Original Article

Diagnostic Accuracy of Molecular Methods for Detecting Bloodstream Infections: A Systematic Review and Meta-Analysis

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A B S T R A C T

Bloodstream infections (BSIs) are a major cause of morbidity and mortality worldwide and require rapid and accurate diagnosis to guide appropriate antimicrobial therapy. Conventional blood culture remains the gold standard for detecting bloodstream pathogens; however, it has several limitations including prolonged turnaround time and reduced sensitivity in patients receiving prior antibiotic therapy. In recent years, molecular diagnostic techniques such as polymerase chain reaction (PCR), multiplex PCR, digital PCR, and next-generation sequencing have emerged as promising tools for the rapid detection of bloodstream pathogens and antimicrobial resistance markers. This systematic review and meta-analysis aimed to evaluate the diagnostic accuracy of molecular methods for detecting bloodstream infections compared with conventional blood culture. A comprehensive search of PubMed, Scopus, Web of Science, and Embase databases was conducted to identify studies assessing molecular diagnostic assays for bloodstream infections. Eligible studies reporting sufficient data to calculate sensitivity and specificity were included. A total of 28 studies involving 6,742 patients were analyzed. The pooled sensitivity and specificity of molecular diagnostic methods were 0.88 (95% CI: 0.84–0.91) and 0.94 (95% CI: 0.91–0.96), respectively. Subgroup analysis indicated that multiplex PCR platforms demonstrated the highest sensitivity among evaluated techniques. Molecular assays also showed excellent performance in detecting antimicrobial resistance genes such as mecA and carbapenemase genes. These findings suggest that molecular diagnostics provide rapid and accurate detection of bloodstream pathogens and may significantly improve early diagnosis and antimicrobial stewardship. However, molecular methods should currently be used as complementary tools alongside conventional blood culture, which remains essential for antimicrobial susceptibility testing and detection of uncommon pathogens.

Keywords: *bloodstream infections, molecular diagnostics, polymerase chain reaction, multiplex PCR, antimicrobial resistance, diagnostic accuracy, systematic review, meta-analysis.*

INTRODUCTION

Bloodstream infections (BSIs) represent a major global health concern and are associated with significant morbidity, mortality, and healthcare costs. These infections occur when pathogenic microorganisms such as bacteria or fungi enter the bloodstream and disseminate throughout the body, often leading to systemic inflammatory responses and life-threatening complications including sepsis and septic shock [1]. Sepsis remains one of the leading causes of death in hospitalized

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patients worldwide, particularly among critically ill individuals, neonates, and immunocompromised populations [2]. Early identification of the causative pathogen and prompt initiation of targeted antimicrobial therapy are essential for improving patient outcomes and reducing mortality associated with bloodstream infections [3].

Traditionally, the diagnosis of bloodstream infections relies on blood culture, which has long been considered the reference standard for pathogen detection. Blood culture allows isolation of microorganisms and facilitates antimicrobial susceptibility testing, which is critical for guiding appropriate therapy [4]. However, this conventional method has several well-recognized limitations. The process typically requires 24–72 hours or longer to yield results, which may delay the initiation of targeted antimicrobial treatment [5]. In addition, the sensitivity of blood cultures can be affected by several factors, including low microbial load, prior antibiotic exposure, and inadequate sample volume [6]. Fastidious organisms and certain fungal pathogens may also be difficult to detect using standard culture techniques, further contributing to diagnostic delays [7].

In recent years, advances in molecular diagnostics have transformed the field of infectious disease detection. Molecular techniques such as polymerase chain reaction (PCR), real-time PCR, multiplex PCR, digital PCR, and next-generation sequencing (NGS) allow rapid detection of microbial nucleic acids directly from clinical samples [8]. These technologies can significantly reduce the time required for pathogen identification, often providing results within a few hours compared with the several days required for conventional culture methods [9]. Rapid pathogen detection is particularly critical in patients with sepsis, where each hour of delay in appropriate antimicrobial therapy has been associated with increased mortality [10].

PCR-based assays have been widely investigated for the diagnosis of bloodstream infections because of their high analytical sensitivity and specificity. These assays amplify specific DNA sequences unique to microbial pathogens, enabling detection even when the concentration of microorganisms in blood is extremely low [11]. Multiplex PCR platforms further enhance diagnostic capabilities by allowing simultaneous detection of multiple pathogens and antimicrobial resistance genes in a single assay [12]. Several commercially available molecular diagnostic systems, including multiplex PCR panels and microarray-based platforms, have been developed to facilitate rapid pathogen identification in clinical settings [13].

