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Comparative Approaches to Antimicrobial Resistance Testing in Sepsis: E-Test and Molecular Diagnostics – A Scoping Review

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Abstract

Sepsis remains a major global health problem with high morbidity and mortality. Rapid antimicrobial susceptibility testing (AST) is essential, but conventional methods are time-consuming and may delay appropriate therapy. This study aimed to compare phenotypic methods, particularly the E-test, and molecular diagnostics for antimicrobial susceptibility testing in sepsis. A scoping review was conducted using PubMed, ScienceDirect, and other sources for studies published between 2016 and 2026. From 214 identified records, 10 studies met the inclusion criteria and were analyzed. Molecular diagnostics provided results within 1–8 hours, while rapid phenotypic methods required 3–7 hours, compared to 48–96 hours for conventional methods. Molecular approaches showed high resistance detection accuracy (up to 99%), whereas phenotypic methods demonstrated high agreement with reference standards (>95–99%). Rapid diagnostics improved antimicrobial therapy optimization, with treatment modification reported in up to 21% of patients. Phenotypic and molecular methods have complementary strengths. Molecular diagnostics offer speed, while phenotypic methods such as the E-test ensure accuracy. An integrated approach may improve antimicrobial stewardship and clinical outcomes in sepsis.

INTRODUCTION

Sepsis remains a major global health burden, characterized by life-threatening organ dysfunction due to a dysregulated host response to infection, and is associated with high morbidity and mortality worldwide, particularly in patients with bloodstream infections (BSIs) (Lamy et al., 2020; Rudd et al., 2020). Early and appropriate antimicrobial therapy is crucial, as delays in treatment are strongly associated with increased mortality (Seymour et al., 2017; Singer, 2016).

Blood culture remains the gold standard for pathogen identification and antimicrobial susceptibility testing (AST) in sepsis. However, conventional culture-based methods require 48–96 hours to produce complete results, leading to delayed targeted therapy and increased reliance on empirical broad-spectrum antibiotics, which contribute to antimicrobial resistance (AMR) (Banerjee & Humphries, 2021; Lamy et al., 2020).

To overcome these limitations, rapid diagnostic technologies have been developed. Molecular methods, such as polymerase chain reaction (PCR) and multiplex panels, enable rapid detection of pathogens and resistance genes within hours and demonstrate high diagnostic performance (MacVane & Dwivedi, 2024; Timbrook et al., 2017). These technologies significantly reduce turnaround time compared to conventional methods and improve antimicrobial management in bloodstream infections.

In contrast, phenotypic AST methods, including minimum inhibitory concentration (MIC)-based techniques such as the E-test, remain essential for accurately determining antimicrobial susceptibility. Although reliable, these methods are growth-dependent and generally require longer processing times. Recent advancements in rapid phenotypic AST have reduced turnaround time to a few hours while maintaining high agreement with standard methods (Idelevich & Becker, 2019; Reszetnik et al., 2024).

A key limitation of molecular diagnostics is their reliance on predefined genetic targets, which may not fully reflect phenotypic resistance. Conversely, phenotypic methods provide a direct assessment of bacterial response to antibiotics, highlighting a critical trade-off between speed and accuracy in antimicrobial resistance testing (Banerjee & Humphries, 2021).

Emerging technologies, including culture-independent diagnostics and next-generation sequencing approaches, aim to further accelerate pathogen detection and resistance profiling, with some platforms capable of producing results within hours (Marino Miguélez et al., 2025; Pinzauti et al., 2025).

Despite these advances, evidence directly comparing phenotypic methods such as the E-test with molecular diagnostics remains limited. Therefore, a scoping review is needed to map and compare current antimicrobial resistance testing approaches in sepsis, focusing on diagnostic performance, turnaround time, and clinical applicability.

METHOD

This study employed a scoping review design following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Extension for Scoping Reviews (PRISMA-ScR) guidelines. Data were collected by identifying, screening, and synthesizing relevant literature from previously published original research articles on antimicrobial resistance testing in sepsis, focusing on phenotypic and molecular diagnostic methods.

The research question was structured using the Population–Concept–Context (PCC) framework. The population included patients with sepsis, septic shock, or bloodstream infections. The concept focused on antimicrobial susceptibility testing methods, including phenotypic and molecular approaches, while the context involved clinical microbiology and hospital settings. The study compared these methods in terms of diagnostic performance, turnaround time, and clinical applicability.

