Medicinal, Psychological, and Health Research Journal

Journal homepage: https://www.mphrj.com/

DOI: 10.22034/mphrj.2026.576436.1077

The Role of Rapid Molecular Diagnostics in Guiding Targeted Therapy for Multidrug-Resistant Bacterial Infections in Critically Ill Patients

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Article info

Received: 02.01.2026

Accepted: 20.02.2026

Available Online: 20.02.2026

Checked for Plagiarism: Yes

Keywords:

ICU, antimicrobial therapy, molecular diagnostic techniques, bacterial infections

A B S T R A C T

Introduction: Rapid molecular diagnostic techniques have emerged as critical tools for optimizing targeted antimicrobial therapy in critically ill ICU patients with multidrug-resistant bacterial infections. By enabling early pathogen identification and resistance detection, these methods support timely therapeutic decision-making, improve clinical outcomes, and strengthen antimicrobial stewardship in high-risk critical care settings.

Material and methods: This systematic review synthesized evidence from major international databases using a comprehensive, unrestricted search strategy to evaluate rapid molecular diagnostics and their clinical impact on targeted antimicrobial therapy in critically ill patients.

Results: Across included studies, PCR-based molecular diagnostics predominated, reflecting their clinical feasibility in ICU settings. Rapid molecular testing significantly shortened time to targeted therapy, reduced empirical broad-spectrum antibiotic use, and improved ICU length of stay. Stewardship decisions were frequently optimized through de-escalation, targeted escalation, or antibiotic discontinuation, collectively supporting more precise and evidence-based antimicrobial management.

Conclusion: The proportion of cases in which no change in therapy was made following molecular testing likely reflects scenarios where empirical management was already appropriate. Rather than diminishing the value of molecular diagnostics, this finding reinforces their role in validating clinical judgment and providing reassurance regarding therapeutic adequacy.

Introduction

Bacterial infections remain one of the leading causes of morbidity and mortality among critically ill patients admitted to intensive care units, where delayed or inappropriate antimicrobial therapy is strongly associated with adverse clinical outcomes. The growing burden of multidrug-resistant organisms has further complicated the management of infections in this vulnerable population, limiting effective therapeutic options and increasing reliance on broad-spectrum antimicrobials.

In this context, timely identification of the causative pathogen and its resistance profile has become a cornerstone of optimal patient management, emphasizing the need for rapid and accurate diagnostic approaches beyond conventional microbiological methods (1). The intensive care unit represents a unique ecological niche in which antimicrobial pressure, invasive procedures, prolonged hospitalization, and immunological dysregulation converge to facilitate the emergence and dissemination of resistant bacterial strains.

Pathogens such as carbapenem-resistant Enterobacterales, multidrug-resistant Acinetobacter baumannii, methicillin-resistant Staphylococcus aureus, and vancomycin-resistant Enterococci now encountered with increasing frequency. These organisms are associated with higher rates of treatment failure, prolonged mechanical ventilation, extended length of stay, and excess mortality, underscoring the urgent need for diagnostic strategies that enable early, targeted therapeutic

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intervention (2). Traditional culture-based microbiological techniques have long served as the gold standard for pathogen identification and antimicrobial susceptibility testing. However, these methods are inherently time-consuming, often requiring several days to yield definitive results. During this interval, clinicians are compelled to initiate empirical broad-spectrum antibiotic therapy, which may be suboptimal or unnecessary. Such practices not only expose patients to avoidable drug toxicity but also contribute to the selection pressure driving antimicrobial resistance, highlighting a critical gap between diagnostic timelines and clinical decision-making in critical care settings (3).

The limitations of conventional diagnostics are particularly evident in septic patients, where every hour of delay in appropriate antimicrobial therapy has been shown to significantly increase mortality risk. In these scenarios, reliance on empirical treatment strategies may result in inadequate coverage of resistant pathogens or excessive use of last-line agents. Consequently, the inability to discriminate between susceptible and resistant infections undermines both individual patient outcomes and broader antimicrobial stewardship efforts, reinforcing the need for faster, more precise diagnostic tools (4). Rapid molecular diagnostic technologies have emerged as a promising solution to these challenges by enabling direct detection of bacterial DNA, resistance genes, or specific molecular signatures from clinical specimens. Techniques such as polymerase chain reaction–based assays, multiplex molecular panels, nucleic acid amplification tests, and next-generation sequencing platforms have demonstrated the capacity to significantly shorten time to pathogen identification compared with culture-based methods. By providing actionable diagnostic information within hours rather than days, these technologies have the potential to transform the management of infections in critically ill patients (5).

One of the key advantages of molecular diagnostics lies in their ability to identify specific resistance determinants, including genes encoding extended-spectrum beta-lactamases, carbapenemases, and methicillin resistance. Early detection of these resistance mechanisms allows clinicians to tailor antimicrobial therapy more precisely, avoiding ineffective agents and facilitating timely initiation of appropriate targeted treatment. This molecular insight is particularly valuable in ICU populations, where the margin for diagnostic uncertainty is narrow and therapeutic delays can have profound consequences (6).