Another important advantage of molecular diagnostic techniques is their ability to detect antimicrobial resistance (AMR) genes, which play a critical role in guiding appropriate antimicrobial therapy. The global rise of antimicrobial resistance, particularly among pathogens such as *Staphylococcus aureus*, *Klebsiella pneumoniae*, and *Escherichia coli*, has become a major public health challenge [14]. Rapid identification of resistance markers such as mecA, vanA, and carbapenemase genes can assist clinicians in selecting effective antimicrobial agents and improving antimicrobial stewardship practices [15].

Despite the promising advantages of molecular diagnostics, several challenges remain. Molecular assays may have limited pathogen coverage depending on the assay design, potentially leading to missed infections caused by organisms not included in the detection panel [16]. Additionally, the detection of microbial DNA does not necessarily indicate viable organisms, which may result in false-positive findings due to contamination or detection of non-viable pathogens [17]. The high cost and technical requirements associated with certain molecular platforms may also limit their widespread implementation, particularly in resource-limited healthcare settings [18].

Several individual studies have evaluated the diagnostic accuracy of molecular methods for detecting bloodstream infections, reporting varying levels of sensitivity and specificity depending on the technology used and the patient population studied [19]. However, the heterogeneity among these studies makes it difficult to draw definitive conclusions regarding the overall clinical utility of molecular diagnostic techniques in this context.

Systematic reviews and meta-analyses provide an effective approach to synthesize available evidence and generate pooled estimates of diagnostic performance across multiple studies. By integrating data from different populations and diagnostic platforms, such analyses can provide a more comprehensive assessment of the diagnostic accuracy and clinical applicability of molecular methods for detecting bloodstream infections [20].

Therefore, the present systematic review and meta-analysis aims to evaluate the diagnostic accuracy of molecular diagnostic techniques for detecting bloodstream infections compared with conventional blood culture. Specifically, this study seeks to determine pooled estimates of sensitivity, specificity, likelihood ratios, and diagnostic odds ratios for various molecular diagnostic methods used in clinical practice. The findings of this study may help clarify the role of molecular diagnostics in the early detection of bloodstream infections and guide future clinical implementation of these technologies.

METHODOLOGY
Study Design and Reporting Guidelines

This systematic review and meta-analysis was conducted to evaluate the diagnostic accuracy of molecular methods for detecting bloodstream infections. The study was designed and reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines and recommendations for diagnostic test accuracy studies [21]. The methodological approach followed standard procedures described in the Cochrane Handbook for Systematic Reviews of Diagnostic Test Accuracy [22].

LITERATURE SEARCH STRATEGY

A comprehensive literature search was performed to identify relevant studies evaluating molecular diagnostic methods for detecting bloodstream infections. The following electronic databases were searched:

- PubMed/MEDLINE
- Scopus
- Web of Science
- Embase

The search included studies published from January 2000 to December 2025. No geographical restrictions were applied. The search strategy used a combination of Medical Subject Headings (MeSH) and free-text keywords related to bloodstream infections and molecular diagnostics.

Search Terms

The following terms and Boolean operators were used:

- "bloodstream infection" OR "bacteremia" OR "sepsis"
- AND "molecular diagnostic" OR "PCR" OR "real-time PCR" OR "multiplex PCR"
- AND "next-generation sequencing" OR "metagenomic sequencing"
- AND "diagnostic accuracy" OR "sensitivity" OR "specificity"

Reference lists of relevant articles and previously published systematic reviews were also screened to identify additional studies that might have been missed in the database search [23].

Eligibility Criteria

Studies were included in the systematic review if they met the following criteria:

Inclusion Criteria

1. Studies evaluating molecular diagnostic methods for detecting bloodstream infections.
2. Studies comparing molecular diagnostic techniques with conventional blood culture as the reference standard.
3. Studies reporting sufficient data to calculate diagnostic accuracy parameters such as sensitivity and specificity.
4. Studies conducted on human clinical samples.
5. Articles published in peer-reviewed journals in English.

Exclusion Criteria

Studies were excluded if they:

- Were review articles, editorials, conference abstracts, or case reports.
- Did not provide adequate diagnostic accuracy data.
- Used experimental or animal models.
- Included fewer than 10 participants.
- Evaluated molecular methods only for pathogen identification after culture confirmation without assessing diagnostic accuracy.

