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REVIEW ARTICLE

Revolutionising Sepsis Management: A Comprehensive Review of Artificial Intelligence Applications

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Abstract

Sepsis is a multifaceted, intricate illness that poses a significant obstacle to global healthcare systems. Severe sepsis patients are usually admitted to the intensive care unit (ICU), where a number of devices are put up to produce high-definition images. The foundation for integrating artificial intelligence (AI) into clinical practice is based on huge and excellent data collection. This review looks at the application of AI in sepsis management. AI is utilised in prompt diagnosis, prognosis assessment, precise treatment and subtyping analysis. Improved detection and response capabilities are provided by an AI-powered early warning systems and targeted treatment can be achieved by using profiling analysis to identify specific indications of sepsis. Precision medicine uses AI to select medications, diagnose bacteria and optimise fluids. Last but not least, the seamless incorporation of AI into the sepsis care domain heralds a paradigm shift that will create new avenues for enhancing prognostic understanding, treatment efficacy and diagnostic precision. AI technologies are developing and further research and cautious application are necessary given their potential to impact the treatment of sepsis in the future.

Key words: Artificial intelligence; Sepsis; Diagnosis; Therapy.

Introduction

Sepsis, a serious public health risk, is characterised by clinical, physiological and metabolic problems caused by infection. It was responsible for almost $20 billion (5.2 %) of all hospital expenses in the United States in 2011. Additionally, there is growing recognition that sepsis survivors frequently experience long-term physical, psychological and cognitive impairments that have substantial health care and social ramifications, such as persistent discomfort, weakness, exhaustion and a reduced quality of life. Furthermore, many survivors have cognitive deficits, anxiety, depression and post-traumatic stress disorder (PTSD), collectively referred to as "post-sepsis syndrome," which may make it challenging for them to take care of themselves, return to their jobs, or engage in social activities. In addition to the individuals impacted, these long-term repercussions have a significant negative impact on their families, healthcare systems and society at large. In order to enhance outcomes for survivors, preventive measures, early intervention and comprehensive post-sepsis care programs are crucial. Additionally, the requirement for continuous rehabilitation and mental health support adds to the total cost of sepsis treatment.[1] Severe circulatory, cellular and metabolic abnormalities are characteristics of septic shock, a kind of sepsis that significantly raises the death risk and, if left untreated, frequently results in multiple organ failure and

irreversible organ damage. The body's immune reaction to infection in septic shock results in extensive vasodilation, a substantial reduction in blood pressure and reduced blood supply to essential organs, all of which interfere with regular cellular and metabolic processes. This results in a cascade of harmful effects, including decreased oxygen delivery to tissues, lactic acidosis and an increase in pro-inflammatory cytokines. Patients in septic shock may experience symptoms such as rapid heart rate, confusion, cold extremities and respiratory distress, all of which require urgent intervention.

Septic shock continues to be a major cause of death in intensive care units across the globe despite advancements in critical care and survival rates are largely dependent on the promptness and efficacy of therapeutic therapies such fluid resuscitation, vasopressors and suitable antimicrobial medications. Early recognition, supportive care and strategies aimed at reversing the underlying infection are critical in reducing mortality rates associated with septic shock.[2] Even though critical care medicine has advanced quickly in recent years, this is still the primary cause of death. This is explained by the enormous variety of sepsis, which makes clinical identification and treatment extremely difficult,[3] which contributes to its intricate diagnosis and management. In particular, diverse sepsis patients may show differently and respond differently to a certain treatment plan, which can provide major challenges for clinical management and research projects.[4] Patients frequently require greatly individualised care plans. However, using traditional evaluation methods to treat sepsis with accuracy and focus is still a difficult endeavour. For example, the popular fast sequential organ failure assessment (qSOFA) is thought to be too sensitive.[5]

Since the term "sepsis" was first used, guidelines for its diagnosis, treatment and prognosis have undergone constant modification due to advances in science, technology and a better comprehension of the intricate pathophysiology that underlies the illness. Early approaches focused primarily on clinical judgment and the

