Review

Jie Yang, Sicheng Hao, Jiajie Huang, Tianqi Chen, Ruoqi Liu, Ping Zhang, Mengling Feng, Yang He, Wei Xiao, Yucai Hong and Zhongheng Zhang*

The application of artificial intelligence in the management of sepsis

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Abstract: Sepsis is a complex and heterogeneous syndrome that remains a serious challenge to healthcare worldwide. Patients afflicted by severe sepsis or septic shock are customarily placed under intensive care unit (ICU) supervision, where a multitude of apparatus is poised to produce high-granularity data. This reservoir of high-quality data forms the cornerstone for the integration of AI into clinical practice. However, existing reviews currently lack the inclusion of the latest advancements. This review examines the evolving integration of artificial intelligence (AI) in sepsis management. Applications of artificial intelligence include early detection, subtyping analysis, precise treatment and prognosis assessment. AI-driven early warning systems provide enhanced recognition and intervention capabilities, while profiling analyzes elucidate distinct sepsis manifestations for targeted therapy. Precision medicine harnesses the potential of artificial intelligence for pathogen identification, antibiotic selection, and fluid optimization. In conclusion, the seamless amalgamation of artificial intelligence into the domain of sepsis management heralds a transformative shift, ushering in novel prospects to elevate diagnostic precision, therapeutic efficacy, and prognostic acumen. As AI technologies develop, their impact on shaping the future of sepsis care warrants ongoing research and thoughtful implementation.

Keywords: diagnosis; treatment; sepsis; artificial intelligence

***Corresponding author: Zhongheng Zhang**, Department of Emergency Medicine, Sir Run Run Shaw Hospital, Zhejiang University School of Medicine, Hangzhou, Zhenjiang Province, China,
E-mail: zh_zhang1984@zju.edu.cn. https://orcid.org/0000-0002-2336-5323
Jie Yang, Jiajie Huang, Tianqi Chen, Yang He, Wei Xiao and Yucai Hong, Department of Emergency Medicine, Sir Run Run Shaw Hospital, Zhejiang University School of Medicine, Hangzhou, Zhenjiang Province, China. https://orcid.org/0009-0006-9846-5448 (J. Yang)
Sicheng Hao, Duke University School of Medicine, Durham, NC, USA
Ruoqi Liu and Ping Zhang, Department of Computer Science and Engineering, The Ohio State University, Columbus, OH, USA. https://orcid.org/0000-0002-4601-0779 (P. Zhang)
Mengling Feng, Saw Swee Hock School of Public Health and Institute of Data science, National University of Singapore, Singapore, Singapore

Introduction

Sepsis, a syndrome characterized by physiological, pathological, and biochemical abnormalities triggered by infection, constitutes a significant public health concern [1]. Sepsis is delineated as a condition wherein life-threatening organ dysfunction ensues due to a maladaptive response of the host to infection. Septic shock, a subtype of sepsis, is characterized by particularly severe circulatory, cellular, and metabolic abnormalities, significantly augmenting the mortality rate [2]. Since the inception of the concept of sepsis, guidelines pertaining to its diagnosis, treatment and prognostication have been consistently evolving (Figure 1). This evolution reflects not only advancements in medical practices but also a continuous deepening of our understanding of the pathophysiological processes underlying sepsis and the synthesis of relevant clinical evidence [1, 3, 4].

In recent years, despite the rapid advancement in critical care medicine, sepsis continues to stand as the foremost cause of mortality among critically ill patients. This can be attributed to the substantial heterogeneity of sepsis, which poses significant challenges to clinical diagnosis and treatment. The intricacies in the diagnosis and treatment of sepsis lie within the heterogeneity of the ailment. Namely, disparate sepsis patients may manifest distinct clinical presentations and respond differently to a particular therapeutic regimen, thereby presenting formidable challenges to both clinical management and research endeavors. Patients often necessitate highly personalized management strategies. Yet, achieving precise and targeted treatment for sepsis through conventional assessment tools remains a formidable task. For instance, the widely employed quick sequential organ failure assessment (qSOFA) is deemed to lack the desired sensitivity [5].