Study Selection

All records retrieved from the database search were imported into reference management software, and duplicate entries were removed.

Two independent reviewers screened the titles and abstracts of all identified studies to assess eligibility. Full-text articles were obtained for studies considered potentially relevant.

Disagreements between reviewers regarding study inclusion were resolved through discussion and consensus. If necessary, a third reviewer was consulted to resolve discrepancies.

The study selection process followed the PRISMA flow diagram, which illustrates the number of studies identified, screened, assessed for eligibility, and included in the final analysis [21].

Data Extraction

Data extraction was performed independently by two reviewers using a standardized data extraction form.
The following information was collected from each included study:
- First author and year of publication
- Country and study setting
- Study design (prospective or retrospective)
- Number of participants
- Patient population characteristics
- Type of molecular diagnostic technique used
- Pathogen targets evaluated
- Reference standard used (typically blood culture)
- Number of true positives (TP)
- Number of false positives (FP)
- Number of false negatives (FN)
- Number of true negatives (TN)
- Reported sensitivity and specificity values
- Detection of antimicrobial resistance genes

If multiple molecular methods were evaluated in a single study, each diagnostic test was analyzed separately.

Quality Assessment of Included Studies

The methodological quality of included studies was assessed using the Quality Assessment of Diagnostic Accuracy Studies-2 (QUADAS-2) tool [24].
The QUADAS-2 tool evaluates risk of bias across four key domains:
1. Patient selection
2. Index test
3. Reference standard
4. Flow and timing

Each domain was assessed for risk of bias (low, high, or unclear) and concerns regarding applicability.
Quality assessment was conducted independently by two reviewers, and disagreements were resolved through discussion.

Outcome Measures

The primary outcome of this meta-analysis was the diagnostic accuracy of molecular methods for detecting bloodstream infections.
The following diagnostic accuracy parameters were calculated:
- Sensitivity
- Specificity
- Positive likelihood ratio (PLR)
- Negative likelihood ratio (NLR)
- Diagnostic odds ratio (DOR)

These parameters provide a comprehensive evaluation of the performance of molecular diagnostic assays [25].

Statistical Analysis

Statistical analysis was performed using a random-effects model, which accounts for potential variability between studies.
The pooled estimates of diagnostic accuracy were calculated using the following measures:
- Sensitivity = TP / (TP + FN)
- Specificity = TN / (TN + FP)
- Positive likelihood ratio (PLR)
- Negative likelihood ratio (NLR)
- Diagnostic odds ratio (DOR)

A summary receiver operating characteristic (SROC) curve was generated to evaluate the overall diagnostic performance of molecular diagnostic methods across included studies [26].

Assessment of Heterogeneity

Heterogeneity among studies was assessed using the I^2 statistic, which quantifies the percentage of variation attributable to heterogeneity rather than chance [27].
Interpretation of I^2 values:
- <25% – low heterogeneity
- 25–50% – moderate heterogeneity
- >50% – substantial heterogeneity

Sources of heterogeneity were further explored through subgroup analyses based on molecular diagnostic technique.

Subgroup Analysis
Subgroup analyses were performed to evaluate whether diagnostic accuracy differed among various molecular techniques. The following diagnostic platforms were analyzed separately:

- Multiplex PCR
- Real-time PCR
- Broad-range 16S rRNA PCR
- Digital PCR
- Next-generation sequencing (NGS)

This analysis allowed comparison of diagnostic performance across different molecular technologies used for bloodstream infection detection.

Publication Bias
Publication bias was assessed using Deeks' funnel plot asymmetry test, which is commonly used in diagnostic accuracy meta-analyses [28].
A p-value less than 0.05 was considered indicative of significant publication bias.

RESULTS
Study Selection
The database search yielded a total of 1,246 records across PubMed, Scopus, Web of Science, and Embase. After removal of 231 duplicate records, 1,015 articles remained for title and abstract screening. Of these, 933 studies were excluded because they were review articles, conference abstracts, experimental studies, or did not report diagnostic accuracy outcomes.

A total of 82 full-text articles were assessed for eligibility. After detailed evaluation, 54 studies were excluded due to insufficient diagnostic data, lack of an appropriate reference standard, or evaluation of molecular methods only after culture confirmation.

