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Artificial intelligence in sepsis management: A bibliometric analysis

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ABSTRACT

Objective: To systematically evaluate the global research landscape of artificial intelligence (AI) applications in sepsis management to identify evolutionary patterns and inform evidence-based clinical decision-making.

Methods: We extracted 1 100 publications from the Web of Science Core Collection (1985-2024), employing Excel, CiteSpace, and VOSviewer for quantitative analysis of national contributions, institutional collaborations, author networks, and keyword evolution.

Results: Our findings reveal exponential growth in publication output since 2017 (annual growth rate: 56.3%), driven by advancements in machine learning and interdisciplinary integration. China and the United States emerged as dominant contributors, collectively accounting for over 60% of total publications. The top three institutions were Harvard University, University of California System and Emory University. Keywords co-occurrence and cluster analysis identified research hotspots such as AI-driven prediction models, immune infiltration, precision medicine and single-cell sequencing. Keywords were categorized into five clusters: clinical management of sepsis, pathological mechanism and biomarkers, complications and monitoring, AI-based research, and diagnostic criteria.

Conclusions: The publications interest in the application of AI in sepsis management is continuously increasing, especially in aspects such as the immune mechanism of sepsis, critical care management, and treatment plans. Moreover, there is great potential for research in precision medicine and single-cell sequencing. Future research should focus more on the application of AI in the prediction and precise intervention of sepsis.

KEYWORDS: Sepsis; Artificial intelligence; Bibliometrics; Sepsis management; Machine learning

Summary

Question: What are the key research trends and future directions of artificial intelligence (AI) in the management of sepsis?

Findings: AI applications in sepsis management have grown rapidly since 2017, with China and the US leading research output. Key focuses include predictive modeling, precision medicine, immune infiltration, and single-cell sequencing.

Meaning: AI holds transformative potential to enhance early diagnosis, risk stratification, and individualized treatment in sepsis, but future progress depends on clinical validation, ethical oversight, and integration of multi-omics technologies.

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1. Introduction

Sepsis, a life-threatening organ dysfunction caused by dysregulated host responses to infection, remains a global health priority due to its high morbidity and mortality rates in intensive care units[1]. While age-standardized incidence and mortality have declined in recent years, sepsis nevertheless continues to impose substantial healthcare burdens worldwide, particularly in regions with limited capabilities for prevention, recognition, or treatment[2]. The heterogeneous nature and nonspecific clinical manifestations of sepsis pose significant challenges to traditional diagnostic tools such as qSOFA[3], SIRS[4], and early warning scores[5]. Conventional clinical decision-making, reliant on physician experience and static indicators, often fails to address the dynamic pathophysiological changes in septic patients. These limitations underscore the urgent need for more timely and accurate prediction methods to improve outcomes.

Artificial intelligence (AI), a concept formally introduced in 1956, has emerged as a transformative approach in sepsis management through advancements in big data analytics and computational technologies. Early applications dating back to the mid-1990s focused on machine learning (ML) models for sepsis prediction[6,7] and prognostic assessment[8]. Subsequent breakthroughs in deep learning have enabled the development of dynamic temporal prediction models that integrate multimodal data, exemplified by systems utilizing real-time analysis of heart rate, systolic blood pressure, and temperature fluctuations for early detection[9]. This technological evolution has progressively expanded AI's role in sepsis care.

Despite rapid growth in AI-related sepsis research, the field remains fragmented due to inconsistent dataset selection, heterogeneous algorithmic approaches, and divergent validation standards across studies. To address this knowledge gap, we conducted a comprehensive bibliometric analysis of global research trends through December 2024. This study systematically maps the intellectual landscape by examining national contributions, institutional collaborations, author networks, keyword evolution, and thematic hotspots. By identifying current research voids, we aim to inform future technological innovations and evidence-based clinical practices, ultimately advancing intelligent sepsis management systems.

2. Methods

2.1. Data sources and search strategy

Data were extracted from the Web of Science Core Collection (WOSCC), a globally recognized academic database selected for its comprehensive coverage across natural sciences, social sciences, and other disciplines, as well as its widespread adoption in bibliometric studies. The search strategy employed the query:

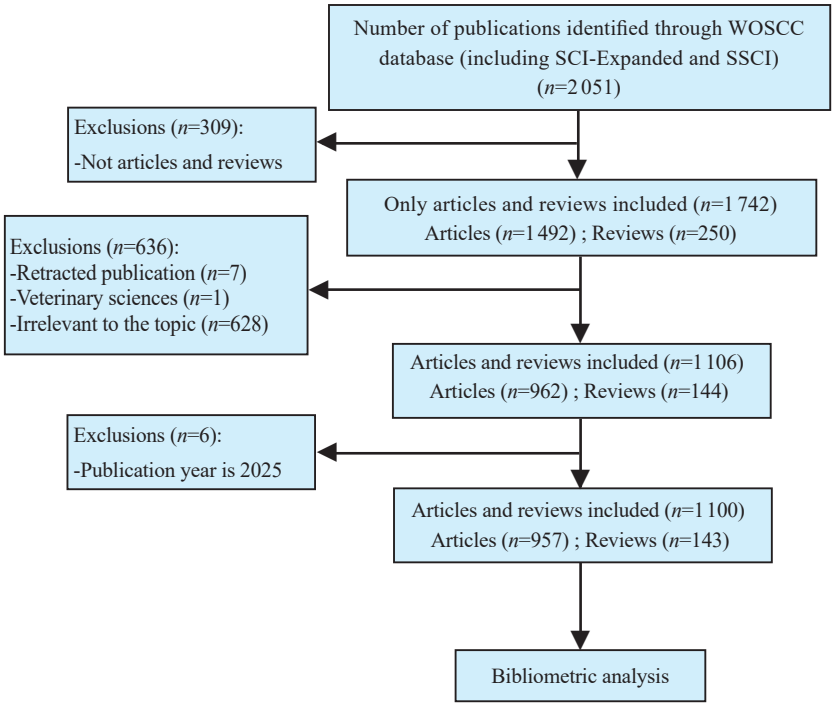


Figure 1. Literature screening flowchart for AI-related studies in sepsis management. AI: artificial intelligence. WOSCC: Web of Science Core Collection.

TS=(sepsis) AND TS= (artificial intelligence *OR* machine learning *OR* deep learning *OR* neural networks *OR* convolutional neural networks *OR* fuzzy logic *OR* reinforcement learning *OR* supervised learning *OR* unsupervised learning *OR* natural language processing *OR* computer vision *OR* big data *OR* computerized analysis). Articles and reviews published through December 2024 were included, while irrelevant studies, veterinary research, and retracted publications were excluded. Six articles originally categorized under 2025 by CiteSpace due to their incorrect categorization in 2025 were excluded through time range configuration to maintain temporal validity. After applying these criteria, 1 100 publications were retained for analysis. A flowchart detailing the screening process is provided in Figure 1.

2.2. Data collection

Three authors independently screened studies, excluding those irrelevant to the search strategy. Discrepancies were resolved through consensus discussions. All metadata (titles, authors, keywords, countries, journals, institutions, and references) were exported from the Web of Science for final analysis.

2.3. Bibliometric analysis

This study employed three analytical tools: Microsoft Office Excel 2019, VOSviewer 1.6.20, and CiteSpace 6.4.R1 Advanced. VOSviewer is a free, open-source software designed for bibliometric analysis and visualization, with a focus on visualizing bibliometric networks and handling large-scale data[10]. It clusters closely related nodes and represents connections between nodes with lines. Additionally, VOSviewer supports two types of visualization maps: overlap and density visualization. CiteSpace, developed by Dr. Chaomei Chen at Drexel University, is a scientific literature analysis tool based on citation analysis theory in scientometrics. It specializes in dynamic visualization to identify and present emerging trends, transient patterns, and critical turning points in a research field[11]. One of its unique features is the dual-map overlay of journal co-citation, which provides a clearer and more intuitive explanation of the cooperative relationships between citing and cited journals and analyzes disciplinary transition trends[12].