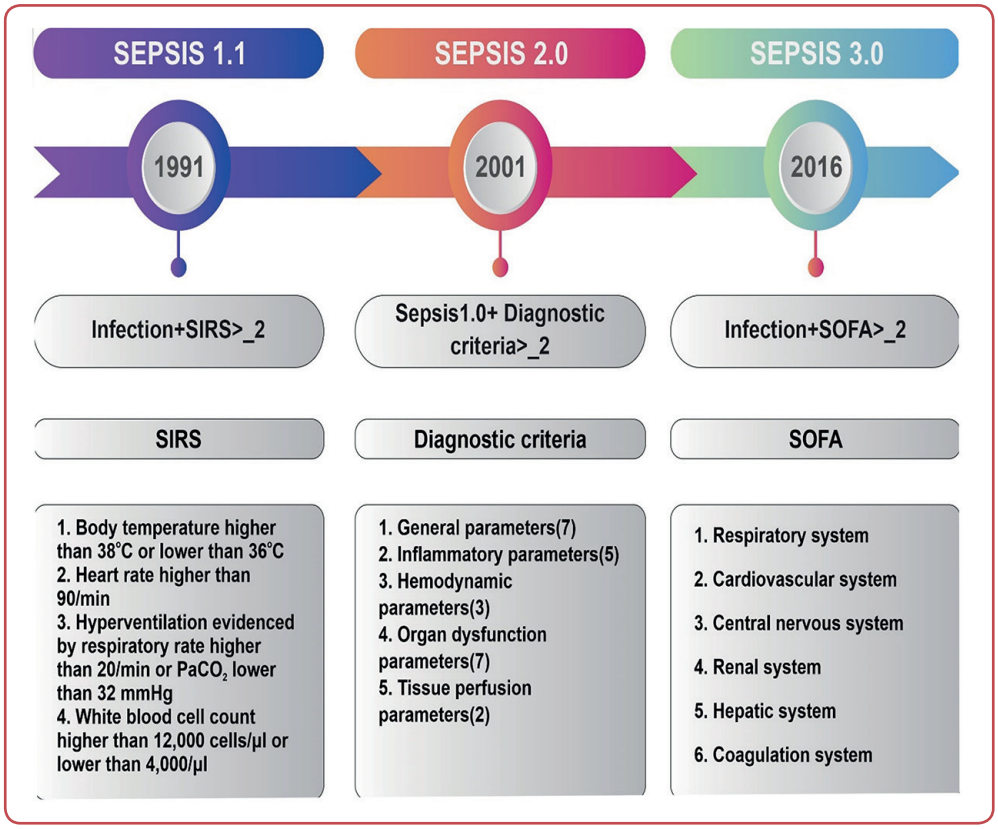

Figure 1: Sepsis development guidelines

The evolution of sepsis classification is based on key criteria revisions over time. Sepsis 1.0, introduced in 1991, primarily relied on the Systemic Inflammatory Response Syndrome (SIRS) criteria as the main diagnostic tool. In 2001, Sepsis 2.0 was introduced, expanding the diagnostic framework by incorporating additional criteria to better define and identify sepsis. The most recent revision, Sepsis 3.0, released in 2016, further refined the diagnostic approach by introducing the Sequential Organ Failure Assessment (SOFA) score as a central criterion, shifting focus towards organ dysfunction as a key marker of sepsis.

identification of infection, but as our knowledge of sepsis progressed, diagnostic criteria became more refined, incorporating biomarkers and advanced imaging techniques to detect sepsis at its earliest stages. The adoption of fluid resuscitation regimens, the creation of sepsis zbundles intended to standardise therapy and the transition from broad-spectrum antibiotics to more targeted medicines are just a few of the notable improvements in management tactics. Additionally, the recognition of septic shock as a distinct and more severe form of sepsis has led to further refinement in treatment protocols, emphasising hemodynamic support, the use of vasopressors and strategies to prevent organ failure. Prognostic models have evolved with the inclusion of new biomarkers, scoring systems and machine learning tools that aim to predict outcomes more accurately and guide treatment decisions. Despite these developments, there are still obstacles to lowering death rates and enhancing the long-term quality of life for sepsis survivors, highlighting the necessity of ongoing study and innovation in the area (Figure 1). The gathering of relevant clinical data, continuous investigation into the pathophysiological mechanisms driving sepsis and improvements in medical techniques have all contributed to this evolution.[1, 3, 4]

As AI becomes more and more integrated into the medical industry, including the intensive care unit, AI is beginning to be applied to the prognosis, diagnosis and treatment of certain severe diseases, such as sepsis, with the potential to revolutionise patient care. AI systems can help with early detection, spot trends that medical professionals might not see right away and tailor treatment regimens to each patient's needs by evaluating massive amounts of clinical data in real time.[6] AI can be used to predict patient outcomes, determine the most effective interventions and optimise the use of resources such as antibiotics and fluid management. Furthermore, AI can continuously monitor patients, enabling more proactive and dynamic decision-making, which is especially critical in life-threatening conditions like sepsis, where rapid intervention is key to improving survival rates and reducing long-term complications. The application of AI technology in critical care has enormous potential to enhance patient outcomes, treatment effectiveness and diagnostic precision as it develops.[7, 8]