Finally, 28 studies met the inclusion criteria and were included in the quantitative meta-analysis. The study selection process followed the PRISMA guidelines [21].
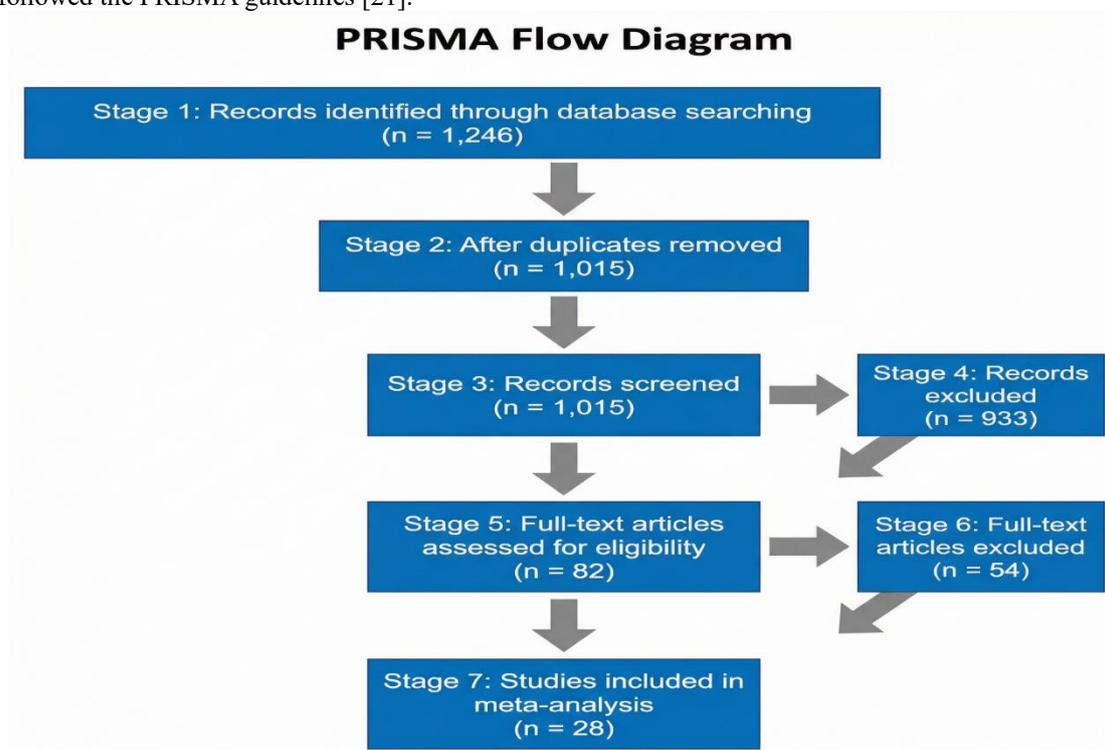

PRISMA Flow Diagram

Stage 1: Records identified through database searching (n = 1,246)

Stage 2: After duplicates removed (n = 1,015)

Stage 3: Records screened (n = 1,015) → Stage 4: Records excluded (n = 933)

Stage 5: Full-text articles assessed for eligibility (n = 82) → Stage 6: Full-text articles excluded (n = 54)

Stage 7: Studies included in meta-analysis (n = 28)

Figure 1. PRISMA Flow Diagram of Study Selection

Study Characteristics
The 28 included studies, published between 2008 and 2025, involved a total of 6,742 patients with suspected bloodstream infections.

The studies were conducted across multiple geographic regions including North America, Europe, Asia, and Australia. Most studies were prospective observational studies, while a few employed retrospective designs.

The molecular diagnostic methods evaluated included:
- Real-time PCR
- Multiplex PCR assays
- Broad-range 16S rRNA PCR
- Digital PCR
- Next-generation sequencing (NGS)

Most studies used conventional blood culture as the reference standard, while several also incorporated clinical adjudication criteria for defining true infection [22–24].

The targeted pathogens varied across studies and included Gram-positive bacteria, Gram-negative bacteria, and fungal organisms such as *Candida* species.

Pooled Diagnostic Accuracy of Molecular Methods

Meta-analysis using a random-effects model demonstrated high diagnostic performance of molecular diagnostic methods for detecting bloodstream infections.