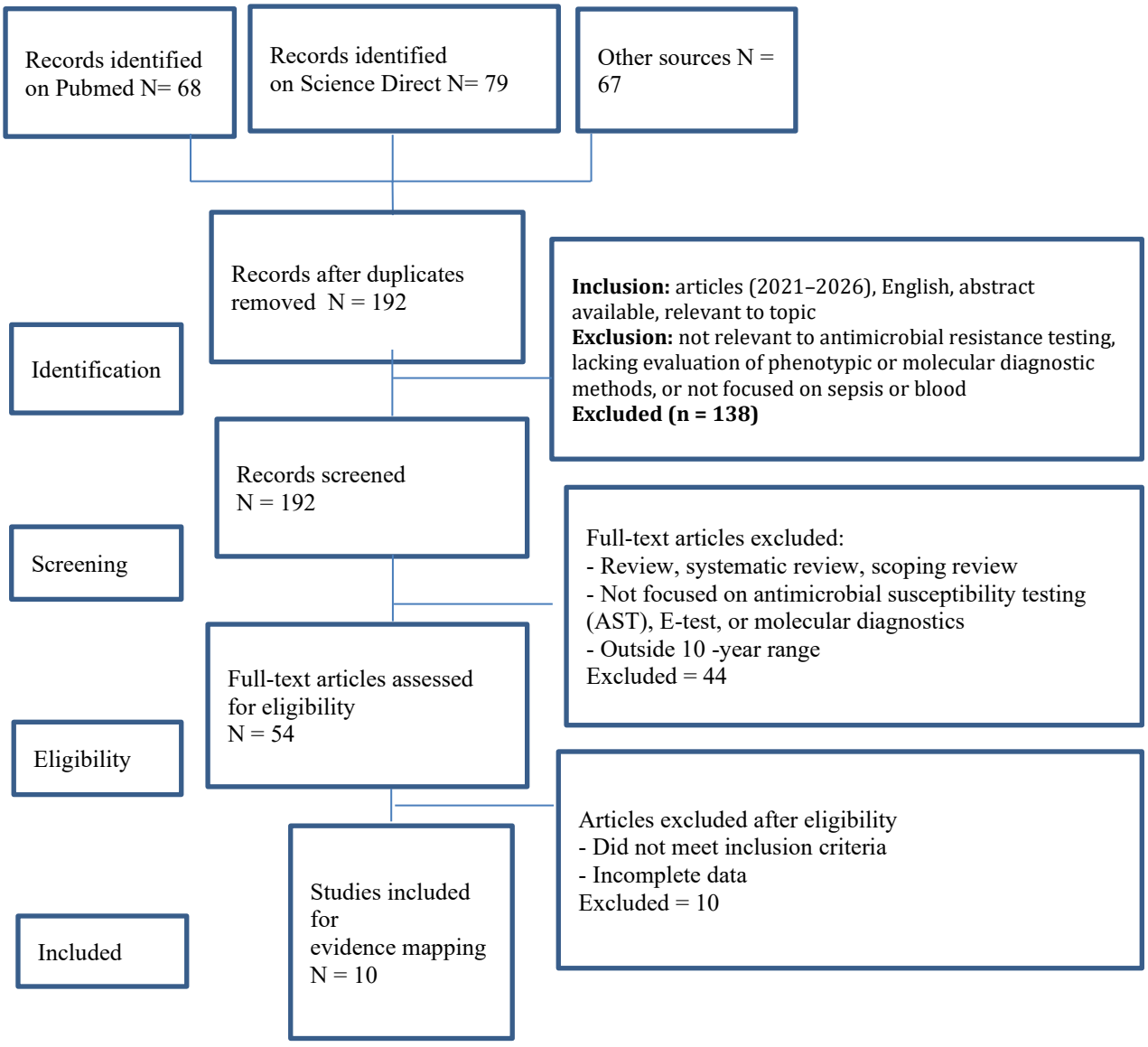
A literature search was conducted in March 2026 across three electronic databases: PubMed, ScienceDirect, and Google Scholar. A total of 214 records were identified, consisting of 68 articles from PubMed, 79 from ScienceDirect, and 67 from other sources. The search strategy combined keywords using Boolean operators: (“sepsis” OR “bloodstream infection”) AND (“antimicrobial susceptibility testing” OR “E-test”) AND (“molecular diagnostics” OR “PCR”), limited to articles published between 2016 and 2026.