Application of AI in sepsis

Sepsis is complex and heterogeneous, which fits well with AI applications. Because of its strong data analytic capabilities, AI may open up new possibilities for addressing the complexity of sepsis by enabling faster and more accurate detection, predicting patient outcomes and personalising treatment strategies. Artificial intelligence (AI) algorithms may detect small trends in vast datasets, such as vital signs, imaging, laboratory results and clinical records, that human practitioners could overlook. This enables earlier intervention and more focused treatments. Furthermore, AI-powered tools can continuously monitor patients in real time, providing dynamic assessments of disease progression and guiding timely adjustments to treatment plans. As AI technology advances, its integration into sepsis care holds promise for improving diagnostic accuracy, reducing mortality rates and enhancing the overall management of this life-threatening condition.[9] Additionally, AI can help optimise resource allocation by predicting which patients are at the highest risk, ensuring that intensive care resources are directed where they are most needed. AI's capacity to handle enormous volumes of data from various sources, such as clinical notes, electronic health records and even patient-reported outcomes, presents the possibility of discovering novel biomarkers for sepsis, which could result in the creation of more accurate diagnostic procedures and treatment plans. As AI continues to evolve, its potential to transform sepsis management extends beyond acute care to include long-term patient monitoring and rehabilitation, further improving outcomes for sepsis survivors.[10] Some recent reviews are mentioned below in which AI is used for sepsis management (Table 1).

In order to clarify the advancements in AI research concerning sepsis detection and therapy, this article will address the technology's present uses, constraints and future prospects, with a focus on its application in early diagnosis, risk stratification, treatment personalisation and predictive modelling. The article will examine how AI technologies, such machine learning and deep learning, are already being used to evaluate enormous volumes of patient data in real time, allowing for more precise and prompt sepsis diagnosis. It will also examine the limitations of these technologies, such as issues related to data quality, model interpretability and the need for large, diverse datasets to train algorithms effectively. The

article will also cover the potential of AI in sepsis care in the future, including how it can be integrated with other cutting-edge technologies like wearable sensors, how it can improve outcomes for sepsis survivors and what obstacles must be overcome before AI-driven solutions can be widely used in clinical practice.[10] AI is used in sepsis for diagnosing (such as identifying the type of sepsis and the pathogen causing it), treating (like suggesting the right antibiotic or adjusting fluids and vasopressors) and predicting outcomes (such as the risk of death or length of hospital stay). The

Table 1: Overview of relevant sepsis reviews

Author	Year	Topic
Liang C et al	2024	Existing knowledge gaps, particularly with regard to the use of corticosteroids, may be filled by integrating artificial intelligence (AI) into the management of sepsis.
Kim MJ et al	2024	The use of AI and machine learning in sepsis care has significantly enhanced personalised medicine and raised treatment accuracy.
Shankar-Hari M et al	2024	AI bioinformatics techniques, supportive software and multiplex technologies should open up new possibilities for managing sepsis.
Santacroce E et al	2024	Clinical data, advanced lab results and machine learning algorithms are now being integrated to enable personalised and targeted therapy.
Zhang S et al	2024	A promising human-AI collaboration model for the future of AI-assisted sepsis diagnosis and other critical medical decision-making is made possible by *SepsisLab*.
Cheungpasitporn W et al	2024	A promising human-AI collaboration model for the future of AI-assisted sepsis diagnosis and other critical medical decision-making is made possible by *SepsisLab*.
Le JP et al	2023	Developments of data science and increase use of machine learning algorithms in vital patient care.
Alves BM et al	2023	Risk assessment for sepsis following flexible ureteroscopy.
O'Sullivan C et al	2023	Neonatal sepsis treatment using machine learning.
van der Vegt AH et al	2023	Predicting sepsis with machine learning methods.
Macias CG et al	2023	Using big data from electronic health records to provide clinical treatment for children.
Sullivan BA et al	2023	Detecting newborn sepsis early with both human and AI.
Su Q et al	2022	Applications of machine learning in acute renal impairment associated with sepsis.
Wei Q et al	2022	AI's use in sepsis prediction and early detection.
Komorowski M et al	2022	Diagnostic methods centred on machine learning and sepsis biomarkers.
Ocampo-Quintero N et al	2022	Improving sepsis control with machine learning methods.
Parra-Rodriguez L et al	2022	Making decisions about antibiotics in the intensive care unit.
Desai MD et al	2022	Prehospital information for the emergency room's early detection of sepsis.
Sahu P et al	2022	Using prediction modelling to identify neonatal sepsis early.
Iregbu K et al	2022	Using data analytics to accurately diagnose sepsis in the early stages of life.
Yan MY et al	2022	Predicting, identifying and detecting sepsis with machine learning using clinical literature.
Yan MY et al	2021	AI applications in real-world healthcare environments.
Hassan N et al	2021	Preventing sepsis through clinical decision-making using AI.
Kausch SL et al	2021	Physiological machine learning algorithms for predicting sepsis in hospitalised patients.
Heming N et al	2021	New and existing approaches to treating sepsis in severely unwell patients.
Nguyen D et al	2021	A current evaluation of AI uses in the intensive care unit.
Van Laere D et al	2020	Supporting hemodynamic intervention in the neonatal critical care unit with machine learning.
Teng AK et al	2020	Solutions using predictive analytics for patients with sepsis.
Luz CF et al	2020	Using machine learning in electronic health records to treat infections.
Fleuren LM et al	2020	Systematic review and meta-analysis of machine learning for sepsis prediction.
Schinkel M et al	2019	Applying AI to sepsis management.
Peiffer-Smadja N et al	2019	Clinical decision support using machine learning in infectious illnesses.
Vodovotz Y et al	2019	Inflammation models based on agents in translational systems biology.
Mei J et al	2019	Refinement of humane endpoints in disease- modelling mice through systematic review and end-point determination based on machine learning.
Rush B et al	2019	Using machine learning on physiological data that is continuously observed.