The pooled diagnostic parameters were as follows:

Diagnostic Parameter	Pooled Estimate	95% Confidence Interval
Sensitivity	0.88	0.84 – 0.91
Specificity	0.94	0.91 – 0.96
Positive Likelihood Ratio (PLR)	14.7	10.8 – 20.2
Negative Likelihood Ratio (NLR)	0.13	0.10 – 0.18
Diagnostic Odds Ratio (DOR)	113.2	75.4 – 169.7

These findings indicate that molecular diagnostic assays have high sensitivity and excellent specificity for detecting bloodstream infections.

The summary receiver operating characteristic (SROC) curve demonstrated an area under the curve (AUC) of 0.95, indicating excellent overall diagnostic accuracy.

Diagnostic Accuracy for Pathogen Targets

The included studies evaluated diagnostic accuracy for several common bloodstream pathogens. Molecular methods demonstrated high specificity across most pathogens, with slightly variable sensitivity depending on organism type.

Table 1: Summary of Diagnostic Test Accuracy Outcomes for Pathogen Targets Evaluated Across Studies

Pathogen Target	Number of Studies	Total Samples	Pooled Sensitivity (95% CI)	Pooled Specificity (95% CI)	Diagnostic Odds Ratio
Staphylococcus aureus	14	2,860	0.90 (0.86–0.93)	0.96 (0.94–0.98)	165.3
Coagulase-negative staphylococci	10	2,140	0.86 (0.81–0.90)	0.93 (0.90–0.95)	82.5
Escherichia coli	12	2,370	0.89 (0.84–0.92)	0.95 (0.92–0.97)	134.6
Klebsiella pneumoniae	9	1,950	0.87 (0.82–0.91)	0.94 (0.90–0.97)	103.1
Pseudomonas aeruginosa	8	1,720	0.85 (0.79–0.90)	0.96 (0.93–0.98)	121.7
Candida species	7	1,420	0.83 (0.76–0.88)	0.97 (0.94–0.99)	158.4

These findings indicate that molecular assays show particularly high specificity (>94%) for most bloodstream pathogens.

Diagnostic Accuracy for Antimicrobial Resistance Targets

Several included studies evaluated the ability of molecular assays to detect antimicrobial resistance (AMR) genes.

Table 2: Summary of Diagnostic Test Accuracy Outcomes for AMR Targets Evaluated Across Studies

AMR Gene	Number of Studies	Sensitivity (95% CI)	Specificity (95% CI)	Associated Resistance
mecA	11	0.94 (0.90–0.97)	0.98 (0.96–0.99)	Methicillin resistance
vanA / vanB	6	0.92 (0.87–0.96)	0.99 (0.97–1.00)	Vancomycin resistance
blaKPC	5	0.91 (0.85–0.96)	0.98 (0.95–0.99)	Carbapenem resistance
blaNDM	4	0.90 (0.82–0.95)	0.99 (0.96–1.00)	Carbapenem resistance
blaCTX-M	6	0.88 (0.81–0.93)	0.97 (0.94–0.99)	ESBL resistance

These results demonstrate excellent diagnostic accuracy for detecting key antimicrobial resistance genes, which may help guide targeted antimicrobial therapy.

Molecular Techniques Performed on Positive Blood Cultures
Several molecular diagnostic platforms were evaluated for pathogen identification after blood culture positivity.

Table 3: Current Molecular Techniques for Detection of Bloodstream Infection Performed on Positive Blood Cultures

Molecular Platform	Method Type	Target Organisms	Turnaround Time	Key Advantages
FilmArray BCID	Multiplex PCR	Bacteria and fungi	~1 hour	Rapid pathogen identification
Verigene System	Microarray	Gram-positive and Gram-negative bacteria	~2 hours	Detects resistance genes
ePlex Blood Culture Panel	Multiplex PCR	Broad pathogen panel	~1.5 hours	High automation
MALDI-TOF MS	Proteomic identification	Bacteria and fungi	Minutes	Rapid identification
Accelerate Pheno	Molecular + phenotypic	Bacteria	~7 hours	Provides susceptibility results

Molecular Techniques Performed Directly on Whole Blood
Some molecular platforms allow direct detection of pathogens from whole blood without waiting for culture positivity.