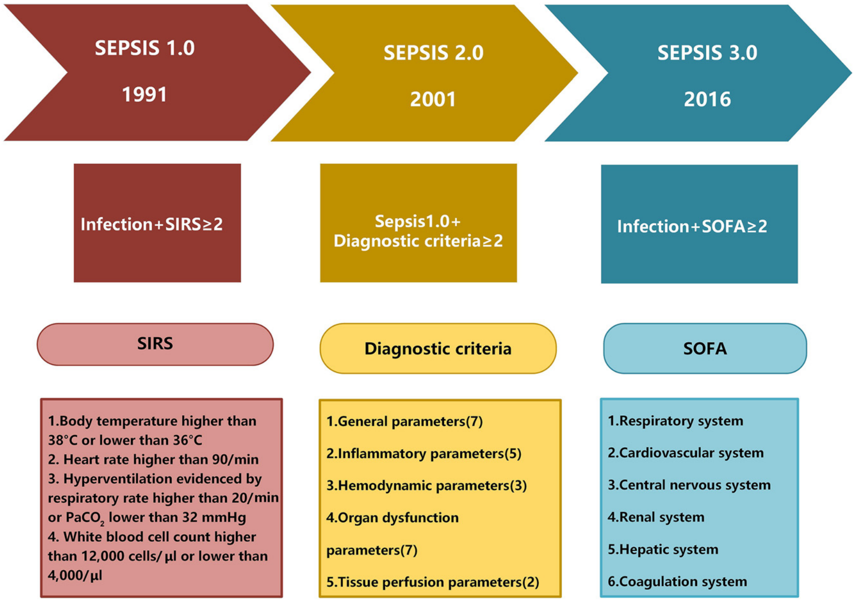

Figure 1: The evolution of guidelines. SOFA, sequential organ failure assessment; SIRS, systemic inflammatory response syndrome.

As the integration of artificial intelligence (AI) into the domain of medicine continually expanding to encompass the field of intensive care [6], AI is beginning to play a role in the diagnosis, prognosis, and treatment of various critical illnesses [7, 8], including sepsis (Table 1).

The intricacy and heterogeneity inherent in sepsis align seamlessly with AI applications. Its robust capacities in data analysis have the potential to introduce fresh avenues for tackling the complexities of sepsis [9, 10]. This article aims to elucidate the progress in AI research pertaining to the diagnosis and treatment of sepsis, engaging in discussions about its current contributions, limitations, and the prospective horizons it holds (Figure 2).

Using the query "Search ('Sepsis'[Mesh]) AND 'Artificial Intelligence'[Mesh] Filters: Review, Systematic Review, in the last 5 years Sort by: Most Recent" on the PubMed

Table 1: Summary of relevant sepsis reviews.

Title	Author	Year	Topic
Making the improbable possible: Generalizing models designed for a syndrome-based, heterogeneous patient landscape	Le JP	2023	The most recent advancements in the field of data science may conceivably enhance the ubiquity of machine learning algorithms in critical patient care
Use of artificial intelligence for sepsis risk prediction after flexible ureteroscopy: a Systematic review	Alves BM	2023	Sepsis risk prediction after flexible ureteroscopy
Machine learning applications on neonatal sepsis treatment: a scoping review	O'Sullivan C	2023	Machine learning applications in neonatal sepsis treatment
Deployment of machine learning algorithms to predict sepsis: systematic review and application of the SALIENT clinical AI implementation framework	van der Vegt AH	2023	Deployment of machine learning algorithms for sepsis prediction
Utilizing big data from electronic health records in pediatric clinical care	Macias CG	2023	Utilizing big data from electronic health records in pediatric clinical care
Artificial and human intelligence for early identification of neonatal sepsis	Sullivan BA	2023	Early identification of neonatal sepsis using artificial and human intelligence
Advances on machine learning applications in sepsis associated-acute kidney injury	Su Q	2022	Machine learning applications in sepsis-associated acute kidney injury
Research progress on application of artificial intelligence in early diagnosis and prediction of sepsis	Wei Q	2022	Application of artificial intelligence in early diagnosis and prediction of sepsis
Sepsis biomarkers and diagnostic tools with a focus on machine learning	Komorowski M	2022	Sepsis biomarkers and diagnostic tools with a focus on machine learning
Enhancing sepsis management through machine learning techniques: a review	Ocampo-Quintero N	2022	Enhancing sepsis management through machine learning techniques

Table 1: (continued)