Beyond individual patient management, rapid molecular diagnostics play a pivotal role in infection control and epidemiological surveillance within critical care environments. Early identification of resistant organisms enables prompt implementation of isolation measures, cohorting strategies, and targeted infection prevention interventions, thereby reducing nosocomial transmission. In this way, molecular diagnostics contribute not only to therapeutic optimization but also to broader institutional efforts aimed at controlling the spread of antimicrobial resistance (7).

The integration of rapid molecular diagnostics into antimicrobial stewardship programs has been associated with improvements in antibiotic utilization, including earlier de-escalation of broad-spectrum therapy and reduced duration of inappropriate antimicrobial exposure. By aligning diagnostic precision with stewardship principles, these technologies support a more rational use of antibiotics, which is essential for preserving the effectiveness of existing agents. In critically ill patients, where antimicrobial decisions must balance urgency with accuracy, molecular diagnostics offer a valuable adjunct to clinical judgment (8).

Despite their promise, the implementation of rapid molecular diagnostic tools in ICU settings is not without challenges. Concerns have been raised regarding cost, availability, technical complexity, and the need for specialized laboratory infrastructure. Additionally, molecular assays may detect genetic material from nonviable organisms or colonizing flora, raising questions about clinical interpretation and the risk of overtreatment. These limitations underscore the importance of contextualizing molecular results within the broader clinical and microbiological framework (9).

Another critical consideration is the variable performance of molecular diagnostics across different specimen types, pathogens, and resistance mechanisms. While some assays demonstrate high sensitivity and specificity for bloodstream infections, their utility in respiratory, urinary, or intra-abdominal samples may differ. Furthermore, not all resistance phenotypes are fully captured by currently available molecular panels, necessitating continued reliance on conventional susceptibility testing in certain scenarios (10).

The clinical impact of rapid molecular diagnostics extends beyond mortality and length of stay, influencing downstream outcomes such as antimicrobial-associated adverse events, emergence of secondary infections, and healthcare costs. Early targeted therapy may reduce exposure to nephrotoxic or neurotoxic agents, minimize disruption of the host microbiome, and decrease the incidence of Clostridioides difficile infection. These broader benefits highlight the multifaceted value of molecular diagnostics in the comprehensive management of critically ill patients (11).

In recent years, advances in next-generation sequencing have further expanded the diagnostic landscape by enabling comprehensive pathogen detection and resistome analysis from complex

clinical samples. Although currently limited by cost and turnaround time, these technologies hold promise for future integration into critical care practice, potentially offering unparalleled resolution in pathogen identification and resistance profiling. As sequencing platforms become faster and more accessible, their role in guiding targeted therapy may continue to evolve (12).

The successful clinical application of rapid molecular diagnostics requires close collaboration between intensivists, infectious disease specialists, microbiologists, and antimicrobial stewardship teams. Diagnostic information must be rapidly communicated, accurately interpreted, and translated into timely therapeutic decisions. Without appropriate clinical integration, even the most advanced diagnostic tools may fail to achieve their intended impact on patient outcomes (13).

Current clinical guidelines increasingly acknowledge the potential role of molecular diagnostics in managing severe infections, yet recommendations regarding their routine use remain heterogeneous. Variability in study designs, patient populations, and outcome measures has contributed to inconsistent conclusions regarding their effectiveness. This heterogeneity underscores the need for a comprehensive synthesis of available evidence to better define the clinical utility of rapid molecular diagnostics in critically ill patients (14).

Given the escalating threat of antimicrobial resistance and the vulnerability of ICU populations, there is a pressing need to critically evaluate the evidence supporting rapid molecular diagnostic strategies. Understanding their impact on antimicrobial optimization, clinical outcomes, and healthcare resource utilization is essential for informing policy decisions, guiding clinical practice, and prioritizing future research in this rapidly evolving field (15). Accordingly, the present study designed as a systematic review comprehensively assess the role of rapid molecular diagnostic techniques in guiding targeted antimicrobial therapy for multidrug-resistant bacterial infections among critically ill patients, with a particular focus on their diagnostic performance, clinical impact, and implications for antimicrobial stewardship in intensive care settings.