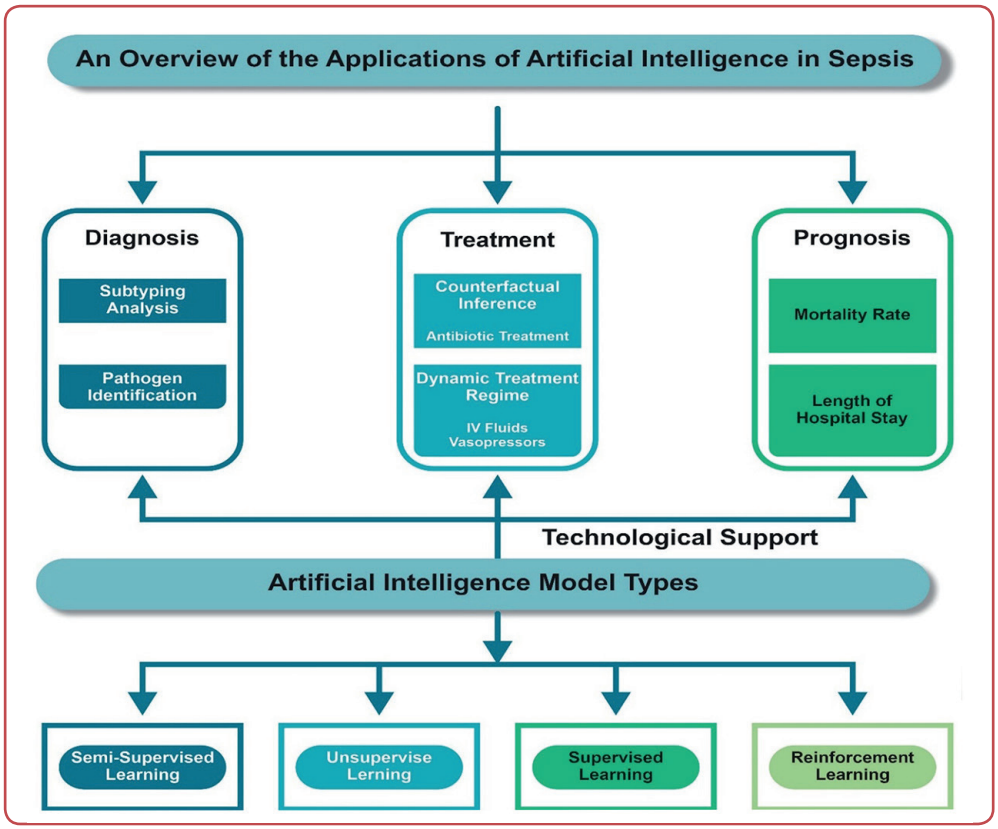

Figure 2: An overview of the application of artificial intelligence (AI) in sepsis
AI is used in sepsis diagnosis (subtyping analysis, pathogen identification), treatment (counterfactual inference-antibiotic treatment, dynamic treatment regime-fluid vasopressor) and prognosis (mortality rate, length of hospital stay). AI has different types of models like semi-supervised learning, unsupervised learning, supervised learning, reinforcement learning.
IV: intravenous;

potential of AI in sepsis care in the future will also be discussed, including how it can be combined with other cutting-edge technologies like wearable sensors, how it can enhance outcomes for sepsis survivors and what challenges need to be addressed before AI-driven solutions are widely applied in clinical practice (Figure 2).

Process of diagnosis in sepsis

Initial warning of sepsis

Early intervention is encouraged by the standard guidelines for managing sepsis and the even more desirable belief is that "prevention is better than cure". Consequently, a number of AI models have been created to forecast the onset of sepsis. Studies conducted in the past have shown that by using AI to continuously monitor clinical data, it is possible to forecast the beginning of sepsis several hours ahead of time with accuracy close to 90 %. This is a significant improvement over the traditional method of assessing illness severity.[11] In order to predict the start of sepsis, several AI models have been developed.[12-15] Nevertheless, these models' usefulness is limited because many of the variables are not regularly monitored in non-intensive care settings.[16] In order to overcome this limitation, scientists have used standard clinical characteristics to create sepsis prediction models that work well in a variety of contexts, such as emergency departments and general wards. Their research has consistently produced positive results.[17-19] Current meta-analyses have demonstrated that ordinary wards and emergency rooms benefit more from AI early warning systems than critical care units do.[20]

