71]	•
Heterogeneity: Tau <sup>2</sup> = 0; Chi <sup>2</sup> = 0.4	9, df = 2	2 (P = 0.7	'8); I <sup>2</sup> = 0%			
Total (common effect, 95% Cl)			100.0%		0.79 [0.79; 0.80]	•
Total (random effect, 95% CI)				100.0%	0.75 [0.69; 0.82]	-
Heterogeneity: Tau <sup>2</sup> = 0.0201; Chi <sup>2</sup>	= 2376	.57, df =	9 (P = 0); I <sup>2</sup> =	100%		
Test for subgroup differences (con	nmon e	ffect): Ch	ni <sup>2</sup> = 664.73, d	lf = 2 (P < 0.	01)	0.75 1 1.5

Test for subgroup differences (random effects):  $\text{Chi}^2 = 14.74$ , df = 2 (P < 0.01)

**Fig. 12** Test set c-index. In the test set, the random forest model was the most frequently employed machine learning model with a c-index of 0.83 (0.82,0.83) in 5 studies. In terms of performance, both the random forest model (n = 5, c-index = 0.83 (0.82,0.83)) and XGBoost (n = 3, c-index = 0.83 (0.82,0.84)) exhibited similar performance. The rest are SVM(n = 3) with c-index 0.66 (0.56, 0.78) SAPS II (n = 2) with c-index 0.76(0.73,0.79) and SOFA(n = 3) with c-index 0.71(0.70,0.71)

Study or			Weight	Weight	Odds Ratio	Odds Ratio
Subgroup	TE	SE	(common)	(random)	IV, Fixed + Random, 95% CI	IV, Fixed + Random, 95% CI
model = LR						
Zhixuan Zeng2021		0.0049				
Wanjun Liu2022		0.0061				•
Total (common effect, 95% CI)			41.4%		0.80 [0.80; 0.81]	•
Total (random effect, 95% CI)				29.1%	0.81 [0.77; 0.85]	· · · · · · · · · · · · · · · · · · ·
Heterogeneity: Tau <sup>2</sup> = 0.0013; Chi <sup>2</sup>	= 41.8	4, df = 1 (	(P < 0.01); I <sup>2</sup> =	: 98%		
model = MLP						
Zhixuan Zeng2021		0.0045				
Wanjun Liu2022		0.0109				<b>†</b>
Total (common effect, 95% CI)			34.3%		0.78 [0.77; 0.78]	
Total (random effect, 95% CI)				29.1%	0.75 [0.68; 0.83]	
Heterogeneity: Tau <sup>2</sup> = 0.0052; Chi <sup>2</sup>	= 76.5	6, df = 1 (	(P < 0.01); l <sup>2</sup> =	:99%		
model = NN						
Zhixuan Zeng2021		0.0054				<b>4</b>
Wanjun Liu2022		0.0129				*
Rodríguez A2021		0.0521				
Total (common effect, 95% CI)			24.3%		0.72 [0.72; 0.73]	
Total (random effect, 95% CI)				41.8%	0.64 [0.54; 0.76]	
Heterogeneity: Tau <sup>2</sup> = 0.0212; Chi <sup>2</sup>	= 323.	72, df = 2	$P < 0.01$ ; $I^2$	= 99%		
Total (common effect, 95% CI)			100.0%		0.77 [0.77; 0.78]	•
Total (random effect, 95% CI)				100.0%	0.72 [0.65; 0.80]	····
Heterogeneity: Tau <sup>2</sup> = 0.0193; Chi <sup>2</sup>						0.75 1 1.5
Test for subgroup differences (cor						0.75 1 1.5
			.2			

Test for subgroup differences (random effects):  $Chi^2 = 8.09$ , df = 2 (P = 0.02)

			Weight	Weight	Odds Ratio	Odds	Ratio		
Study	TE	SE	(common)	(random)	IV, Fixed + Random, 95% CI	IV, Fixed + R	andom, 95% Cl		
Zhixuan Zeng2021	-0.34	0.0057	1.2%	10.1%	0.71 [0.70; 0.72]	•			
Rodríguez A2021	-0.53	0.0473	0.0%	8.5%	0.59 [0.54; 0.65]				
Zhixuan Zeng2021	-0.24	0.0045	1.9%	10.1%	0.79 [0.78; 0.79]				
Zongqing Lu2021	-0.36	0.0254	0.1%	9.6%	0.70 [0.67; 0.74]	+			
Zhixuan Zeng2021	-0.29	0.0051	1.5%	10.1%	0.75 [0.74; 0.76]	٠			
Zongqing Lu2021	-0.21	0.0189	0.1%	9.8%	0.81 [0.78; 0.84]	+			
J E García-Gallo2018	-0.23	0.0006	94.3%	10.1%	0.79 [0.79; 0.79]				
Zongqing Lu2021	-0.51	0.0295	0.0%	9.4%	0.60 [0.57; 0.64]	+			
Lin PC2021	-0.56	0.2085	0.0%	2.1%	0.57 [0.38; 0.86]				
Alireza Rafiei2020	-0.43	0.0118	0.3%	10.0%	0.65 [0.64; 0.67]	+			
Alireza Rafiei2020	-0.33	0.0078	0.6%	10.1%	0.72 [0.71; 0.73]	*			
Total (common effect, 95% CI	)		100.0%		0.79 [0.79; 0.79]	1			
Total (random effect, 95% CI)				100.0%	0.71 [0.66; 0.75]	<u> </u>			
Heterogeneity: Tau <sup>2</sup> = 0.0113; Chi	<sup>2</sup> = 1026	.22, df =	10 (P < 0.01)	; I <sup>2</sup> = 99%		I	1		
<b>12</b> Fig. 13 Test set c-index The LP $(n - 2)$ MLP $(n - 2)$ and NN $(n - 3)$ models showed c-index 0.81 $(0.770.85)$ 0.75 $(0.680.83)$ and 0.64 $(0.540.76)$									

Fig. 13 Test set c-index. The LR(n = 2), MLP(n = 2) and NN(n = 3) models showed c-index 0.81(0.77,0.85) 0.75(0.68,0.83) and 0.64(0.54,0.76)

## Limitations

This study also has some limitations. First, this study focused on the accuracy of machine learning models and did not include risk factors that lead to the high incidence rate of sepsis in ICU patients. Second, some included models contained special variables related to the diagnosis of sepsis (such as infection indicators), which are valuable for further validation and research in subsequent studies.

## **Supplementary Information**

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Additional file 1. PRISMA 2020 Checklist.

Additional file 2.

Additional file 3.

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Not applicable.

#### Authors' contributions

Zhenyu Yang formulated the research purpose, searched, and screened the literature, processed the data and wrote the article. Xiaoju Cui participated in the literature collection and screening work. Zhe Song participated in data analysis work. Xiaoju Cui supervised the study. Zhenyu Yang and Zhe Song participated in text correction and format proofreading work.

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#### Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

#### Declarations

#### Ethics approval and consent to participate

This study does not involve ethical issues and therefore does not require approval from the ethics committee.

#### **Consent for publication**

This study is based on published research and does not contain data from any individual person, therefore the consent for publication is not applicable.

#### **Competing interests**

The authors declare that they have no competing interests.

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