Title	Author	Year	Topic
Antibiotic decision-making in the ICU	Parra-Rodriguez L	2022	Antibiotic decision-making in the intensive care unit
Can prehospital data improve early identification of sepsis in emergency department? An integrative review of machine learning approaches	Desai MD	2022	Prehospital data for early identification of sepsis in the emergency department
Prediction modelling in the early detection of neonatal sepsis	Sahu P	2022	Prediction modeling in early detection of neonatal sepsis
Global health systems' data science approach for precision diagnosis of sepsis in early life	Iregbu K	2022	Data science approach for precision diagnosis of sepsis in early life
Sepsis prediction, early detection, and identification using clinical text for machine learning: a systematic review	Yan MY	2022	Sepsis prediction, early detection, and identification using clinical text for machine learning
Role of artificial intelligence applications in real-life clinical practice: Systematic review	Yin J	2021	Role of artificial intelligence applications in real-life clinical practice
Preventing sepsis; how can artificial intelligence inform the clinical decision-making process? A systematic review	Hassan N	2021	Preventing sepsis: Artificial intelligence in clinical decision-making
Physiological machine learning models for prediction of sepsis in hospitalized adults: An integrative review	Kausch SL	2021	Physiological machine learning models for sepsis prediction in hospitalized adults
Sepsis in the critically ill patient: current and emerging management strategies	Heming N	2021	Current and emerging management strategies for sepsis in the critically ill patient
AI in the intensive care unit: Uu-to-date review	Nguyen D	2021	AI applications in the intensive care unit: Up-to-date review
Machine learning to support hemodynamic intervention in the neonatal intensive care unit	Van Laere D	2020	Machine learning to support hemodynamic intervention in the neonatal intensive care unit
A review of predictive analytics solutions for sepsis patients	Teng AK	2020	Predictive analytics solutions for sepsis patients
Machine learning in infection management using routine electronic health records: Tools, techniques, and reporting of future technologies	Luz CF	2020	Machine learning in infection management using electronic health records
Machine learning for the prediction of sepsis: a systematic review and meta-analysis of diagnostic test accuracy	Fleuren LM	2020	Systematic review and meta-analysis of machine learning for sepsis prediction
Clinical applications of artificial intelligence in sepsis: a narrative review	Schinkel M	2019	Clinical applications of artificial intelligence in sepsis: A narrative review
Machine learning for clinical decision support in infectious diseases: a narrative review of current applications	Peiffer-smadja N	2019	Machine learning for clinical decision support in infectious diseases
Agent-based models of inflammation in translational systems biology: a decade later	Vodovotz Y	2019	Agent-based models of inflammation in translational systems biology: A decade later
Refining humane endpoints in mouse models of disease by systematic review and machine learning-based endpoint definition	Mei J	2019	Refining humane endpoints in mouse models of disease by systematic review and machine learning-based endpoint definition
Applying machine learning to continuously monitored physiological data	Rush B	2019	Applying machine learning to continuously monitored physiological data

platform, located 34 pertinent articles resembling recent reviews (Table 1). Subsequently, five reviews that exhibited limited relevance to this manuscript were excluded and tabulated. It is worth noting that prior related reviews predominantly concentrated on the diagnosis and treatment of sepsis or were specialized in areas such as neonatology. Furthermore, in the temporal context of the retrieved articles, the majority of comprehensive reviews date back to approximately two to three years ago. This review serves as a summative synthesis of the latest literature regarding the prediction and treatment of sepsis (Table 2).

Diagnosis in sepsis

Early warning of sepsis

The conventional guidelines for sepsis management advocate for early intervention, and the even more preferable notion is one of "prevention is better than cure." Consequently, multiple AI models have been devised to forecast the occurrence of sepsis. Retrospective studies have demonstrated that through continuous monitoring of clinical data via AI, the onset of sepsis can be predicted several