In this study, we primarily utilized Excel to analyze the publication output of literature related to AI-related studies in sepsis management. VOSviewer and CiteSpace were employed to examine collaborative relationships among countries, authors, and institutions, as well as to conduct co-citation analysis of journals, keyword clustering, and timeline visualization. Notably, to enhance the accuracy and scientific rigor of our analysis, we merged synonyms of keywords in CiteSpace. This step was necessary because different authors might use varying keywords to describe the same or similar concepts, or employ abbreviations for proper nouns, which could otherwise result in fragmented displays of similar keywords during the analysis.

3. Results

This study analyzed 1 100 publications from 75 countries, involving 363 institutions and 749 authors. They were published in 422 journals and cited 17 205 references from 848 journals.

3.1. Annual number of publications and cumulative number of publications

Figure 2A illustrates publication trends from 1985 to 2024. Pre-2017, research output remained low but stable, followed by a sharp rise with an annual growth rate of 56.3% after 2017. By 2024, annual publications peaked at 326, with 94.5% of all studies published in the last eight years (2017-2024). This surge likely stems from rapid advances in AI/ML, interdisciplinary integration of critical care and computer science, and growing clinical demand for innovations such as early warning systems and dynamic prognostic models.

Table 1. Top 10 countries in the number of publications on AI in sepsis management.

Rank	Number of publications	Countries	Percentage	Citations
1	390	People's Republic of China	35.45	3 422
2	346	USA	31.45	11 229
3	63	UK	5.73	2 887
4	56	Italy	5.09	741
5	54	Germany	4.91	1 314
6	48	South Korea	4.36	495
7	46	Netherlands	4.18	2 122
8	39	India	3.55	258
9	38	Australia	3.45	1 022
10	36	Canada	3.27	761

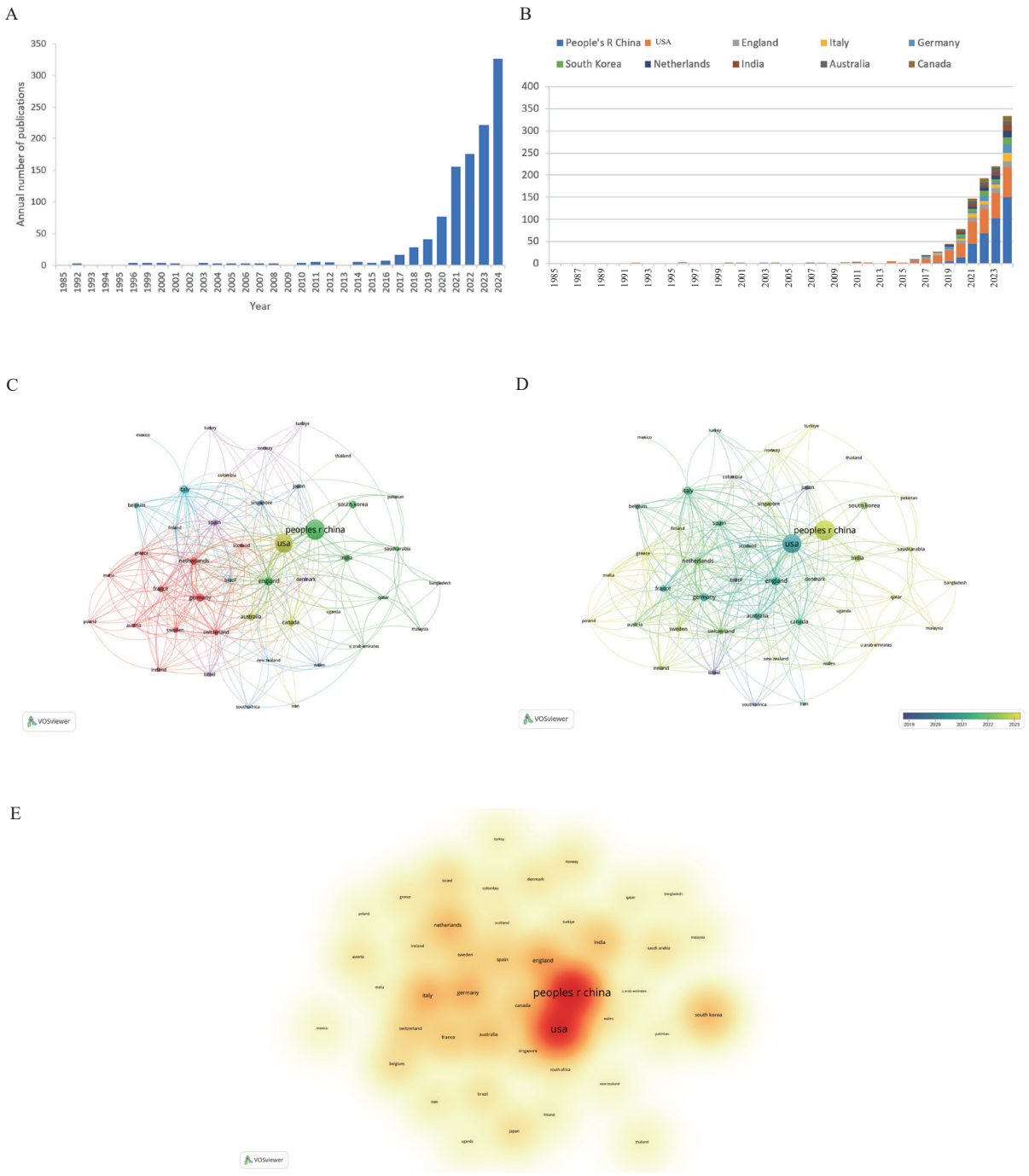


Figure 2. (A) Annual and cumulative number of publications related to AI in sepsis management. (B) Trends in the number of articles published by the top 10 countries over the past 40 years. (C) Countries with more than 4 publications. Each node represents a country, the size of the node represents the number of articles published, the links between nodes represent the cooperation of countries, and the thickness of the lines represents the intensity of the cooperation. (D) Overlay visualization: average year of publication by country. (E) Density visualization of countries.

3.2. Distribution of countries

A total of 75 countries contributed to AI-related sepsis research. Table 1 ranks the top 10 countries by publication volume: China (390), the United States (346), the United Kingdom (63), and Italy (56) led productivity. China and the U.S. collectively accounted for >60% of total output. However, the U.S., China, the UK, and New Zealand dominated citation metrics. Despite leading in publication output since 2021, China lags behind the U.S. in citations, possibly due to its recent surge in publishing that has yet to translate into global academic influence. Figure 2B traces national productivity trends over four decades, showing the U.S. as the earliest contributor (1985) until China surpassed it in 2021.

VOSviewer analysis (threshold: ⩾4 publications per country) identified 44 nations forming 6 clusters (Figure 2C). China, represented by the largest node, maintained strong collaborations

Table 2. Top 10 keywords by frequency in CiteSpace and VOSviewer.