The variety of infection locations and patient variances pose significant obstacles to the accurate identification of sepsis. Research indicates that applying machine learning and big data to screening methods can increase the sensitivity and precision of sepsis detection.[21] Over and be-

yond the typical clinical data that is standardised and quantified,[22] Promising diagnostic models that incorporate unstructured textual data have also included vital signs and laboratory results. These models can increase the percentage of early sepsis diagnoses by 32 % and reduce the percentage of false positives by 17 %.[15] For instance, about 9 0% of people with acute respiratory distress syndrome can be identified by AI systems trained on image-formatted chest X-rays.[23]

More proof of a strong link between early implementation of sepsis warning systems and decreased rates of in-hospital mortality, organ failure and shorter hospital stays was recently presented by multicentre prospective cohort research.[24] The previously cited research highlights the potential benefits of AI in accurately detecting sepsis early on and improving patient outcomes. As such, there is much space for refining and enhancing AI's diagnostic capabilities. To facilitate wider clinical integration, AI models' predictions must be simple to understand. Clinical practitioners need to be able to understand the predictive principles of the models in order for them to believe and accept the predictions or recognise instances in which the forecasts are incorrect.[25] Consequently, by making prediction logic visible, transparent and open, researchers have created interpretable AI models[26-28] trying to further harness their medical significance.

Analysis of sepsis subtyping

Sepsis is a complicated illness that is difficult to reduce to a single clinical manifestation because of its variability. As a result, a new area of research has focused on using AI algorithms for sepsis subtyping. The most recent definition of sepsis-3 uses the sequential organ failure assessment (SOFA) score to determine organ dysfunction. Six different organ systems heart, circulatory, central nervous system, kidneys, respiration, coagulation and liver are all thoroughly assessed by the SOFA score. Moreover, these characteristics are also applied to the subtype categorisation with the goal of identifying changes that are clinically meaningful. According to research findings, using machine learning to analyse clinical features in the past, sepsis may be classified into four phenotypes: α, β, γ and δ.[29] These subgroups reflect various sepsis presentations or clinical profiles, each with its own distinct traits and patient outcomes. People with the β phenotype are more likely to have chronic illnesses and renal issues, while people with the γ phenotype are more likely to have inflammation and lung issues. Similar to this, three different subtypes of acute kidney damage linked to sepsis-related renal dysfunction have been identified based on immunological patterns, biochemical markers and clinical outcomes,[30] although these subtyping methods help to understand the heterogeneity of sepsis, they do not offer mechanistic insights that could guide treatment decisions. Furthermore, after doing a thorough examination of patient data, researchers were able to divide sepsis into two subgroups according to variations in gene expression. Significant variations exist between these categories in terms of mortality and how they react to hormone treatment. A significant immunosuppression is present in one group and the usage of hormones is linked to a higher death rate in this group.[31]

Additionally, secondary analyses of five randomised controlled trials using machine learning approaches have separated acute respiratory distress syndrome (ARDS) into hyper-inflammatory and hypo-inflammatory subgroups. Treatment results and responses differ among these subgroups.[32] Then, in another multicentre retrospective investigation, these experimental results were validated.[33] Furthermore, research has demonstrated that the molecular abnormalities previously identified in ARDS are present across a range of sepsis cohorts with varying responses to activated protein C. These molecular phenotypes might indicate characteristics of a serious disease that goes beyond the patient syndrome diagnosis and is curable.[34] When seen through the lens of inflammatory response, the information above only partially explains the variability of sepsis. In addition to providing novel insights for future mechanistic research, clinical diagnostics, pathogen identification and antibiotic susceptibility testing, this machine learning-driven subtyping of sepsis enhances our comprehension of disease evaluation and therapy. The early stages of antibiotic therapy for sepsis primarily employ empirical approaches due to the delayed arrival of data on antimicrobial susceptibility and pathogen detection. A number of AI algorithms have been created to increase clinical microbiology diagnosis accuracy. Transcriptomics, microbiome, genomics, gene sequences, colony morphology, microscopic pictures and clinical data are just a few of the many sources of information that these models incorporate.[35] Several researchers have

successfully employed spectral analysis of blood samples in conjunction with AI models to rapidly identify 30 common bacteria and fungus as well as suggestions for treatment susceptibility, with an accuracy rate of over 80 %.[36] This strategy has the potential to shorten the wait times for antibiotic susceptibility tests and microbiological cultures if it is successfully applied in clinical settings. Furthermore, to improve empirical antibiotic treatment, AI models that forecast infections and drug resistance have been created.[37-41]

Personalised sepsis treatment

To support or maintain tissue perfusion in the event of early fluid resuscitation, venous return and cardiac output can be raised. On the other hand, substantial organ oedema brought on by fluid administration may potentially limit oxygen transport and cause organ failure. Vasopressor drugs, on the other hand, can be used to reduce the amount of fluid administered while maintaining perfusion and reversing hypotension. A current RCT (randomised controlled experiment),[42] researchers found that, in contrast to a liberal fluid approach, the trial's restrictive fluid approach did not substantially lower (or raise) mortality in septic patients with hypotension within 90 days of discharge. Reinforcement learning models in sepsis management[43] are applied to analyse many (usually unsatisfactory) treatment selections in order to attain optimal treatment.