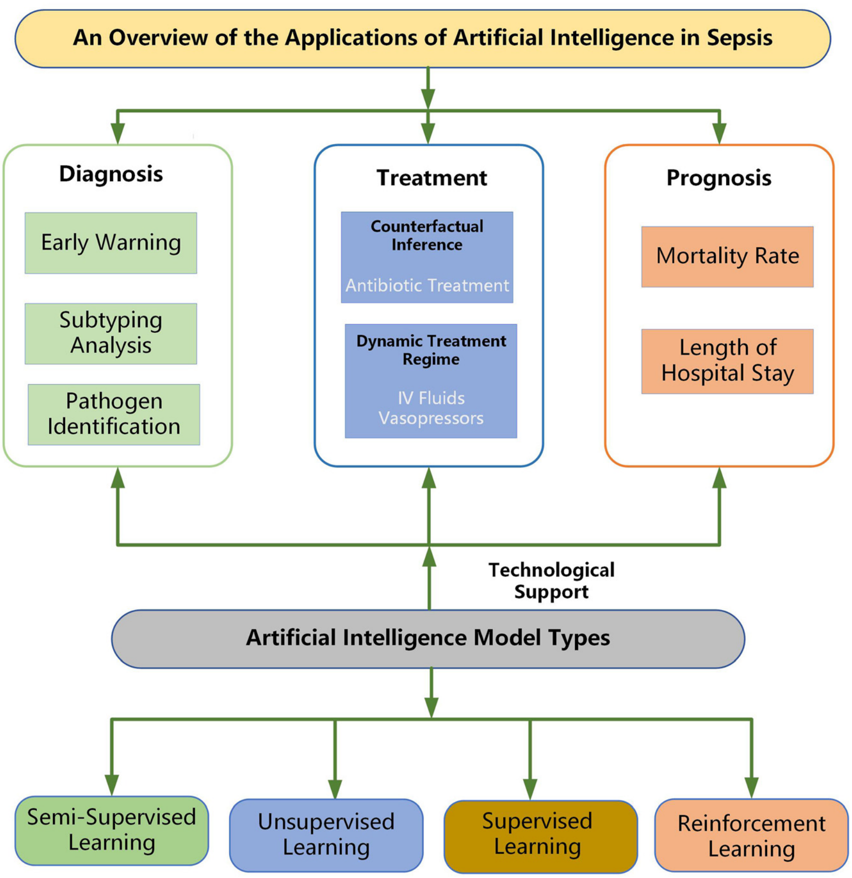

Figure 2: An overview of the application of artificial intelligence in sepsis. IV fluids, intravenous fluids.

hours in advance with an accuracy nearing 90 %, a substantial improvement over traditional disease severity scoring [11]. Historically, man prediction y AI models for sepsis prediction and identification primarily focused on critically ill patients [12–15]. However, numerous variables within these models are not routinely measured in non-intensive care settings, thereby limiting their applicability [16].

To address this constraint, researchers have leveraged routine clinical variables to devise sepsis prediction models suitable for various settings, including general wards and emergency rooms, with consistently positive research outcomes [17–19]. Recent meta-analyses have revealed that the benefits of AI early warning systems are more pronounced in emergency departments and general wards than in intensive care units [20]. Beyond conventional clinical data, research endeavors have also incorporated biomarker features derived from transcriptomics to construct machine learning models capable of identifying patients at risk of postoperative infections or sepsis within the first three clinical days.

The diversity of infection sites and individual patient variations present considerable challenges for the precise diagnosis of sepsis. Research has indicated that screening tools based on big data and machine learning can enhance the sensitivity and accuracy of sepsis diagnosis [21]. Beyond the conventional quantifiable structured clinical data [22], encompassing vital signs and laboratory findings, diagnostic models incorporating unstructured textual data have demonstrated promise. These models can elevate early sepsis diagnosis rates by 32 % and decrease false positive rates by 17 % [15]. For instance, AI models trained on chest X-rays in image format can identify around 90 % of patients with acute respiratory distress syndrome [23].

A recent multicenter prospective cohort study further revealed a significant correlation between the proactive application of early sepsis warning systems and reduced in-hospital mortality, organ failure incidence, and shorter hospital stays [24]. The aforementioned studies underscore the promising prospects of AI in the accurate early identification of sepsis and improvement of patient outcomes. However, the majority of models encompass only a fraction of clinical data variables, leaving a plethora of clinical information unexplored. Consequently, there exists ample room for optimizing and augmenting the diagnostic proficiency of AI. To facilitate broader clinical integration, AI model predictions must

Table 2: Latest sepsis prediction and treatment reviews.