Inclusion criteria were original research articles evaluating phenotypic and/or molecular antimicrobial susceptibility testing in sepsis or bloodstream infections, reporting diagnostic performance, turnaround time, or clinical impact, published in English and available in full text. Exclusion criteria included review articles, studies unrelated to antimicrobial susceptibility testing, biomarker-only studies, and articles with insufficient data.

After removing 22 duplicate records, 192 articles remained for screening. During title and abstract screening, 138 articles were excluded due to irrelevance. A total of 54 articles underwent full-text review, of which 44 were excluded for not meeting the inclusion criteria,

resulting in 10 studies included in the final analysis. The selection process followed the PRISMA-ScR framework and was presented in a flow diagram.

Data extraction was performed using a standardized form, including author, year, study design, population, diagnostic methods, and key outcomes such as turnaround time, diagnostic accuracy, agreement with reference methods, and clinical impact. Formal quality appraisal was not conducted, as this is consistent with scoping review methodology, which aims to map existing evidence rather than assess study quality.



Picture 1. PRISMA-based flow diagram

Table 1. Comparative Approaches to Antimicrobial Resistance Testing in Sepsis: E-test and Molecular Diagnostics – A Scoping Review

No	Author, Title	Aim	Results	Conclusion
1	Giacobbe et al., 2022 – *T2Bacteria and T2Resistance Assays in Critically Ill Patients with Sepsis or Septic Shock: A Descriptive Experience*	To evaluate the use of molecular diagnostics in patients with sepsis	Pathogens were detected in 26% of cases and resistance genes in 11%; results were obtained faster than conventional blood culture; antibiotic therapy was modified in 21% of patients	Molecular diagnostics facilitate earlier pathogen detection and support timely therapeutic decision-making
2	Chilleri et al., 2026 – *Evaluation of the Performance of Novel Gram-Negative and Gram-Positive Sepsis Panels for the Rapid Diagnosis of Bloodstream Infections*	To assess the performance of molecular panels for pathogen and resistance gene detection	Identification agreement reached 89%, while resistance gene detection accuracy was up to 99%; results were available within approximately 1 hour	Molecular panels provide rapid and highly accurate detection, although limited to predefined targets
3	Migliorisi et al., 2024 – *The Rapid Phenotypic Susceptibility Testing in Real-Life Experience: How the MIC Values Impact on Sepsis Fast Diagnostic Workflow*	To evaluate rapid phenotypic AST based on MIC in sepsis	Average turnaround time was ~7 hours; essential agreement exceeded 98% compared to standard methods; very low categorical errors were observed	Rapid phenotypic AST provides highly accurate results and enables earlier MIC-guided therapy
4	Zalas-Więcek et al., 2022 – *The Accelerate Pheno™ System—A New Tool in Microbiological Diagnostics of Bloodstream Infections: A Pilot Study from Poland*	To evaluate the effectiveness of the Accelerate Pheno system for AST in bloodstream infections	Microorganism identification rate was 88.9%; AST was successful in 84.4% of samples; AST results were available within 5–6 hours; agreement with standard methods ranged from 96–100%; diagnostic time was reduced by up to 63 hours	The system significantly accelerates AST while maintaining high accuracy compared to conventional methods
5	Park et al., 2025 – *Comparative Assessment of Rapid Identification and Antimicrobial Susceptibility Testing Methods for Bloodstream Infections in a Non-24/7 Clinical Microbiology Laboratory*	To compare multiple rapid identification and AST methods with conventional techniques	Rapid methods reduced turnaround time to less than 24 hours; molecular methods were faster for identification, while phenotypic methods provided more reliable AST results; laboratory workflow significantly influenced performance	Combining rapid diagnostic approaches improves efficiency and clinical utility in BSI management
6	Matúšková et al., 2026 – *Rapid Bacterial Identification and Quantitative Antimicrobial Susceptibility Assessment from Positive Blood Cultures to Optimize Bloodstream Infection Management*	To evaluate MALDI-TOF combined with rapid AST compared to standard workflow	Identification accuracy reached 93%; AST agreement was up to 99.3%; minimal error rates were observed; overall diagnostic time was significantly reduced	This approach enables faster diagnosis and supports optimization of antimicrobial therapy
7	Caunedo-Jiménez et al., 2023 – *Clinical Utility of the FilmArray® Blood Culture Identification (BCID) Panel for the Diagnosis of Neonatal Sepsis*	To assess the accuracy of a molecular BCID panel in neonatal sepsis	Sensitivity was 66.7%, while specificity reached 100%; high negative predictive value; results were obtained within a few hours	Molecular diagnostics are useful for early clinical decision-making, particularly for ruling out infection
8	So et al., 2023 – *Large-*	To evaluate the	Identification agreement was	BCID panels