AI has also proven to be useful in directing fluid resuscitation and sepsis care. A model can identify individuals with oliguria and predict post-resuscitation urine output after training on the MIMIC database.[44] When it comes to evaluating fluid responsiveness and volume status in severe patients, AI models trained on echocardiographic data show promise, yielding sensitivities related to the passive leg raising test.[45] An AI model utilising the random forest method found that fluid overload is a major risk factor for sepsis patients who are admitted and have low bicarbonate, high lactate and postoperative outcomes. Because of this, a lactate-guided method of fluid resuscitation might not be suitable for this particular subset of sepsis patients.[46] Although these models perform well in research settings, more thorough validation is needed to determine their clinical relevance.

Causal inference has drawn a lot of attention in the present healthcare environment, particularly when it comes to the treatment of sepsis. Complex confounding variables must usually be taken into account when drawing causal conclusions from real-world data. When dealing with a small number of these confounding variables, traditional statistical methods such as stratification, multivariable regression analysis adjustment and propensity score analysis are employed. However, when working with high-dimensional datasets, confounding factor removal is difficult and requires more sophisticated machine learning techniques.

More recently, scientists[47] have put forth a novel paradigm intended to measure the impact of therapy on sepsis patients by means of causal inference. This study's central model, T4, takes a novel approach. Using static data and historical time series, it cyclically encodes patient information to estimate individual treatment effects (ITEs) first. Subsequently, it interprets the possible results for various treatment plans. The study generates balanced mini-batches of data and accounts for confounding influence to lessen the impact of confounding factors. Additionally, the model makes treatment recommendations intelligible by analysing contributions at the global and variable levels using attention processes and variable importance analysis. It is possible to prevent too optimistic therapy recommendations by measuring the model's uncertainty. The study illustrates the model's capacity to pinpoint exact medical care and identify successful treatment plans through a comparison with two real-world electronic health record (EHR) datasets.

Sepsis prognostication

A crucial component of diagnosing and treating sepsis is prognostic evaluation and AI has shown some benefits in this area. According to a randomised controlled study, employing AI models decreased hospital stay length from 13.0 to 10.3 days and in-hospital mortality from 21.30 to 8.96 percent when compared to the control group.[48] Three different machine learning models have been created by researchers using XGBoost, SAPS-II scoring prediction and traditional logistic regression.[49] The XGBoost model performed better than all other models developed to forecast the 30-day death rate among sepsis patients

in the MIMIC-III database, with an accuracy of 85 %. The use of AI models in emergency rooms and general wards was linked to shorter hospital stays and a decreased incidence of in-hospital mortality, according to a multi-centre prospective study based on actual data.[50] In a different multi-centre retrospective analysis, hospitals that used AI models had lower average hospital stays, fewer ICU admissions and lower fatality rates than conventional hospitals with patients not in the ICU.[51] Additionally, a retrospective cohort study that trained machine learning models to predict in-hospital mortality and examined the relationship between urine output and survival found a clear link between sepsis patient death and low urine production.[52] Further research is necessary to completely evaluate the therapeutic efficacy of AI models and their connection to the prognosis of sepsis.[53]

Online resources

More and more digital resources are being available online as the Internet develops. These resources include both pre-existing model alterations and the training data needed for AI. We shall go into more detail about these two factors later. The creation of significant amounts of high-granularity data in the course of daily practice is what defines the medical industry. These days, hospital information systems carefully preserve these records, primarily for use in routine clinical applications. An in-depth analysis of such concealed massive data in healthcare environments might significantly improve our comprehension of the biology of sepsis and have an impact on medical practices. Numerous databases on acute care have been made available to the public, resulting in hundreds of research publications in academic journals. AI-based medical big data models, however, often need a considerable quantity of data for training a quantity that might exceed the capacity of a single hospital or even a treatment group. For this reason, finding and using huge, publicly available databases on the internet is crucial when it comes to training and validating models. We have performed a brief summary of the available internet datasets on sepsis, containing MIMIC-IV,[54] eICU,[55] AmsterdamUMCdb,[56] HiRID[57] PIC[58] Zhejiang Province ICU[59] and INSPIRE,[60] in an attempt to aid readers in their further investigation (Table 2).