Title	Year	Model	Application
Early detection of sepsis utilizing deep learning on electronic health record event sequences	2020	Deep learning	Early warning of sepsis
A novel artificial intelligence based intensive care unit monitoring system: using physiological waveforms to identify sepsis	2021	Machine learning	Early warning of sepsis
Prospective, multi-site study of patient outcomes after implementation of the TREWS machine learning-based early warning system for sepsis	2022	Machine learning	Early warning of sepsis
Predicting sepsis onset using a machine learned causal probabilistic network algorithm based on electronic health records data	2023	Machine learning	Early warning of sepsis
Machine learning of cell population data, complete blood count, and differential count parameters for early prediction of bacteremia among adult patients with suspected bacterial infections and blood culture sampling in emergency departments	2023	Machine learning	Early warning of sepsis
Derivation, validation, and potential treatment implications of novel clinical phenotypes for sepsis	2019	Machine learning	Subtyping analysis of sepsis
Utilization of deep learning for subphenotype identification in sepsis-associated acute kidney injury	2020	Deep learning	Subtyping analysis of sepsis
Deep learning-based clustering robustly identified two classes of sepsis with both prognostic and predictive values	2020	Deep learning	Subtyping analysis of sepsis
Development and validation of parsimonious algorithms to classify acute respiratory distress syndrome phenotypes: a secondary analysis of randomised controlled trials	2020	Machine learning	Subtyping analysis of sepsis
Identifying molecular phenotypes in sepsis: An analysis of two prospective observational cohorts and secondary analysis of two randomised controlled trials	2023	Machine learning	Subtyping analysis of sepsis
The artificial intelligence clinician learns optimal treatment strategies for sepsis in intensive care	2018	Reinforcement learning	Precision treatment of sepsis
Rapid identification of pathogenic bacteria using Raman spectroscopy and deep learning	2019	Deep learning	Precision treatment of sepsis
Accurate prediction of blood culture outcome in the intensive care unit using long short-term memory neural networks. Artificial intelligence in medicine	2019	Machine learning	Precision treatment of sepsis
A machine learning approach for predicting urine output after fluid administration	2019	Machine learning	Precision treatment of sepsis
Machine learning in the clinical microbiology laboratory: has the time come for routine practice? Clinical microbiology and infection	2020	Machine learning	Precision treatment of sepsis
Using machine learning techniques to aid empirical antibiotic therapy decisions in the intensive care unit of a general hospital in Greece	2020	Machine learning	Precision treatment of sepsis
Towards personalized guidelines: using machine-learning algorithms to guide antimicrobial selection	2020	Machine learning	Precision treatment of sepsis
Machine learning methods to improve bedside fluid responsiveness prediction in severe sepsis or septic shock: an observational study	2021	Machine learning	Precision treatment of sepsis
Fluid overload phenotypes in critical Illness – A machine learning approach	2022	Machine learning	Precision treatment of sepsis
Estimating treatment effects for time-to-treatment antibiotic stewardship in sepsis	2023	Counterfactual inference	Precision treatment of sepsis
Predicting 30-days mortality for MIMIC-III patients with sepsis-3: a Machine learning approach using Xgboost	2020	Machine learning	Prognostication in sepsis
Effect of a sepsis prediction algorithm on patient mortality, length of stay and readmission: a Prospective multicentre clinical outcomes evaluation of real-world patient data from US hospitals	2020	Machine learning	Prognostication in sepsis
Automated identification of adults at risk for in-hospital clinical deterioration	2020	Machine learning	Prognostication in sepsis
Association between urine output and mortality in critically Ill patients: a machine learning approach	2022	Machine learning	Prognostication in sepsis

possess readily interpretable characteristics. The predictive principles of the models must be comprehensible to clinical practitioners, fostering their trust and acceptance of the predictions, or enabling them to identify cases of erroneous predictions [25]. Consequently, researchers have developed interpretable AI models through making prediction logic transparent, open, and visualizable [26–28], aiming to better harness their medical value.

Subtyping analysis of sepsis

The heterogeneity of sepsis renders it challenging to simplify into a singular clinical presentation. Therefore, the utilization of AI algorithms for sepsis subtyping has emerged as a research focus in recent years. In the most recent definition of sepsis-3, organ dysfunction assessment is conducted through the utilization of the sequential organ failure assessment (SOFA) score. The SOFA score comprehensively evaluates the functioning of six distinct organ systems, which include respiration, coagulation, liver, cardiovascular, central nervous system, and renal functions. Furthermore, these parameters are also utilized for the classification of subtypes, aiming to discern clinically significant variations. Research reports have highlighted that retrospective analysis of clinical variables using machine learning can classify sepsis into four phenotypes: α, β, γ, and δ [29]. These subtypes represent distinct clinical profiles or manifestations of sepsis, each with its unique characteristics and patient outcomes. Patients with the β phenotype exhibit a higher prevalence of chronic illnesses and renal impairments, while those with the γ phenotype experience a greater incidence of inflammation and pulmonary dysfunction. Similarly, concerning renal functions system sepsis-related acute kidney injury has been divided into three distinct subtypes based on biochemical markers, immune patterns, and clinical outcomes [30]. While these subtyping approaches aid in comprehending sepsis heterogeneity, they lack mechanistic insights that could provide therapeutic guidance.

Furthermore, researchers have classified sepsis into two subtypes based on differences in gene expression among septic patients through extensive data analysis. These subtypes exhibit significant differences in mortality rates and responses to hormone therapy. One category displays pronounced immune suppression, with its elevated mortality rate linked to hormone application [31].

Similarly, by applying machine learning algorithms to secondary analyses of five randomized controlled trials, acute respiratory distress syndrome (ARDS) has been categorized into two subtypes: hyperinflammatory and hypoinflammatory. These subtypes exhibit distinct clinical outcomes and responses to treatment [32]. Subsequently, these experimental findings were validated in another multicenter retrospective study [33]. Furthermore, researchers have demonstrated through their studies that the molecular phenotypes previously identified in ARDS can also be identified in multiple sepsis cohorts, with varying responses to activated protein C. These molecular phenotypes may represent treatable characteristics of severe diseases that extend beyond patient syndrome diagnoses [34].