No	Author, Title	Aim	Results	Conclusion
	Scale Clinical Evaluation of Rapid Blood Culture Identification Panels for Bloodstream Infections at a Tertiary Hospital	performance of BCID panels in bloodstream infections	93%; turnaround time ranged from 0.5 to 8 hours; capable of simultaneous pathogen and resistance gene detection	effectively accelerate diagnosis and improve antimicrobial management
9	Marino Miguélez et al., 2025 – *Culture-free detection of bacteria from blood for rapid sepsis diagnosis*	To develop a culture-independent bacterial detection method	Bacteria were detected directly from blood within ≤2 hours; capable of detecting low bacterial concentrations; no culture step required	Culture-free technologies show strong potential for future sepsis diagnostics
10	Olsson et al., 2025– *Multicenter evaluation of the QuickMIC® rapid AST system in clinical practice: impact on turnaround time compared to routine AST systems*	To evaluate the performance of the QuickMIC rapid phenotypic AST system	Accuracy exceeded 95%; results were obtained in ~3 hours compared to 9–19 hours with conventional methods; high essential agreement observed	QuickMIC enables rapid and accurate AST and has the potential to replace conventional methods

RESULTS AND DISCUSSION

A total of 10 studies were included in this scoping review, consisting of original research evaluating antimicrobial resistance testing approaches in sepsis and bloodstream infections. The studies investigated phenotypic antimicrobial susceptibility testing (AST), molecular diagnostics, and emerging technologies (Giacobbe et al., 2022; Park et al., 2025).

The diagnostic approaches were categorized into three groups: phenotypic AST methods (MIC-based systems such as E-test), molecular diagnostics targeting pathogens and resistance genes, and comparative or integrated approaches (Migliorisi et al., 2024; Zalas-Więcek et al., 2022). All studies reported a significant reduction in turnaround time with rapid diagnostics compared to conventional culture-based methods (48–96 hours) (Banerjee & Humphries, 2021) . Molecular diagnostics provided results within approximately 1–8 hours, while rapid phenotypic AST methods required about 3–7 hours, with some systems achieving results in ~3 hours (Park et al., 2025; Zalas-Więcek et al., 2022) . Emerging technologies enabled detection in less than 2 hours (Marino Miguélez et al., 2025) .

High diagnostic performance was observed across studies. Molecular methods demonstrated identification agreement of approximately 89–93% and resistance detection accuracy up to 99% (Chilleri et al., 2026; So et al., 2023). Phenotypic methods showed higher agreement with reference standards (>95–99%) and minimal error rates, indicating strong reliability for determining antimicrobial susceptibility (Matúšková et al., 2026; Migliorisi et al., 2024). Comparatively, molecular diagnostics offered faster results but were limited to predefined resistance targets and did not always reflect phenotypic resistance (Banerjee & Humphries, 2021). In contrast, phenotypic methods, including E-test, provided a direct assessment of bacterial response and more comprehensive susceptibility data, although with slightly longer processing times (Idelevich & Becker, 2019).

Several studies reported clinical benefits from rapid diagnostics, including earlier optimization of antimicrobial therapy and treatment modification in up to 21% of patients (Giacobbe et al., 2022). Additionally, emerging technologies such as culture-independent and microfluidic-based methods demonstrated promising potential to further accelerate sepsis diagnostics (Marino Miguélez et al., 2025).