Table 2: Intensive care databases

Name	Data collection timeframe	Patients (n)	Country	Patient sources	Website
MIMIC-IV	2008–2019	299,712	The United States	Admitted to intensive care units at the Beth Israel Deaconess Medical Centre (BIDMC)	https://physionet.org/content/mimiciv/2.2/
eICU	2014–2015	Over 200,000	The United States	Admitted to one of 208 hospitals across the United States' 335 units	https://physionet.org/content/eicu-crd/2.0/
AmsterdamUMCdb	2003–2016	20,109	The Netherlands	Admitted to intensive care units at an academic medical centre 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/
Zhejiang ProvinceICU	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	Underwent anaesthesia for surgery at an academic institution	https://www.physionet.org/content/inspire/0.1/

Some models have already been used in healthcare settings as a result of AI advances. For example, the Neonatal Early-onset Sepsis (EOS) Calculator was developed using a predictive risk model with a nested case-control design that includes 608,014 neonates delivered in 14 US hospitals at a gestational age of 34 weeks or more. To enhance this model even more, recursive partitioning and logistic regression were applied. Using the EOS Calculator, the probability of end-of-life syndrome (EOS) can be estimated based on four clinical neonatal risk indicators and five objective maternal risk variables. It assigns newborns to one of three risk categories and provides advice for appropriate care, including when to begin or cease empirical antibiotic medication.

In addition, scientists have developed a model called PEDSEPS-GBM (http://yinglab.top/PEDSEPS-GBM) using statistical and machine learning techniques. In support of this approach, a user-friendly online calculator has been created to assist medical professionals in prompt detection of paediatric sepsis. Converting academic research discoveries into useful medical interventions is a major difficulty in the quickly developing field of AI. We think there is no question that the health of individuals with sepsis would improve if these new discoveries could be developed into instruments that medical professionals might utilise.

The limitations of AI's applications

Insufficient global applicability

It has the ability to drastically alter clinical diagnosis and treatment, transforming the use of existing clinical data by offering more precise, fast and individualised insights. However, there are significant constraints that must be acknowledged, such as the requirement for a variety of high-quality datasets, the need for transparent and interpretable AI models, the potential for algorithmic bias and the challenge of integrating AI systems into existing clinical workflows without compromising patient care. Additionally, AI-driven decisions should always be complemented by clinical expertise, as AI models may not fully capture the complexity of individual patient case.[61]

AI has several limitations that can affect its effectiveness in clinical settings. One key issue is biased datasets, as AI models can be influenced by limited or unrepresentative data, such as a lack of diversity in ethnic groups, outdated technologies, or variations in clinical practices over time. Additionally, there are challenges related to model design, including overfitting, where a model is too specific to past data and under-fitting, where it fails to capture important patterns. The lack of interpretability, which means AI models might not be able to adequately explain how they arrive at their conclusions, is another drawback. In terms of research design, much of the AI research is based on retrospective data, which examines past patient outcomes, rather than prospective investigations that test AI in real-time or future scenarios, limiting its reliability. Lastly, the size and representativeness of the datasets used for training are crucial, as AI needs large and diverse datasets to function well. If the data is too small or not reflective of the broader population, the AI's accuracy and effectiveness can be compromised (Figure 3). The generalisability of AI models is among the most crucial of these. Because different hospitals have distinct operating methods, database architecture, hardware and software systems, patient demographics and epidemiological aspects of disease, moving a model developed at one hospital to another may not always yield the desired results.[61] For instance, the University of Michigan Hospital's AI system had an overabundance of warnings as a result of changes in the patient demographics brought on by the COVID-19 epidemic. In 2020, the hospital decided to stop using the AI model due to the inadvertent rise in medical expenses.[62,63] To deliver long-term therapeutic benefit, it may be crucial to bridge the gap between "computational" and "clinical medicine" and improve the general application of AI models by enabling them to self-update.[64]

Minimal clinical importance

The restricted use of AI models by medical professionals is another significant problem. According to investigations, healthcare workers don't fully comprehend AI because of its complex algorithmic logic, which doesn't necessarily follow standard medical reasoning.[65] Predictive models in particular frequently fail to earn the trust of medical practitioners when the system issues alarms prior to the start of illness. This is because patients had not yet displayed any signs of decline at that point. In the end, only 13 % of