Rank	CiteSpace		VOSviewer	
	Keywords	Frequency	Keywords	Frequency
1	sepsis	475	sepsis	780
2	machine learning	442	machine learning	438
3	mortality	319	mortality	359
4	definition	227	definition	227
5	model	175	prediction	203
6	prediction	151	model	183
7	artificial intelligence	140	artificial intelligence	129
8	score	116	score	117
9	intensive care unit	101	diagnosis	98
10	critical care	97	prognosis	92

with the U.S. and UK. The green cluster, led by China, primarily included Asian nations (*e.g.*, South Korea, India) with dense intra-regional connections. The U.S.-led yellow cluster demonstrated extensive international linkages despite smaller national nodes. Temporal overlay visualization (Figure 2D) highlighted recent research activity (2019-2023) in China and other Asian countries. Chinese research predominantly focuses on developing sepsis predictive models[13,14], emphasizing early detection and forecasting complications and mortality. In contrast, U.S. studies prioritize clinical validation and translational research of ML models, alongside mechanistic exploration of sepsis, exemplified by identifying novel clinical phenotypes[15]. These divergent research priorities likely stem from disparities in healthcare data ecosystems and clinical implementation contexts between the two nations.

3.3. Distribution of institutions and authors

A total of 363 institutions have published research related to AI and sepsis, among which 46 institutions have published more than 10 papers (Figure 3). The institution with the most publications is Harvard University (41), followed by the University of California (38), Emory University (35), Harvard University Medical Affiliates (24) and Chinese Academy of Medical Sciences (21). The last university is located in China. Supplementary Table 1 shows the top 10 research institutions ranked by the number of publications.

A total of 749 authors have contributed to these studies (Figure 3). The top 5 authors in the field of AI and sepsis, ranked by the number of publications, are Rishikesan Kamaleswaran (19), Shamim Nemati (10), Ritankar Das (7), Azra Bihorac (7), and Matthew M. Churpek (6). Supplementary Table 2 shows the top 10 authors ranked by the number of publications.

3.4. Distribution of journals

A total of 1 100 cited documents were published in 422 different journals. Figure 4A shows the co-citation journal map created by CiteSpace, while Figure 4B shows the 78 journals with more than 100 citations of AI and sepsis papers created by VOSviewer. Figure 4C uses CiteSpace to create a dual-map overlay, which illustrates the thematic distribution of journals, citation trajectories, and changes in research centers. The graph shows that the main themes of the cited journals are molecules, biology, genetics, health, nursing, and medicine, while the main themes of the citing journals are pharmaceuticals, medicine, and clinical. The shift in journal themes from basic to clinical research reflects the field's movement toward clinical applications, which is the ultimate goal of AI in sepsis.

3.5. Keyword co–occurrence cluster analysis

The keyword co-occurrence network in AI-related sepsis research was visualized using CiteSpace and VOSviewer (Figure 5A & 5B). CiteSpace generated a keyword co-occurrence network (Figure 5A), labeling keywords with occurrence frequencies greater than 70. VOSviewer identified 3 413 keywords, with 145 keywords exceeding 8 occurrences (Figure 5B). Table 2 lists the top 10 high-frequency keywords identified by CiteSpace and VOSviewer respectively. Overlapping keywords include "sepsis", "machine learning", "mortality", "definition", "prediction", "model", and "artificial intelligence" indicating that AI is primarily applied to construct predictive models for sepsis and support clinical decision-making to reduce mortality. Here, "artificial intelligence" represents a broad field encompassing technologies that simulate human intelligence, while "machine learning", as a subfield of AI, focuses more on algorithm development and is frequently employed in predictive modeling or decision-making systems (*e.g.*, deep learning, random forests). The separate categorization of these two keywords and the higher frequency of ML compared to AI reflect an evolving research emphasis in sepsis-related studie: investigations increasingly prioritize ML-driven algorithmic development for clinical applications. The overlay visualization map (Figure 5C) displays the average time of keyword appearances. Nearly all

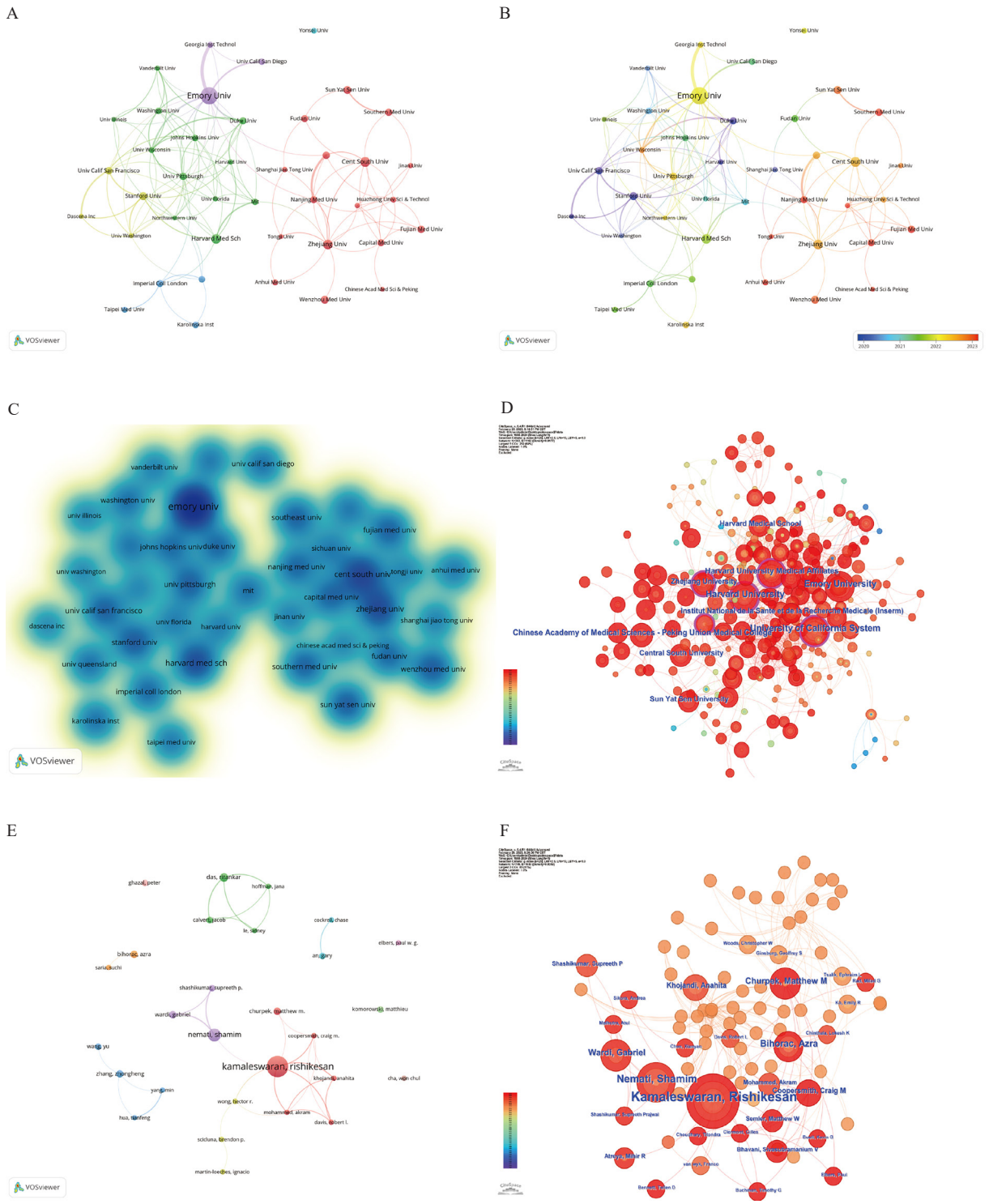


Figure 3. Distribution of institutional collaboration and author networks in AI and sepsis research. (A), (B), and (C) represent the institution map, temporal distribution of institutions, and density visualization of institutions with more than 10 publications displayed by Vosviewer, respectively. (D) The institutional collaboration network created by Citespace. (E) Author collaboration network created by Vosviewer for authors with more than 5 publications. (F) Author collaboration network created by Citespace for authors with more than 3 publications. Each node represents an institution or an author, and the size of the node indicates the number of publications. Connections between nodes represent collaborations among those nodes, with the thickness of the lines indicating the strength of the collaboration.