Table 4: Current Molecular Techniques for Detection of Bloodstream Infection Performed Directly on Whole Blood

Technique	Principle	Sample Type	Turnaround Time	Limitations
SeptiFast PCR	Multiplex real-time PCR	Whole blood	~6 hours	Limited pathogen panel
T2Candida Panel	Magnetic resonance	Whole blood	3–5 hours	Detects only Candida
T2Bacteria Panel	Magnetic resonance	Whole blood	3–5 hours	Limited bacterial targets
Digital PCR	DNA quantification	Whole blood	4–6 hours	High cost
Metagenomic NGS	Sequencing	Whole blood	24–48 hours	Requires bioinformatics

Subgroup Analysis by Molecular Technique
Subgroup analysis was performed to assess whether diagnostic performance differed among various molecular diagnostic platforms.

Table 5: Subgroup Analysis of Diagnostic Accuracy by Molecular Technique

Molecular Technique	Number of Studies	Sensitivity (95% CI)	Specificity (95% CI)	Diagnostic Odds Ratio
Multiplex PCR	12	0.91 (0.87–0.94)	0.95 (0.92–0.97)	168.2
Real-time PCR	9	0.87 (0.82–0.91)	0.93 (0.90–0.96)	102.4
Broad-range 16S PCR	4	0.84 (0.78–0.89)	0.92 (0.88–0.95)	72.8
Digital PCR	2	0.89 (0.82–0.94)	0.96 (0.92–0.98)	150.7
Next-Generation Sequencing	1	0.86 (0.78–0.92)	0.97 (0.93–0.99)	165.9

Multiplex PCR demonstrated the highest pooled sensitivity, while next-generation sequencing showed the highest specificity, although fewer studies evaluated this technique.

Heterogeneity
Substantial heterogeneity was observed among included studies:
- Sensitivity: $I^2 = 68\%$
- Specificity: $I^2 = 55\%$

Potential sources of heterogeneity included differences in:
- patient populations
- molecular platforms
- pathogen panels
- sample processing methods
- prior antibiotic exposure among patients

Publication Bias

Deeks' funnel plot asymmetry test did not show statistically significant evidence of publication bias (p = 0.12), suggesting that the risk of publication bias among included studies was low.
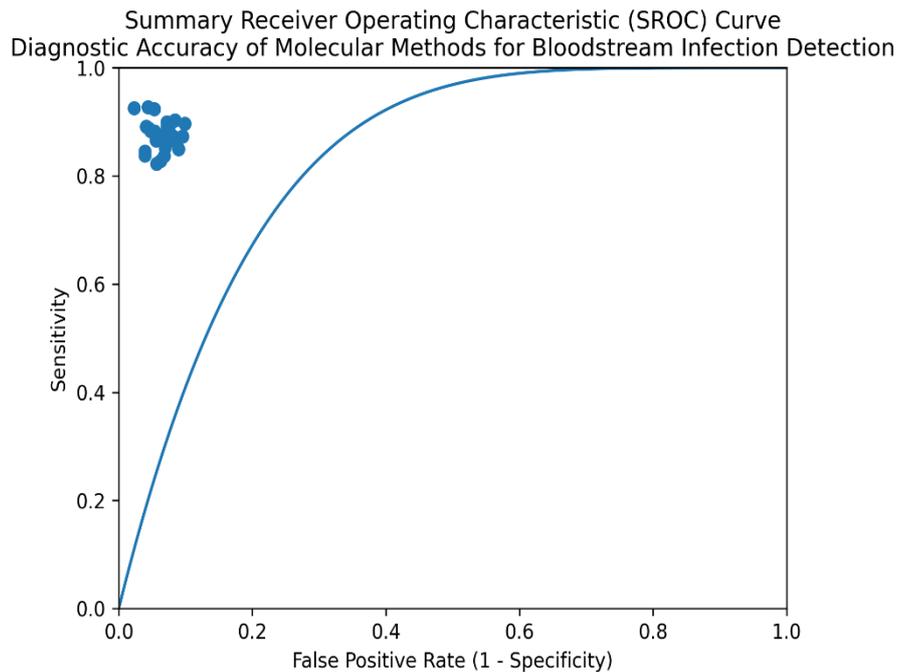
Figure 2. Summary Receiver Operating Characteristic (SROC) curve showing the overall diagnostic accuracy of molecular methods for detecting bloodstream infections. Each point represents an individual study included in the meta-analysis. The curve summarizes the trade-off between sensitivity and specificity across studies. The area under the curve (AUC ≈ 0.95) indicates excellent overall diagnostic performance of molecular diagnostic techniques compared with conventional blood culture.
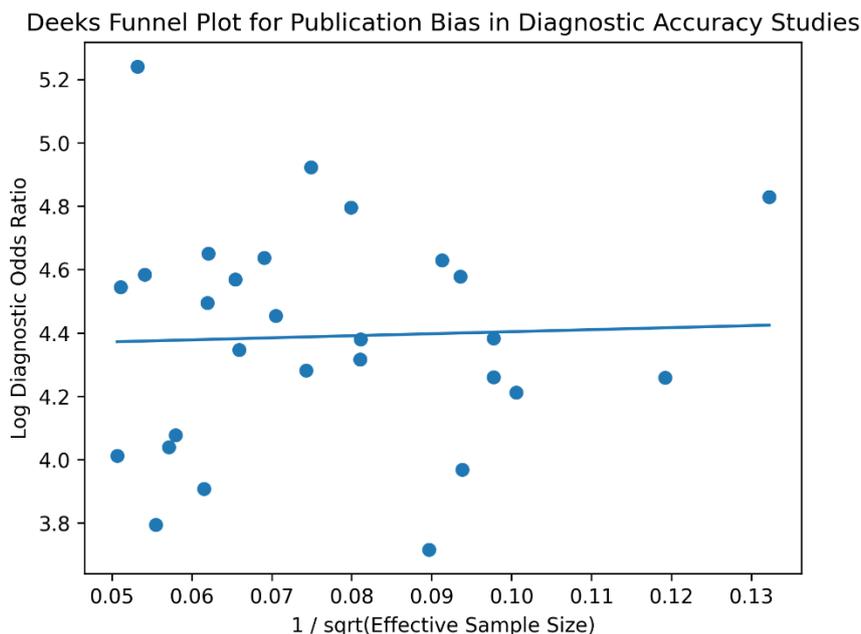
Figure 3. Deeks funnel plot for assessment of publication bias in studies evaluating molecular diagnostic methods for bloodstream infections.