The conclusions drawn from the aforementioned studies, viewed through the lens of inflammatory response, partially illuminate the heterogeneity of sepsis. This machine learning-driven sepsis subtyping expands our perspective on disease assessment and treatment, offering novel insights for future mechanistic research and clinical diagnostics.

Pathogen identification and antimicrobial susceptibility testing

Due to the lag in pathogen diagnosis and antimicrobial susceptibility results, early-stage antibiotic administration for sepsis mainly relies on empirical approaches. To enhance the efficiency of clinical microbiology diagnostics, various AI algorithms have been developed. These models draw from diverse data sources, including microbiota, genomics, gene sequences, colony morphology, microscopic images, transcriptomics, and clinical data [35]. Notably, some researchers have combined spectral analysis of blood samples with AI models to rapidly identify 30 common bacteria and fungi, along with drug susceptibility recommendations, achieving an accuracy surpassing 80 % [36]. If effectively implemented in clinical settings, this approach possesses the potential to reduce the waiting time for microbiological cultures and antimicrobial susceptibility testing. Furthermore, AI models designed to predict pathogens and drug resistance have been developed to assist and optimize empirical antibiotic therapy [37–41].

Precision treatment of sepsis

Early fluid resuscitation can enhance or maintain tissue perfusion by increasing venous return and cardiac output. However, fluid administration may also lead to significant organ edema, resulting in organ dysfunction and impaired oxygen delivery. Conversely, vasopressor agents can be employed to reverse hypotension and maintain perfusion while limiting fluid administration. In a recent randomized controlled trial [42], researchers found that in septic patients with hypotension, a restrictive fluid strategy employed in the trial did not significantly reduce (or increase) mortality within 90 days of discharge when compared to a liberal fluid strategy. In the management of sepsis, reinforcement learning models [43] are utilized to achieve optimal treatment by analyzing numerous (mostly suboptimal) treatment decisions.

Additionally, AI has demonstrated its utility in guiding fluid resuscitation and management for sepsis. After training on the MIMIC database, a model can predict post-resuscitation urine output and identify patients with oliguria [44]. AI models that have been trained using echocardiographic parameters demonstrate the capacity to evaluate volume status and fluid responsiveness in critically ill patients, yielding sensitivities on par with the passive leg raising test [45]. An AI model employing random forest algorithm research discovered that sepsis patients admitted with high lactate levels, low bicarbonate levels, and postoperative complications are at high risk of fluid overload. Therefore, this subset of sepsis patients might not be suitable for a lactate-guided fluid resuscitation strategy [46]. While these models exhibit promising performance in research settings, their clinical utility is yet to be comprehensively validated.

In the current healthcare landscape, causal inference has become a highly examined area of research, especially in the context of sepsis management. Causal inference from real-world data typically involves addressing complex confounding factors. When dealing with a limited number of such confounding factors, conventional statistical methods like stratification, propensity score analysis, and multivariable regression analysis adjustment are used. However, in high-dimensional datasets, controlling for confounding factors is not straightforward and necessitates the use of more advanced machine learning methods.

More recently, researchers [47] have introduced a novel framework aimed at estimating treatment effects for sepsis patients through causal inference. The core model of this study, named T4, employs a unique approach. It first estimates individual treatment effects (ITEs) by cyclically encoding patient information from historical time series and static data. Subsequently, it decodes the potential outcomes under different treatment sequences. To mitigate the impact of confounding factors, the study utilizes balancing matching to construct balanced mini-batches of data and adjusts for the influence of confounders. Furthermore, the model provides interpretability for treatment recommendations by analyzing contributions at both global and variable levels through attention mechanisms and variable importance analysis. Quantifying the model's uncertainty helps prevent overconfident treatment suggestions. The research demonstrates the model's application in two real-world electronic health record (EHR) datasets, showcasing its ability to identify effective treatment strategies and pave the way for personalized and precise medical care.

Prognostication in sepsis

Prognostic assessment is a pivotal aspect of sepsis diagnosis and treatment, and AI has demonstrated certain advantages in prognosis analysis. A randomized controlled trial indicated that the application of AI models reduced in-hospital mortality from 21.30 % to 8.96 % compared to the control group, along with a decrease in average hospital stay from 13.0 to 10.3 days [48]. Researchers have employed conventional logistic regression, SAPS-II scoring prediction, and XGBoost algorithms to construct three distinct machine learning models [49]. These models were designed to anticipate the 30-day mortality rate among sepsis patients in the MIMIC-III database, with the XGBoost model demonstrating the highest accuracy, reaching 85 %. A multi-center prospective study grounded in real-world data suggested that the application of AI models in general wards and emergency patients correlated with reduced in-hospital mortality rates and shorter hospital stays [50]. Another multi-center retrospective study involving non-intensive care unit (ICU) patients indicated that hospitals utilizing AI models exhibited lower mortality rates, ICU admission rates, and shorter average hospital stays compared to traditional hospitals [51]. Furthermore, in a retrospective cohort study, training machine learning models to predict in-hospital mortality and examining the interaction between urine output and survival revealed a close correlation between low urine output and sepsis patient mortality [52]. Further research is needed to comprehensively evaluate the clinical efficacy of AI models and their correlation with sepsis prognosis [53].