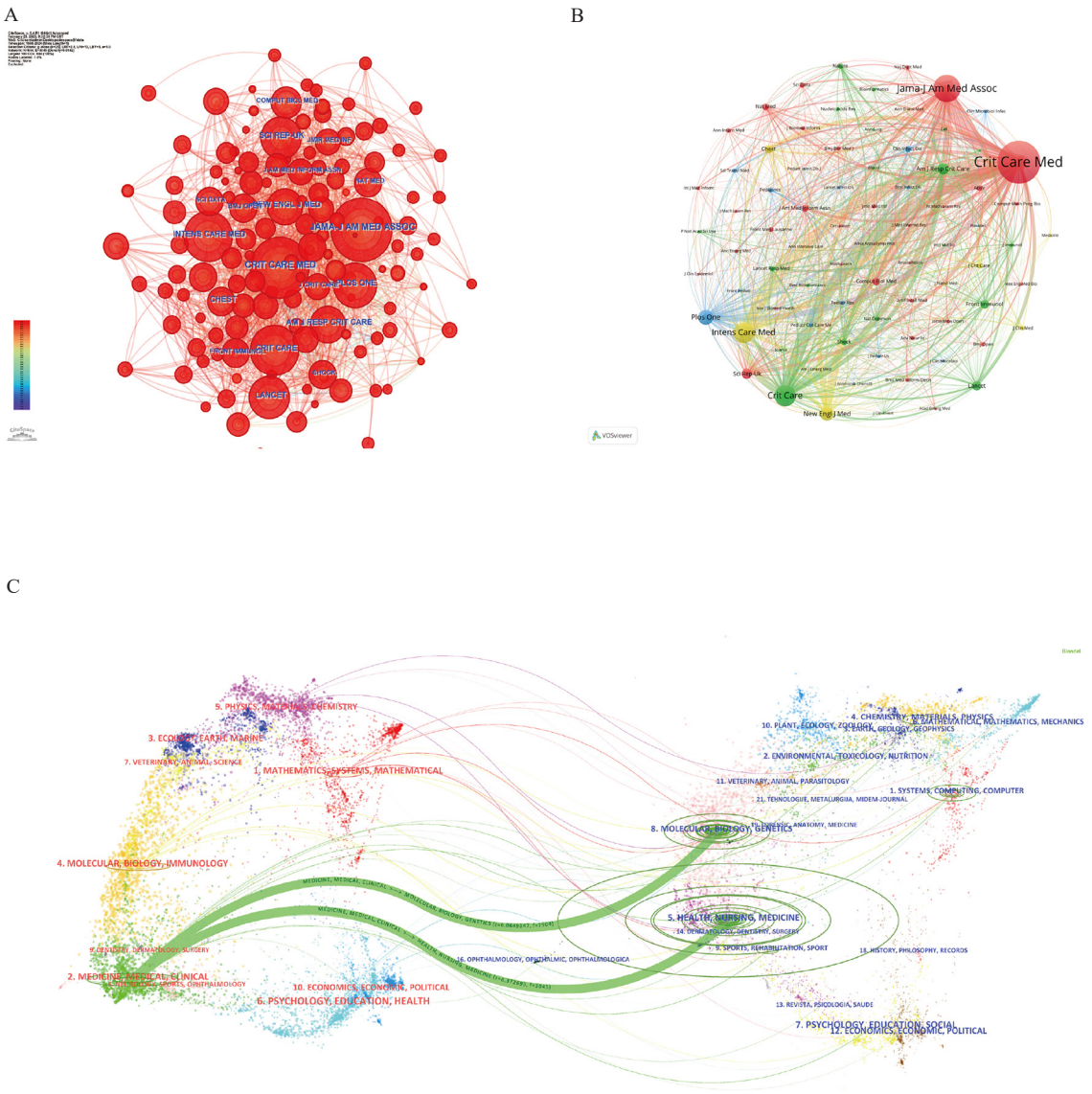


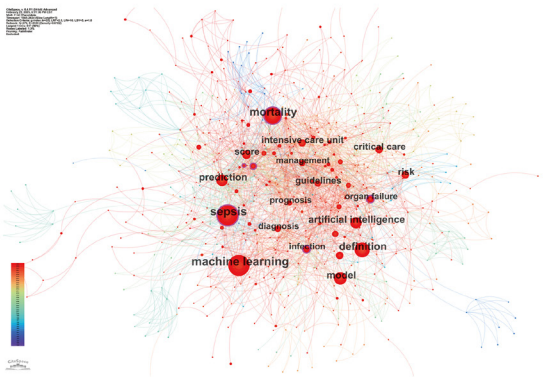
Figure 4. Distribution of co-citation journal networks in the field of AI and sepsis. (A) Co-citation journal network distribution created by Citespace for top 130 journals. (B) Co-citation journal map created by Vosviewer for journals with more than 100 citations. Each node represents a journal, and the size of the node indicates the number of citations. Connections between nodes represent co-citation relationships between journals, with the thickness of the lines indicating the strength of these relationships. (C) Dual-map overlay created by Citespace. The left side represents citing journals, symbolizing the knowledge frontier; the right side represents cited journals, symbolizing the knowledge base. Lines represent citation links between journals.

keywords emerged post-2018, with most high-frequency terms averaging appearance in 2021-2022, signifying a surge in research activity during this period.

Supplementary Table 3 lists six keywords identified by CiteSpace with centrality over 0.1. Among these, “sepsis”, “mortality”, “organ failure”, and “infection” exhibit both high frequency and centrality (>0.1), indicating their central role in research focus. Notably, “epidemiology” and “C-reactive protein” also demonstrate significant centrality (>0.1), despite their lower frequencies (61 and 23 occurrences, respectively), underscoring their critical roles in advancing sepsis-related studies.

Cluster analysis was performed using the log-likelihood ratio (LLR) ranking algorithm in CiteSpace, revealing the top ten clusters (Figure 5D). The top five representative keywords within each cluster are detailed in Supplementary Table 4. The clustering quality was evaluated using modularity (Q) and mean silhouette (S) values. A Q>0.3 indicates significant modular structure, while S>0.5 suggests reasonable clustering, and S>0.7 reflects high reliability. In this map, the modularity Q value was 0.598 and the Silhouette S value was 0.812, indicating the high reliability of the clustering labels. Generally, these clusters were divided into five research categories: Core clinical management scenarios of sepsis (*e.g.*, #0, #2); Pathological mechanisms and biomarkers (*e.g.*, #1, #9); Sepsis-related complications and monitoring (*e.g.*, #3, #4, #6); AI-driven research applications (*e.g.*, #7, #8) and diagnostic criteria for sepsis (*e.g.*, #5)

A



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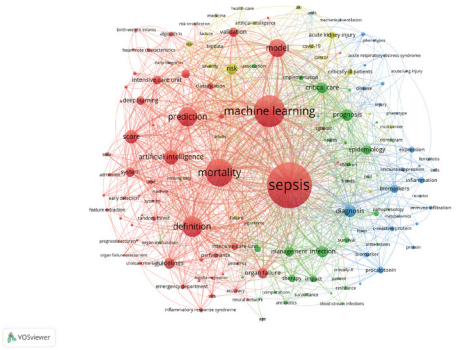