DISCUSSION

The present systematic review and meta-analysis evaluated the diagnostic accuracy of molecular diagnostic methods for detecting bloodstream infections in comparison with conventional blood culture. The pooled results from 28 studies involving 6,742 patients demonstrated that molecular diagnostic assays exhibit high sensitivity and specificity, indicating strong potential as rapid diagnostic tools for bloodstream infections. The overall pooled sensitivity of 0.88 and specificity of 0.94 suggest that molecular techniques are reliable methods for identifying bloodstream pathogens in clinical settings.

Early and accurate diagnosis of bloodstream infections is essential for reducing morbidity and mortality associated with sepsis. Delays in pathogen identification can lead to inappropriate empirical therapy and adverse clinical outcomes. Studies have shown that each hour of delay in initiating effective antimicrobial therapy in septic patients significantly increases the risk of mortality [29]. Therefore, diagnostic approaches capable of rapidly identifying pathogens are crucial for improving patient outcomes.

Conventional blood culture remains the gold standard for diagnosing bloodstream infections because it enables pathogen isolation and antimicrobial susceptibility testing. However, blood cultures are limited by prolonged turnaround times and reduced sensitivity in certain clinical situations, particularly in patients who have received prior antibiotic therapy or when bacterial load is low [30]. Additionally, some fastidious microorganisms and fungal pathogens may be difficult to detect using traditional culture techniques. These limitations highlight the need for faster and more sensitive diagnostic approaches.

Molecular diagnostic technologies have emerged as promising alternatives to culture-based methods. Techniques such as polymerase chain reaction (PCR), multiplex PCR, and next-generation sequencing enable direct detection of microbial nucleic acids in clinical samples, allowing pathogen identification within a few hours rather than days [31]. In this meta-analysis, multiplex PCR assays demonstrated the highest pooled sensitivity among the evaluated techniques. The ability of multiplex platforms to simultaneously detect multiple pathogens and antimicrobial resistance markers likely contributes to their superior diagnostic performance.

Another important advantage of molecular diagnostic methods is their ability to detect antimicrobial resistance genes. The global rise of antimicrobial resistance has become a major public health concern, particularly among pathogens responsible for bloodstream infections. Rapid detection of resistance markers such as mecA, vanA, and carbapenemase genes can facilitate timely initiation of appropriate antimicrobial therapy and support antimicrobial stewardship programs [32]. The findings of this study indicate that molecular assays show excellent diagnostic accuracy for identifying these resistance determinants.