Discussion

This scoping review highlights the evolving landscape of antimicrobial resistance testing (AST) in sepsis, demonstrating a shift from conventional culture-based methods toward rapid phenotypic and molecular diagnostics. Although traditional methods remain the reference standard, their prolonged turnaround time limits timely clinical decision-making, which is critical in sepsis management (Banerjee & Humphries, 2021; Lamy et al., 2020).

A. Comparison Between Phenotypic and Molecular Approaches

Phenotypic methods, including E-test and other minimum inhibitory concentration (MIC)-based techniques, directly assess bacterial response to antibiotics, providing a reliable representation of antimicrobial susceptibility. This explains the high agreement rates (>95–99%) observed across studies, confirming their role as the gold standard (Migliorisi et al., 2024; Zalas-Więcek et al., 2022). However, these methods depend on bacterial growth, resulting in longer turnaround times compared to molecular approaches (Idelevich & Becker, 2019) .

In contrast, molecular diagnostics detect resistance genes and allow rapid pathogen identification, often within a few hours (Banerjee & Humphries, 2021; Timbrook et al., 2017). Despite their speed, these methods are limited to predefined genetic targets and may not accurately reflect phenotypic resistance, especially in cases involving unknown resistance mechanisms (Banerjee & Humphries, 2021). This discrepancy highlights a critical trade-off between speed and accuracy in AST.

B. Clinical Impact of Rapid Diagnostics

Rapid diagnostic methods significantly influence clinical decision-making by enabling earlier optimization of antimicrobial therapy. Studies included in this review reported treatment modifications in up to 21% of patients, emphasizing the clinical relevance of rapid AST (Giacobbe et al., 2022).

Moreover, rapid diagnostics support antimicrobial stewardship by reducing unnecessary use of broad-spectrum antibiotics, which is a key driver of antimicrobial resistance (Timbrook et al., 2017). However, evidence regarding their impact on long-term outcomes, such as mortality and length of hospital stay, remains inconsistent, suggesting that diagnostic improvements must be integrated with clinical workflows to achieve maximal benefit (Banerjee & Humphries, 2021).

C. Emerging Technologies and Future Directions

Emerging technologies, including culture-independent diagnostics and microfluidic-based platforms, offer promising solutions to overcome current limitations. These approaches enable pathogen detection and susceptibility assessment directly from blood samples within hours, significantly reducing diagnostic delays (Marino Miguélez et al., 2025) .

Additionally, ultra-rapid AST systems have demonstrated the potential to further reduce turnaround time while maintaining high accuracy, representing a major advancement in sepsis diagnostics (Idelevich & Becker, 2019). However, challenges related to cost, accessibility, and clinical validation remain barriers to widespread implementation.

Strengths and Limitations

This review provides a comprehensive overview of current AST approaches in sepsis and highlights key differences between diagnostic methods. However, the limited number of included studies and heterogeneity in study designs may affect generalizability. Additionally, no formal quality assessment was conducted, consistent with scoping review methodology.

CONCLUSION

This scoping review, titled *"Comparative Approaches To Antimicrobial Resistance Testing In Sepsis: E-Test And Molecular Diagnostics – A Scoping Review,"* highlights significant advancements in antimicrobial susceptibility testing (AST) for sepsis, particularly the transition from conventional culture-based methods to rapid phenotypic and molecular diagnostics. While phenotypic methods such as the E-test remain highly accurate and are capable of reflecting true antimicrobial susceptibility, their reliance on bacterial growth limits turnaround time. In contrast, molecular diagnostics provide rapid detection of pathogens and resistance genes, enabling earlier clinical decision-making, although they may not fully represent phenotypic resistance.

The findings of this review demonstrate that each diagnostic approach has distinct strengths and limitations, with phenotypic methods offering high accuracy and molecular techniques providing speed. Therefore, no single method is sufficient to meet the complex diagnostic demands of sepsis. A combined diagnostic strategy that integrates molecular and phenotypic approaches appears to be the most effective solution, balancing rapid detection with reliable susceptibility assessment.

Furthermore, this review identifies a critical gap in the literature, namely the limited availability of direct comparative studies between phenotypic and molecular AST methods. Future research should focus on head-to-head comparisons, evaluation of clinical outcomes, and cost-effectiveness analyses to guide implementation in clinical practice. Overall, optimizing antimicrobial susceptibility testing through integrated approaches has the potential to improve antimicrobial stewardship and patient outcomes in sepsis management.

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