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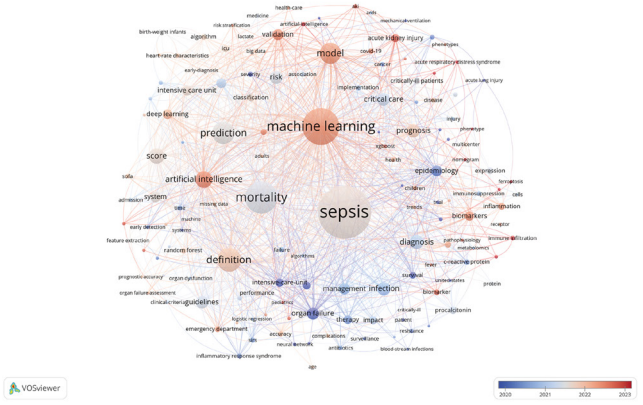

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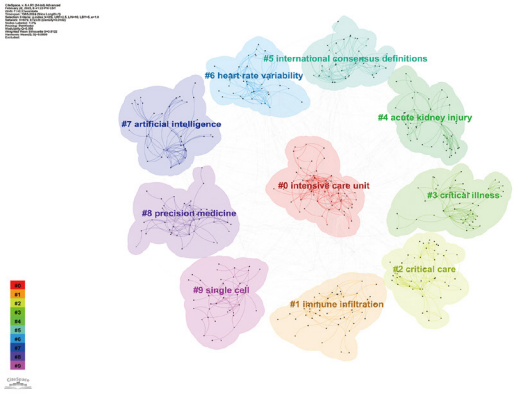

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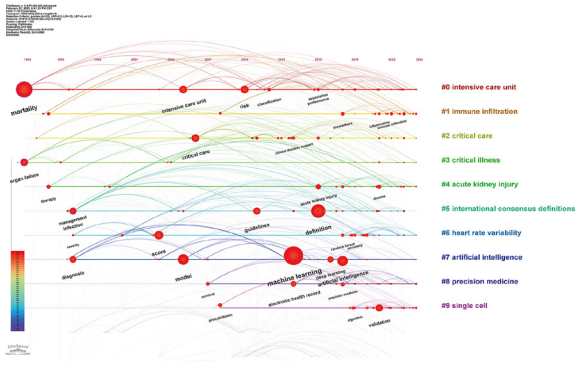

F

Top 20 Keywords with the Strongest Citation Bursts

Keywords	Year	Strength	Begin	End	1985 - 2024
trial	1993	2.72	1993	2021	
epidemiology	2004	2.45	2004	2011	
program	2013	2.54	2013	2018	
early detection	2014	2.65	2014	2021	
goal directed therapy	2014	2.37	2014	2019	
blood stream infections	2015	2.43	2015	2018	
artificial neural networks	2016	2.16	2016	2020	
guidelines	2011	3.61	2017	2020	
intensive care unit	2005	3.36	2017	2018	
clinical trials	2017	2.24	2017	2020	
inflammatory response syndrome	2012	3	2018	2020	
antimicrobial therapy	2018	2.8	2018	2021	
vital signs	2019	3.71	2019	2021	
definition	2016	3.18	2019	2020	
admission	2019	3.01	2019	2021	
electronic health record	2014	2.32	2019	2020	
response system	2019	2.3	2019	2020	
onset	2020	2.82	2020	2021	
intensive care	2012	2.51	2022	2024	
cells	2008	2.13	2022	2024	

Figure 5. (A) Keyword co-occurrence network generated by CiteSpace. (B) Keyword co-occurrence map from VOSviewer (minimum occurrence count >8). (C) Overlay visualization from VOSviewer: The average time of keywords appearance. (D) Keyword clustering analysis network. (E) Timeline visualization. (F) Top 20 burst keywords.

The timeline map generated by CiteSpace (Figure 5E) visualizes the emergence and evolution of research themes over time. For instance: Cluster #7 (artificial intelligence) first appeared in 1996, later branching into subtopics such as "models", "machine learning", "deep learning", and "artificial intelligence". The most studied term, "machine learning", emerged around 2013 and gained significant focus post-2020, primarily for predictive modeling. Cluster #8 (precision medicine) originated around 2007, reflecting the relatively late integration of AI into sepsis-related precision medicine research. Additionally, the relatively recent emergence of cluster keywords such as "immune infiltration", "single-cell", and "acute kidney injury" suggests their potential as frontier areas in AI-driven sepsis-related research.

Keyword bursts, identified by CiteSpace (Figure 5F), highlight emerging research frontiers and hotspots in AI-driven sepsis studies. Notably, terms such as "intensive care" and "cells" have shown sustained prominence since 2022, reflecting that current research focuses on sepsis management in critical care settings. Simultaneously, AI-driven sepsis research has shifted from population-level to cellular-level investigations. AI is poised to drive advancements in decoding immune cell dynamics to guide individualized therapies, integrating AI with single-cell sequencing for dynamic cellular data analysis, identifying critical cell sub-populations and developing targeted therapeutic strategies in the future.

4. Discussion

4.1. Research hotspots and frontiers in AI–driven sepsis studies

Keyword analysis reveals a pivotal frontier in AI applications for sepsis management: leveraging AI to characterize sepsis at the cellular level for precision medicine. The emergence of terms such as "immune infiltration" "precision medicine" and "cells" epitomizes a shift in sepsis pathophysiology research—from population-level investigations toward single-cell resolution analyses[16].

4.2. AI in the pathological mechanisms of sepsis

Recent studies have shown that exploring the complex pathological mechanisms of sepsis at the cellular level, such as immune dysregulation, mitochondrial dysfunction, and coagulation abnormalities, is the biological basis for accurate typing. AI has emerged as a powerful tool to unravel sepsis pathology by enabling multi-omics integration, causal network construction and single-cell resolution.

Current AI-driven research on the pathological mechanisms of sepsis primarily focuses on identifying biomarkers and conducting immune infiltration analyses to validate interactions between biomarkers and immune cells. For example, a study integrating Weighted Gene Co-expression Network Analysis with three ML methods—LASSO, Random Forest, and Boruta—identified three potential biomarkers for diagnosing sepsis[17]. Subsequent immune infiltration and single-cell analyses further dissected the immune microenvironment, pinpointing molecular compounds and docking sites. These findings position the identified genes as mechanistic nodes for therapeutic intervention. Besides this, a ML model has been able to identify 20 genetic markers in peripheral blood immune cells of children with sepsis in pediatric ICU to predict the severity and mortality of sepsis[18]. Notably, biomarkers linked to dysfunctional cells in organs—such as tissue macrophages and vascular endothelial cells—are increasingly recognized as critical players in sepsis progression. Despite progress, most sepsis biomarkers exhibit limited clinical utility, with only a small fraction adopted in routine practice[19]. A key challenge lies in optimally combining biomarkers to enhance diagnostic accuracy[20].

Growing evidence suggests a potential link between sepsis and mitochondrial dysfunction. One study conducted bioinformatics analysis on datasets related to septic cardiomyopathy to explore the interaction between mitochondrial metabolism and the immune microenvironment for the first time[21]. Using three ML algorithms (SVM-RFE, LASSO, and RF), the study identified six mitochondrial-associated differentially expressed genes, revealing the interplay between mitochondrial metabolism and immune infiltration in septic cardiomyopathy. Another study applied WGCNA and ML to investigate mitochondrial-related genes (MiRGs) in sepsis[22]. Three hub MiRGs were identified, with further analysis linking them to immune cell infiltration. These studies explore the pathological mechanism of sepsis from the perspective of mitochondrial metabolism and immune disorders, which is expected to promote mitochondrial targeted therapy. Future research should deepen exploration of MiRG functions, employing gene-editing technologies to regulate mitochondrial-related genes and develop targeted therapeutics to advance sepsis management.