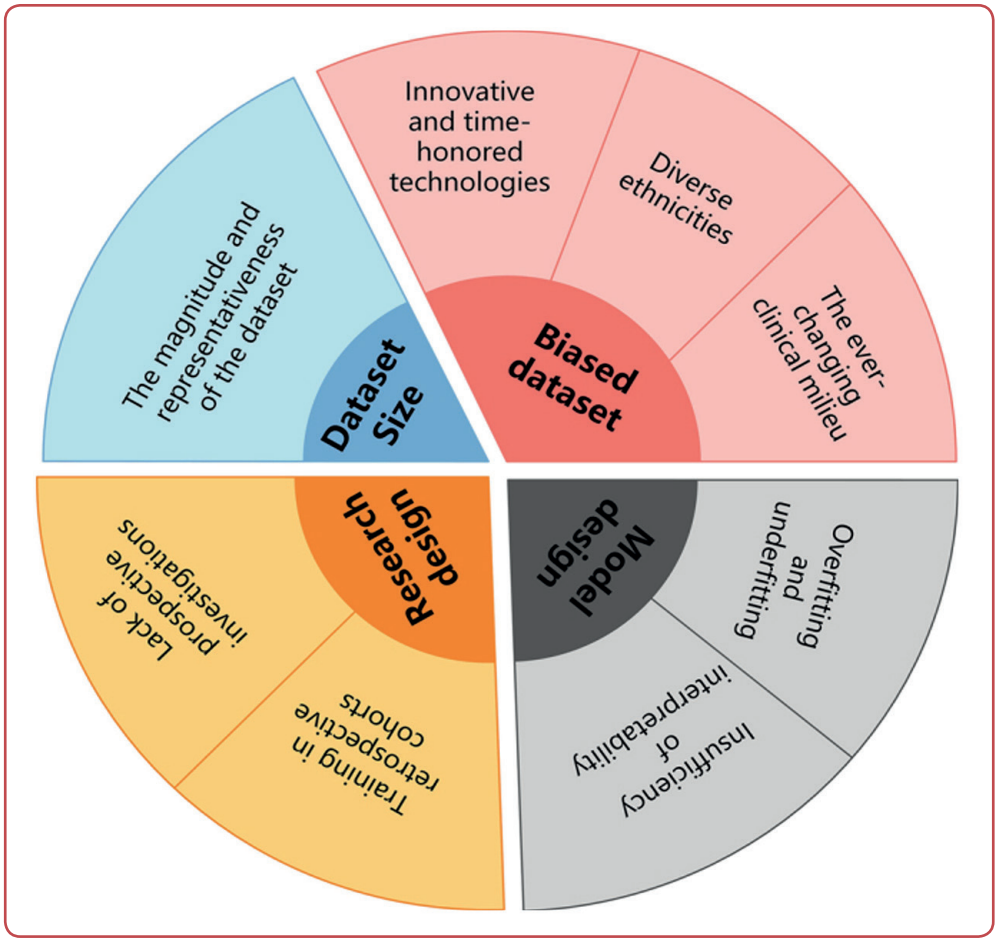

Figure 3: *Artificial intelligence limitations*

Biased dataset (Innovative and time-honoured technologies, diverse ethnicities, the ever-changing clinical milieu); Model design (overfitting and underfitting, insufficiency of interpretability); Research design (training in retrospective cohorts, lack of prospective investigations); Dataset size (the magnitude and representativeness).

physicians and 38 % of nurses think that models utilising AI improve medical diagnosis and treatment.[65] Recent studies show that antibiotic delivery time can be accelerated by an average of 1.8 hours if sepsis signals from the system can be assessed and verified by doctors within 3 hours. Therefore, rather than focusing on improving the predictive or diagnostic accuracy of AI models, care needs to be taken with the varying opinions that medical personnel have about AI. The model's usefulness depends critically on how much healthcare practitioners understand, apply and embrace it.[66] The attention of future research should be on increasing the trust that physicians have in AI models, enhancing their applicability for clinical diagnostic procedures and closely examining their real effect on patient outcomes.[67]

Conclusion

Sepsis's diversity and complexity make it a great "data soil" for AI research. AI has enormous potential to improve the prognosis of sepsis by utilising its powerful data processing skills. It might lead to new developments in sepsis management, lower mortality rates and improve current diagnostic choices. But actual AI research is still in its early stages, with issues including limited alignment with conventional diagnostic logic and inadequate general application. These restrictions provide significant obstacles to future research on the medicinal potential of AI and highlight significant problems that must be addressed. Additionally, we address the application of AI-driven large language models in sepsis and other general medical scenarios. The quick adoption of sophisticated chatbots highlights the immense potential of large language model AI systems for skilful

knowledge processing and language manipulation. Numerous studies have demonstrated AI chatbots' advantages over conventional physicians and their effectiveness in treating a variety of conditions and populations with health-related behaviours. For sepsis patients, on the other hand, the situation can be different because they often arrive with severe problems, such as cognitive disturbance and behavioural changes, this makes it more difficult for them to converse using complex language models. Earlier reported instances of effectiveness frequently dealt with milder problems without having a significant influence on behaviour or communication. Thus, targeting critically sick patients with the advantages of big models might be one avenue for future applications. To sum up, AI's capacity for making decisions is still far from what human medicine can accomplish. The transition from "code" to "clinical" is still difficult, time-consuming and full of roadblocks.

Ethics

This study did not directly involve with human participants or experimental animals. Therefore, the ethics approval was not required in this paper.

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Conflicts of interest

The authors declare that there is no conflict of interest.

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Data access

The data that support the findings of this study are available from the corresponding author upon reasonable individual request.

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