Online resources

As the Internet continues to evolve, an increasing wealth of digital resources becomes accessible online. These resources encompass not only the training data required for artificial intelligence but also pre-existing model transformations. Subsequently, we will expound on these two aspects.

The field of medicine is characterized by the generation of substantial high-granularity data in daily practice. Presently, these data are meticulously archived within hospital information systems, primarily for routine clinical use. The profound exploration of such latent big data within healthcare institutions may contribute significantly to gaining deeper insights into the pathophysiology of sepsis and guiding healthcare practices.

Several publicly accessible intensive care databases have been established, yielding hundreds of scientific achievements published in scholarly journals. However, medical big data models based on artificial intelligence often necessitate a substantial volume of data for training, a magnitude that may not align with what a treatment group or even a single hospital can provide. Consequently, in the

Table 3: Publicly accessible intensive care databases.

Name	Data collection timeframe	Patients volume	Country	Patient sources	Website
MIMIC-IV	2008–2019	299,712	The United States	Admitted to intensive care units at the beth Israel deaconess medical center (BIDMC)	https://physionet.org/content/mimiciv/2.2/
eICU	2014–2015	Over 200,000	The United States	Admitted to one of 335 units at 208 hospitals located throughout the US	https://physionet.org/content/eicu-crd/2.0/
AmsterdamUMCdb	2003–2016	20,109	The Netherlands	Admitted to intensive care units at an academic medical center in Amsterdam	https://github.com/AmsterdamUMC/AmsterdamUMCdb
HiRID	2008–2016	34,000	Switzerland	Admissions to the department of intensive care medicine of the bern University hospital	https://physionet.org/content/hirid/1.1.1/
PIC	2010–2018	12,881	China	Paediatric patients (aged 0–18 years) admitted to critical care unit	https://physionet.org/content/picdb/1.1.0/
ZhejiangProvinceICU	2012–2022	7,638	China	Admitted to intensive care units and emergency intensive care units at Zhejiang provincial People's hospital	https://www.nature.com/articles/s41597-023-01952-3
INSPIRE	2011–2020	130,000	South Korea	Nderwent anesthesia for surgery at an academic institution	https://www.physionet.org/content/inspire/0.1/

context of model training and validation, the identification and utilization of existing large open databases on the internet hold paramount importance. We have conducted a concise overview of the online databases related to sepsis that are accessible, such as MIMIC-IV [54], eICU [55], AmsterdamUMCdb [56], HiRID [57], PIC [58], Zhejiang Province ICU [59] and INSPIRE [60],with the aim of assisting readers in furthering their research endeavors (Table 3).

With the advancement of artificial intelligence, certain models have already been applied in clinical settings. The Neonatal early-onset sepsis (EOS) Calculator, for instance, is founded on a predictive risk model developed through a nested case-control design involving 608,014 newborns born in 14 U. S. hospitals, each with a gestational age of 34 weeks or more. This model underwent further refinement using logistic regression and recursive partitioning. The EOS Calculator (http://kp.org/eoscalc) estimates the risk of EOS based on five objective maternal risk factors and four clinical neonatal risk factors. It classifies newborns into three risk categories and provides corresponding management recommendations, including the initiation or cessation of empiric antibiotic therapy.

Furthermore, researchers have employed statistical and machine learning approaches to develop a model known as PEDSEPS-GBM (http://yinglab.top/PEDSEPS-GBM). They have also created a user-friendly web calculator for this model to assist clinicians in early detection of sepsis in children. In the rapidly evolving landscape of artificial intelligence, the translation of academic research findings into practical clinical technologies presents a new challenge. If these recent advancements can be translated into tools available to clinicians, we believe it would undoubtedly benefit the health of sepsis patients.