4.3. AI–based precision medicine for sepsis

Precision medicine is becoming important in sepsis management[23]. As established earlier, AI enables the stratification of patient phenotypes by elucidating cellular-level heterogeneity, thereby constructing a multi-dimensional framework integrating genomic, biological, and environmental determinants for sepsis precision medicine. At present, AI-based precision medicine for sepsis can be divided into the following four aspects: endotype stratification, dynamic monitoring, precision therapeutics and outcome redefinition.

ML, a subset of AI, has been applied to cluster septic patients into phenotypes. A prior ML-based clustering study identified four coagulopathic phenotypes in severe sepsis patients. Recombinant human thrombomodulin therapy was associated with reduced in-hospital mortality only in the severe coagulopathy phenotype, characterized by low platelet counts, elevated fibrin degradation products and *D*-dimer levels, and multi-organ dysfunction, which illustrated ML's capability to identify optimal clinical phenotypes for targeted therapies[24]. However, determining individual patient phenotypes remains challenging. To address the challenge of phenotype identification, Goto *et al.*[25] developed and validated an ML model to predict rhTM-responsive phenotypes, aiding clinicians in optimizing therapeutic strategies. Additionally, a review summarized AI-driven sepsis subtyping approaches, including classifications based on infection characteristics, site of infection, pathogens, hemodynamic patterns, routine clinical data, and molecular omics[26]. These phenotype classifications hold promise for enabling more precise therapies and enhancing patient care. While AI has identified numerous subtypes, the clinical relevance of each novel subtype requires rigorous evaluation. Future studies should deepen understanding of existing phenotypes, and the utility of biological phenotypes must be validated in prospective clinical trials.

Given the rapid clinical deterioration characteristic of sepsis in ICUs, predictive modeling of dynamic physiological trajectories has emerged as a cornerstone of precision critical care. Widely adopted ML algorithms, including XGBoost and Random Forest, demonstrate significant utility for early sepsis risk stratification in heterogeneous patient populations[27]. In a pivotal comparative study by Yang *et al*., 23 predictive models underwent rigorous validation *via* training-test set partitioning. The Random Forest model (test set n=9, accuracy=0.911) and XGBoost algorithm (test set n=7, accuracy=0.957) achieved superior predictive performance for sepsis incidence, evidenced by elevated accuracy and C-index metrics—enabling phenotype-specific intervention. Complementing this, Hou *et al*. developed an XGBoost model (AUC=0.857) that outperformed conventional logistic regression and SAPS-Ⅱ scores in predicting 30-day mortality among Sepsis-3 patients within the MIMIC-Ⅲ database[13], validating its role in prognostic precision. To translate these advances into bedside precision medicine, future development must prioritize non-invasive predictive biomarkers that enhance model fidelity and clinical interoperability. Dynamic monitoring of vital signs and evaluation of therapeutic effect are key steps in the treatment and prognosis of sepsis. One study raised the concept of heterogeneous treatment effects, which may lead to an ineffective average treatment effect in patients with sepsis and clinicians being unable to accurately evaluate interventions[28]. In comparative assessments of therapeutic effects across different ICU patient stratification models, unsupervised modeling demonstrates superior capability to stratify sepsis patients' therapeutic responses solely based on baseline characteristics—a finding consistently validated in other studies. AI is also gradually applied to the precision medicine of neonatal sepsis. The difference between neonates and adults is a challenge for AI models to assess their optimal antibiotic dosage and prognosis. A study utilized the CatBoost ML algorithm to develop a clinical decision support system for optimizing dosing regimens of five antibiotics commonly used in neonatal sepsis—amoxicillin, ceftazidime, cefotaxime, meropenem, and latamoxef. This approach significantly enhanced predictive accuracy for all five agents, thereby enhancing precision medicine in neonatal sepsis management[29].

In summary, current research prioritizes two interconnected domains: 1) leveraging cellular biomarkers and immune signatures to decode sepsis mechanisms, and 2) advancing AI-driven precision medicine. This dual focus underscores the field's evolution toward granular, biologically grounded AI solutions to address sepsis heterogeneity.

4.4. AI applications in sepsis prediction and diagnosis

Based on the rapid progression of sepsis, the atypical early symptoms and the lag of traditional diagnostic methods, AI is crucial in the early prediction and accurate diagnosis of sepsis, and can effectively guide subsequent personalized treatment and prognosis[30]. A study has shown that the SERA algorithm will convert the electronic medical record (EMR) combined with unstructured clinical records to demonstrate superior accuracy (AUC 0.94, sensitivity 0.87, specificity 0.87)[31]. In the clinical classification of sepsis, there is a study that uses k-means clustering to analyze 29 variables in the EMR of patients at admission (including demographic variables, vital signs, inflammatory markers, markers of organ dysfunction or damage, and lactate levels, *etc.*), develops a concise classifier model that can identify four clinical subtypes of sepsis patients and confirms that there are significant differences between different subtypes. Therefore, clinicians can make different treatments based on AI diagnosis for different subtypes to achieve the best efficacy[32].

Early prediction of mortality in patients with sepsis can also provide effective decision-making for clinical treatment and prognostic assessment. A multicenter retrospective cohort study used ML methods to analyze EMR in patients with sepsis to evaluate the model's performance in predicting sepsis outcomes within 24 hours of ICU admission in healthcare facilities in the United States and China[33]. The researchers extracted and analyzed 31 clinical data from patients' EMR, including demographic data and laboratory indicators. The final prediction model showed good performance in predicting mortality in sepsis patients in the test concentration, with an AUC of over 0.8 and an accuracy of more than 70%. This

study suggests that ML-based sepsis prediction models can improve clinical outcomes by conducting accurate risk assessments within the critical first 24 hours of ICU admission. Despite the differences between the healthcare systems in the United States and China, the algorithm maintains reliable predictive performance, showing broad applicability. In addition, another study used ML to find a U-shaped relationship between stress hyperglycemia ratio and 28-day mortality in sepsis patients – higher SHR values were significantly associated with an increased risk of adverse events[34].

CiteSpace's hotspot analysis suggests that recent research on AI for sepsis has shifted from a "population level" to a "cellular" focus, AI-driven diagnostic research focuses more on identifying sensitive biomarkers and optimizing diagnostic tools. In addition to traditional markers such as procalcitonin and C-reactive protein, "omics"-derived biomarkers – genomic, transcriptome, proteome and metabolome – are also gaining traction[35]. The integration of single-cell RNA sequencing and ML techniques can identify key immune genes in sepsis. Biological association networks and ML were used to collect blood samples from patients with sepsis in the ICU and healthy volunteers undergoing routine examinations at the same time within 24 hours of admission. Total RNA was extracted to identify differentially expressed genes, key genes are then identified and their cell localization can be determined by single-cell sequencing[36]. In addition, other studies have combined key genes for platelets with a large amount of RNA-seq data to develop a new prognostic model for patients with sepsis, emphasizing the importance of platelets in sepsis[37]. Transcriptomics-based classifiers show particular promise for rapid, cost-effective point-of-care diagnosis through host gene expression profiles[38].

4.5. Research on AI in the clinical management of sepsis

Sepsis is a leading cause of death worldwide, affecting in-hospital survival and post-discharge quality of life, as well as the risk of readmission[39]. Therefore, initiating early treatment for sepsis patients is crucial. The 2021 International Guidelines for the Management of Sepsis and Septic Shock mention that the clinical management of sepsis patients includes initial resuscitation, infection control, hemodynamic management, adjunctive therapies, and monitoring and assessment. The application of AI in sepsis precision medicine research emerged relatively late, and while ML for treatment monitoring has been gradually introduced, its application in clinical practice still needs to be improved.