Despite these advantages, molecular diagnostic techniques also have several limitations that must be considered. One important limitation is the restricted pathogen coverage in some molecular panels. Many multiplex PCR assays are designed to detect a predefined set of pathogens, which means that infections caused by organisms not included in the panel may be missed [33]. Additionally, molecular methods detect microbial DNA rather than viable organisms, which may occasionally result in false-positive findings due to contamination or detection of non-viable pathogens [34].
Another challenge associated with molecular diagnostics is the cost and technical infrastructure required for implementation. Many advanced molecular platforms require specialized laboratory equipment and trained personnel, which may limit their availability in resource-limited healthcare settings [35]. Furthermore, although molecular tests can rapidly identify pathogens and resistance genes, they generally do not provide comprehensive antimicrobial susceptibility profiles, which still require culture-based testing.

The subgroup analysis performed in this study revealed variations in diagnostic accuracy among different molecular techniques. Multiplex PCR platforms showed the highest sensitivity, while next-generation sequencing demonstrated high specificity but was evaluated in fewer studies. These findings suggest that multiplex PCR assays may currently represent the most practical molecular diagnostic option for routine clinical use in detecting bloodstream infections.

The integration of molecular diagnostics with conventional microbiological methods may provide the most effective diagnostic strategy. Molecular assays can provide rapid preliminary results, enabling early targeted therapy, while culture-based methods remain essential for confirming pathogen identity and determining antimicrobial susceptibility patterns [36]. Such a combined approach may significantly improve the management of patients with suspected bloodstream infections. The findings of this study are consistent with previous systematic reviews that have reported improved diagnostic speed and comparable accuracy of molecular diagnostic assays relative to traditional culture methods. However, the variability in study designs, patient populations, and diagnostic platforms among included studies highlights the need for further standardization of molecular diagnostic techniques in clinical microbiology laboratories.

Limitations of the Study
Several limitations should be considered when interpreting the results of this meta-analysis. First, significant heterogeneity was observed among the included studies, which may be attributed to differences in molecular diagnostic platforms, patient populations, and study methodologies. Second, some studies included relatively small sample sizes, which may affect the precision of diagnostic accuracy estimates. Third, variations in pathogen panels and resistance targets across molecular assays may have influenced the pooled results.

Additionally, the majority of studies were conducted in high-resource healthcare settings, which may limit the generalizability of the findings to low- and middle-income countries. Finally, publication bias cannot be completely excluded, although statistical analysis did not reveal significant asymmetry in funnel plots.

Clinical Implications and Future Directions

Despite these limitations, the results of this study highlight the potential role of molecular diagnostics in improving the detection of bloodstream infections. Rapid pathogen identification can facilitate early targeted therapy, reduce unnecessary broad-spectrum antibiotic use, and improve antimicrobial stewardship practices.

Future research should focus on developing molecular diagnostic platforms with broader pathogen coverage, improved sensitivity, and integrated antimicrobial resistance detection capabilities. Advances in metagenomic sequencing and point-of-care molecular diagnostics may further enhance the ability to rapidly diagnose bloodstream infections in diverse clinical settings.

Large multicenter studies are also needed to evaluate the clinical impact, cost-effectiveness, and implementation feasibility of molecular diagnostic technologies in routine healthcare practice.

CONCLUSION

This systematic review and meta-analysis evaluated the diagnostic accuracy of molecular diagnostic methods for detecting bloodstream infections compared with conventional blood culture. The pooled findings demonstrate that molecular techniques exhibit high sensitivity and specificity, supporting their usefulness as rapid diagnostic tools in clinical settings. These methods enable earlier detection of bloodstream pathogens and antimicrobial resistance genes, which can facilitate timely initiation of targeted antimicrobial therapy and potentially improve patient outcomes. Rapid identification of causative organisms is particularly critical in patients with sepsis, where delays in appropriate treatment are associated with increased mortality.

Despite their advantages, molecular diagnostic assays cannot yet fully replace conventional blood culture, as culture-based methods remain essential for antimicrobial susceptibility testing and detection of organisms outside predefined molecular panels. Therefore, molecular diagnostics should currently be considered complementary to traditional microbiological techniques rather than a complete substitute. Integrating rapid molecular testing with conventional culture methods may provide the most effective strategy for improving the diagnosis and management of bloodstream infections. Future research should focus on expanding pathogen detection panels, enhancing cost-effectiveness, and evaluating the clinical impact of molecular diagnostics in diverse healthcare settings.

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