Limitations of applying artificial intelligence

Insufficiency in universal applicability

Despite revolutionizing the utilization of current clinical data and its potential to play a significant role in clinical diagnosis and treatment, there exist considerable obstacles that cannot be ignored (Figure 3). Among these, a pivotal issue pertains to the universal applicability of AI models. Introducing a model developed by one hospital into another often fails to yield anticipated results, due to variations in operational methods, software and hardware systems, database structures, patient demographics, and epidemiological characteristics of diseases among different medical institutions [61]. For example, the AI system at the University of Michigan Hospital encountered an excess of alerts due to shifts in patient demographics arising from the COVID-19 pandemic. This inadvertently increased the healthcare burden, leading the hospital to suspend the operation of the AI model in 2020 [62, 63]. This demonstrates that establishing AI models is not a one-time endeavor; continuous

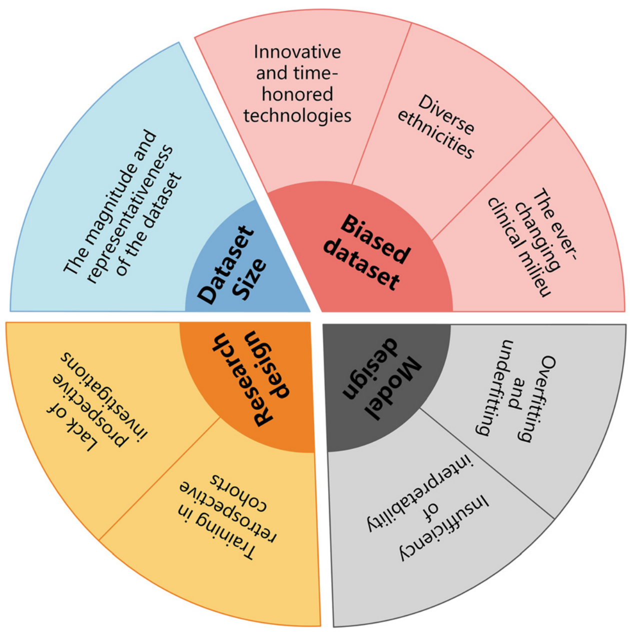

Figure 3: Limitations of applying artificial intelligence.

consideration of factors such as patient populations, disease progression, clinical guidelines, and hospital environments is essential. To realize lasting clinical value, it might be necessary to endow AI models with the capability for ongoing self-updates, thereby enhancing their universal applicability to bridge the gap between "computational" and "clinical medicine" [64].

Limited clinical relevance

Another prominent issue is the limited acceptance of AI models by medical professionals. Investigations reveal that healthcare personnel possess incomplete understanding of AI due to the intricate algorithmic logic, which may not always align with conventional medical reasoning [65]. Particularly concerning predictive models, alerts issued by the system before the onset of illness often struggle to gain the trust of healthcare professionals. This is because, at that point, patients have not yet displayed signs of deterioration. Ultimately, only 12 % of doctors and 38 % of nurses believe that AI models enhance diagnostic and treatment services [65]. Recent research indicates that if sepsis alerts from the system can be evaluated and confirmed by physicians within 3 h, antibiotic administration time can be advanced by an average of 1.8. Hence, beyond striving to enhance the accuracy of AI model predictions or diagnoses, attention must be directed towards the subjective attitudes of medical staff towards AI. The degree of awareness, experiential usage, and acceptance of the model by healthcare professionals constitute crucial factors in determining its practical effectiveness [66]. Future research should focus on reinforcing the trust medical personnel have in AI models, enhancing their alignment with clinical diagnostic processes, and comprehensively assessing their genuine impact on clinical outcomes [67].

Conclusion and prospects

In summary, the complexity and heterogeneity of sepsis offer fertile "data soil" for the development of AI. Leveraging its robust data processing capabilities, AI holds immense potential for improving sepsis prognosis. It could optimize existing diagnostic decisions, reduce mortality rates, and usher in new breakthroughs in sepsis management [68]. However, current practical research on AI remains in its nascent stages, grappling with challenges like insufficient universal applicability and limited alignment with traditional diagnostic logic. These constraints significantly impede the exploration of AI's clinical utility, posing critical problems to be addressed in future studies.

Furthermore, considering the perspective of AI-powered large language models, we discuss the application of such models in sepsis and even broader medical contexts. The rapid deployment of advanced chatbots underscores the astonishing potential of large language model AI systems in adept language manipulation and knowledge processing. Multiple studies have demonstrated the effectiveness of AI chatbots in health behavior interventions among diverse populations under specific conditions [69], and their advantages compared to traditional doctors [70]. However, the scenario might differ for sepsis patients, who frequently present with severe conditions, including cognitive impairment and behavioral disruptions, limiting their ability to interact with large language models. Previously proven examples of efficacy often concerned milder illnesses without significant impacts on communication and behavior. Thus, adapting the strengths of large models to critically ill patients could be a prospective avenue for future applications.

In conclusion, the decision-making capabilities of AI presently remain distant from the realm of human medical expertise. The journey from "code" to "clinical" continues to be challenging, replete with obstacles, and protracted.

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