4.6. Fluid resuscitation

The latest Surviving Sepsis Campaign guidelines recommend an initial fluid resuscitation with at least 30 mL/kg (based on ideal body weight) of crystalloid fluids[40]. Most patients require ongoing fluid administration after the initial resuscitation phase. Careful management of fluid volumes is crucial to avoid both over-resuscitation and under-resuscitation. After the initial fluid resuscitation, the use of AI can help assess intravascular volume status and organ perfusion to guide further fluid administration.

A team developed a novel ML-based fluid responsiveness algorithm using only arterial blood pressure waveform data as input[41]. Compared to pulse pressure variation (a widely used FR predictor), this model significantly improved FR prediction accuracy. It guides clinicians to maximize the benefits of fluid bolus therapy, mitigate fluid toxicity risks, and achieve targeted resuscitation in critically ill patients with circulatory shock. Another study employed ML to compare mortality outcomes in sepsis patients receiving balanced crystalloids versus saline for fluid resuscitation[42]. The study found that an ML algorithm developed from bedside vital signs prospectively identified Group D sepsis who may have a substantial mortality reduction from the use of balanced crystalloids compared with normal saline. These findings may optimize intravenous fluid selection in sepsis and could potentially inform future sepsis resuscitation guidelines.

4.7. Control of infection in sepsis management

One study employed a Long Short-Term Memory network to develop the T4 model[43]. Utilizing 22 time-varying variables (including vital signs, laboratory test results, *etc*.) and 4 static variables (age, gender, *etc.*), the T4 model was able to recommend effective treatment strategies, offering potential clinical insights to assist clinicians in determining the optimal timing for antibiotic administration in sepsis patients. However, although the T4 algorithm addresses the issue of optimal timing for antibiotic dosing in sepsis patients, it does not differentiate between specific antibiotics and their corresponding side effects, nor does it incorporate antibiotic choice or side effects into its treatment optimization framework. Wendland *et al*. developed OptAB, the first AI-based, online-updatable model for optimal antibiotic selection, based on a hybrid neural network differential equation algorithm[44]. By processing specific characteristics of patient data, including irregular measurements, a high proportion of missing values, and time-dependent confounding, this model enables clinicians to compare predicted outcomes for individual patients under different antibiotic choices over time. It guides clinicians in selecting the optimal antibiotic for sepsis patients while simultaneously considering contraindications and side effects, thereby maximizing the probability of treatment success.

In conclusion, this bibliometric analysis investigates the application of AI in sepsis research from 1985 to 2024, leveraging 1 100 articles from the WOSCC database to evaluate publication trends, contributions by countries, institutions, authors, and journals, as well as thematic evolution and future directions. The field has

experienced exponential growth since 2017, with publication numbers exhibiting exponential growth, highlighting its expanding research potential. Emerging areas such as precision medicine and single-cell sequencing, though relatively recent, demonstrate significant promise for future advancements. Current research hotspots focus on AI-driven critical care management and cellular-level exploration of immune mechanisms and therapeutic strategies. To propel the field forward, future efforts should address ethical and regulatory challenges such as data privacy and algorithmic fairness, advance multicenter clinical trials to validate the generalizability of AI models, develop personalized AI-driven treatment models for sepsis, and prioritize transitioning AI applications from predictive modeling to mechanistic exploration and precision interventions, while integrating advanced technologies like multi-omics and gene editing to deepen our understanding of sepsis pathophysiology and develop targeted therapies.

However, this study has several limitations. First, the analysis in this study was based solely on articles from the WOSCC database, excluding relevant literature from other databases, which may result in incomplete coverage and omission of significant studies. Second, this study exclusively analyzed English-language literature, which may overlook significant studies published in other languages, introducing potential bias. Third, this study utilized only two software tools (CiteSpace and VOSviewer), omitting other platforms (*e.g.*, online bibliometric tools), thereby limiting multi-platform validation. Fourth, while bibliometric analysis outcomes are objective, the interpretation of results remains inherently subjective, as different researchers may derive varying conclusions from identical data.

Conflict of interest statement

The authors report no conflict of interest.

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Data availability statement

The data supporting this bibliometric analysis are publicly available from the Web of Science Core Collection. Any additional details can be obtained from the corresponding authors upon reasonable request.

Authors' contributions

MW conceptualized the study, supervised the research process, and revised the manuscript for important intellectual content. LYZ, WL, and WBZ conducted the literature search and data extraction, performed the bibliometric analysis, and drafted the initial manuscript. JWB, YYYS, and ZS assisted in data analysis and interpretation, and contributed to the discussion section of the manuscript. MW and WL provided clinical expertise in sepsis management, reviewed the manuscript for clinical accuracy, and offered critical feedback.

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References

[1] Mizera J, Bystron A, Matuszewska K, Pilch J, Giordano U. Knowledge, management, and complications of sepsis and septic shock: A significant therapeutic challenge in the intensive care unit. *J Acute Dis* 2024; **13**(2): 53-59.

[2] Rudd KE, Johnson SC, Agesa KM, Shackelford KA, Tsoi D, Kievlan DR, et al. Global, regional, and national sepsis incidence and mortality, 1990-2017: Analysis for the global burden of disease study. *Lancet* 2020; **395**(10219): 200-211.

[3] Churpek MM, Snyder A, Han X, Sokol S, Pettit N, Howell MD, et al. Quick sepsis-related organ failure assessment, systemic inflammatory response syndrome, and early warning scores for detecting clinical deterioration in infected patients outside the intensive care unit. *Am J Respir Crit Care Med* 2017; **195**(7): 906-911.

[4] Raith EP, Udy AA, Bailey M, Mcgloughlin S, Macisaac C, Bellomo R, et al. Prognostic accuracy of the SOFA Score, SIRS Criteria, and qSOFA Score for in-hospital mortality among adults with suspected infection admitted to the intensive care unit. *JAMA* 2017; **317**(3): 290.

[5] Holland M, Kellett J. A systematic review of the discrimination and absolute mortality predicted by the National Early Warning Scores according to different cut-off values and prediction windows. *Eur J Intern Med* 2022; **98**: 15-26.

[6] Jaimes F, Farbiarz J, Alvarez D, Martinez C. Comparison between logistic regression and neural networks to predict death in patients with suspected sepsis in the emergency room. *Crit Care* 2005; **9**(2):

R150-R156.

[7] Sutherland A, Thomas M, Brandon RA, Brandon RB, Lipman J, Tang B, et al. Development and validation of a novel molecular biomarker diagnostic test for the early detection of sepsis. *Crit Care* 2011; **15**(3): R149.

[8] Xu P, Lin Z, Meng H, Yan S, Yang Y, Liu X, et al. A metabonomic approach to early prognostic evaluation of experimental sepsis. *J Infect* 2008; **56**(6): 474-481.

[9] Danner OK, Hendren S, Santiago E, Nye B, Abraham P. Physiologically-based, predictive analytics using the heart-rate-to-systolic-ratio significantly improves the timeliness and accuracy of sepsis prediction compared to SIRS. *Ame J Surg* 2017; **213**(4): 617-621.

[10]van Eck NJ, Waltman L. Software survey: VOSviewer, a computer program for bibliometric mapping. *Scientometrics* 2010; **84**(2): 523-538.

[11]Chen C. CiteSpace II: Detecting and visualizing emerging trends and transient patterns in scientific literature. *J Ame Soc Info Sci Tech* 2006; **57**(3): 359-377.

[12]Chen C, Leydesdorff L. Patterns of connections and movements in dual-map overlays: A new method of publication portfolio analysis. *J Assoc Inf Sci Technol* 2014; **65**(2): 334-351.

[13]Hou N, Li M, He L, Xie B, Wang L, Zhang R, et al. Predicting 30-days mortality for MIMIC-III patients with sepsis-3: A machine learning approach using XGboost. *J Transl Med* 2020; **18**(1): 462.

[14]Yue S, Li S, Huang X, Liu J, Hou X, Zhao Y, et al. Machine learning for the prediction of acute kidney injury in patients with sepsis. *J Transl Med* 2022; **20**(1): 215.

[15]Seymour CW, Kennedy JN, Wang S, Chang CH, Elliott CF, Xu Z, et al. Derivation, validation, and potential treatment implications of novel clinical phenotypes for sepsis. *JAMA* 2019; **321**(20): 2003-2017.

[16]Cajander S, Kox M, Scicluna BP, Weigand MA, Mora RA, Flohé SB, et al. Profiling the dysregulated immune response in sepsis: overcoming challenges to achieve the goal of precision medicine. *Lancet Respir Med* 2024; **12**(4): 305-322.

[17]Jiang J, Chen Y, Su Y, Zhang L, Qian H, Song X, et al. Identification and experimental validation of diagnostic and prognostic genes CX3CR1, PID1 and PTGDS in sepsis and ARDS using bulk and single-cell transcriptomic analysis and machine learning. *Front Immunol* 2024; **15**: 1480542.

[18]Banerjee S, Mohammed A, Wong HR, Palaniyar N, Kamaleswaran R. Machine learning identifies complicated sepsis course and subsequent mortality based on 20 genes in peripheral blood immune cells at 24 H post-ICU admission. *Front Immunol* 2021; **12**: 592303.

[19]Nora D, Salluh J, Martin-Loeches I, Povoa P. Biomarker-guided antibiotic therapy - strengths and limitations. *Ann Transl Med* 2017; **5**(10): 208.

[20]Zhang X, Zhang Y, Yuan S, Zhang J. The potential immunological mechanisms of sepsis. *Front Immunol* 2024; **15**: 1434688.

[21]Li Y, Yu J, Li R, Zhou H, Chang X. New insights into the role of mitochondrial metabolic dysregulation and immune infiltration in septic cardiomyopathy by integrated bioinformatics analysis and experimental validation. *Cell Mol Biol Lett* 2024; **29**(1): 21.

[22]Shu Q, She H, Chen X, Zhong L, Zhu J, Fang L. Identification and experimental validation of mitochondria-related genes biomarkers associated with immune infiltration for sepsis. *Front Immunol* 2023; **14**: 1184126.

[23]Shah FA, Meyer NJ, Angus DC, Awdish R, Azoulay É, Calfee CS, et al. A Research agenda for precision medicine in sepsis and acute respiratory distress syndrome: An official American thoracic society research statement. *Am J Respir Crit Care Med* 2021; **204**(8): 891-901.

[24]Kudo D, Goto T, Uchimido R, Hayakawa M, Yamakawa K, Abe T, et al. Coagulation phenotypes in sepsis and effects of recombinant human thrombomodulin: An analysis of three multicentre observational studies. *Crit Care* 2021; **25**(1): 114.

[25]Goto T, Kudo D, Uchimido R, Hayakawa M, Yamakawa K, Abe T, et al. Web-based application for predicting the potential target phenotype for recombinant human thrombomodulin therapy in patients with sepsis: Analysis of three multicentre registries. *Crit Care* 2022; **26**(1): 145.

[26]Liu B, Zhou Q. Clinical phenotypes of sepsis: A narrative review. *J Thorac Dis* 2024; **16**(7): 4772-4779.

[27]Yang Z, Cui X, Song Z. Predicting sepsis onset in ICU using machine learning models: A systematic review and meta-analysis. *BMC Infect Dis* 2023; **23**(1): 635.

[28]Linck EJG, Goligher EC, Semler MW, Churpek MM. Toward precision in critical care research: Methods for observational and interventional studies. *Crit Care Med* 2024; **52**(9): 1439-1450.

[29]Tang BH, Yao BF, Zhang W, Zhang XF, Fu SM, Hao GX, et al. Optimal use of beta-lactams in neonates: Machine learning-based clinical decision support system. *EBioMedicine* 2024; **105**: 105221.

[30]Wang Y, Gao Z, Zhang Y, Lu Z, Sun F. Early sepsis mortality prediction model based on interpretable machine learning approach: Development and validation study. *Intern Emerg Med* 2025; **20**(3): 909-918.

[31]Goh KH, Wang L, Yeow AYK, Poh H, Li K, Yeow JJL, et al. Artificial intelligence in sepsis early prediction and diagnosis using unstructured data in healthcare. *Nat Commun* 2021; **12**(1): 711.

[32]van Amstel R, Rademaker E, Kennedy JN, Bos L, Peters-Sengers H, Butler JM, et al. Clinical subtypes in critically ill patients with sepsis: Validation and parsimonious classifier model development. *Crit Care* 2025; **29**(1): 58.

[33]Shi S, Zhang L, Zhang S, Shi J, Hong D, Wu S, et al. Developing a rapid screening tool for high-risk ICU patients of sepsis: Integrating electronic medical records with machine learning methods for mortality prediction in hospitalized patients-model establishment, internal and external validation, and visualization. *J Transl Med* 2025; **23**(1): 97.

[34]Yan F, Chen X, Quan X, Wang L, Wei X, Zhu J. Association between the stress hyperglycemia ratio and 28-day all-cause mortality in critically ill patients with sepsis: A retrospective cohort study and predictive model establishment based on machine learning. *Cardiovasc Diabetol* 2024; **23**(1): 163.

[35]Komorowski M, Green A, Tatham KC, Seymour C, Antcliffe D. Sepsis biomarkers and diagnostic tools with a focus on machine learning. *EBioMedicine* 2022; **86**: 104394.

[36]Wang H, Len L, Hu L, Hu Y. Combining machine learning and single-cell sequencing to identify key immune genes in sepsis. *Sci Rep* 2025; **15**(1): 1557.

[37]Shen L, Tao C, Zhu K, Cai L, Yang S, Jin J, et al. Key platelet genes play important roles in predicting the prognosis of sepsis. *Sci Rep* 2024; **14**(1): 23530.

[38]Lukaszewski RA, Jones HE, Gersuk VH, Russell P, Simpson A, Brealey D, et al. Presymptomatic diagnosis of postoperative infection and sepsis using gene expression signatures. *Intensive Care Med* 2022; **48**(9): 1133-1143.

[39]Desposito L, Bascara C. Review: Sepsis guidelines and core measure bundles. *Postgrad Med* 2024; **136**(7): 702-711.

[40]Prescott HC, Ostermann M. What is new and different in the 2021 Surviving Sepsis Campaign guidelines. *Med Klin Intensivmed Notfmed* 2023; **118**(Suppl 2): 75-79.

[41]Gupta CB, Basu D, Williams TK, Neff LP, Johnson MA, Patel NT, et al. Improving the precision of shock resuscitation by predicting fluid responsiveness with machine learning and arterial blood pressure waveform data. *Sci Rep* 2024; **14**(1): 2227.

[42]Bhavani SV, Holder A, Miltz D, Kamaleswaran R, Khan S, Easley K, et al. The precision resuscitation with crystalloids in sepsis (PRECISE) Trial: A trial protocol. *JAMA Netw Open* 2024; **7**(9): e2434197.

[43]Liu R, Hunold KM, Caterino JM, Zhang P. Estimating treatment effects for time-to-treatment antibiotic stewardship in sepsis. *Nat Mach Intell* 2023; **5**(4): 421-431.

[44]Wendland P, Schenkel-Haeger C, Wenningmann I, Kschischo M. An optimal antibiotic selection framework for sepsis patients using artificial intelligence. *NPJ Digit Med* 2024; **7**(1): 343.