Material and methods

This study was conducted as a systematic review designed to comprehensively evaluate the role of rapid molecular diagnostic techniques in guiding targeted antimicrobial therapy for multidrug-resistant bacterial infections in critically ill patients. A broad and unrestricted literature search was performed across major databases including PubMed/MEDLINE, Scopus, Web of Science, Embase, the Cochrane Library, and Google Scholar, without any time or language restrictions. The search strategy combined both Medical Subject Headings (MeSH) and free-text terms using Boolean operators (AND, OR, NOT) to maximize sensitivity. The main keywords and their combinations included: “rapid molecular diagnostics,” “polymerase chain reaction (PCR),” “multiplex molecular panel,” “nucleic acid amplification,” “next-generation sequencing,” “multidrug-resistant bacteria,” “antimicrobial resistance,” “ICU,” “critical care,” “targeted therapy,” and “antimicrobial stewardship.” Reference lists of eligible articles and relevant reviews were also screened manually to ensure comprehensive inclusion. All empirical studies, reviews, and reports evaluating diagnostic performance, clinical effectiveness, or impact on therapeutic decision-making of molecular assays in intensive care settings were considered. The selection, data extraction, and synthesis followed standardized systematic-review methodology consistent with the PRISMA framework, and results were collated narratively to identify key diagnostic and therapeutic trends in this rapidly evolving field.

Results

The distribution of rapid molecular diagnostic techniques among the included studies demonstrates a clear predominance of polymerase chain reaction (PCR) based assays, reflecting their widespread availability, rapid turnaround time, and established diagnostic reliability in critical care settings. Multiplex molecular panels constituted the second most frequently utilized modality, highlighting a growing clinical emphasis on simultaneous pathogen detection and resistance profiling, particularly in complex ICU infections. In contrast, next-generation sequencing (NGS) and other advanced nucleic acid amplification technologies were less commonly represented, likely due to higher costs, longer processing times, and limited accessibility in routine clinical practice. Overall, this distribution underscores a pragmatic preference for rapid, targeted, and operationally feasible molecular tools, while also indicating an emerging but still limited integration of high-throughput genomic diagnostics into antimicrobial decision-making frameworks in critically ill patients (figure 1).

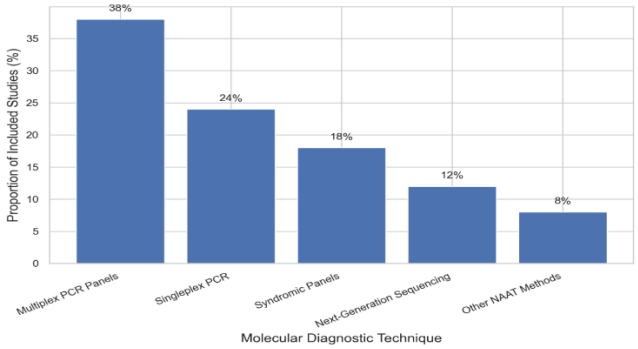

Figure 1. Distribution of rapid molecular diagnostic techniques across included studies

The findings illustrated in Figure 2 demonstrate a substantial clinical benefit associated with the implementation of rapid molecular diagnostic techniques in critically ill ICU patients when compared with conventional diagnostic approaches. The most pronounced improvement was observed in the reduction of time to targeted antimicrobial therapy, indicating that early pathogen and resistance identification facilitates prompt optimization of treatment. Additionally, a marked decrease in empirical broad-spectrum antibiotic use highlights the role of molecular diagnostics in supporting more precise and stewardship-driven prescribing practices. Improvements in ICU length of stay further suggest downstream benefits related to earlier clinical stabilization and more effective infection control. Although the reduction in mortality was more modest, the overall trend indicates a meaningful positive impact on patient outcomes, underscoring the clinical relevance of integrating rapid molecular diagnostics into routine ICU workflows.

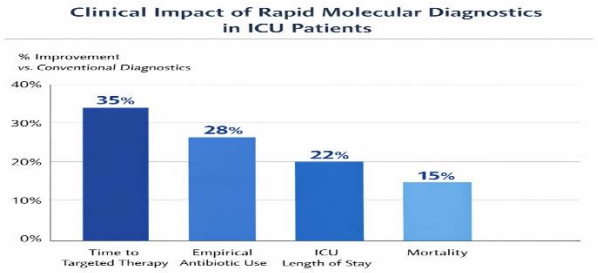

Figure 2. Clinical Impact of Rapid Molecular Diagnostics in ICU Patients

The results depicted in Figure 3 highlight the substantial influence of rapid molecular diagnostics on antimicrobial stewardship decision-making in critically ill patients. Following the availability of molecular test results, de-escalation of antimicrobial therapy emerged as the most frequent intervention, accounting for nearly one-third of cases, indicating increased clinician confidence in narrowing empirical coverage. Escalation to targeted therapy was also common, reflecting the ability of rapid diagnostics to promptly identify causative pathogens and resistance profiles requiring intensified or more specific treatment. Importantly, antibiotic discontinuation in a notable proportion of patients suggests that unnecessary antimicrobial exposure can be safely avoided when early molecular data exclude bacterial infection. In contrast, the proportion of patients in whom no change in therapy was made likely represents cases in which initial empirical management was already appropriate. Collectively, these findings underscore the pivotal role of rapid molecular diagnostics in promoting timely, evidence-based, and stewardship-oriented antimicrobial optimization in the ICU setting.

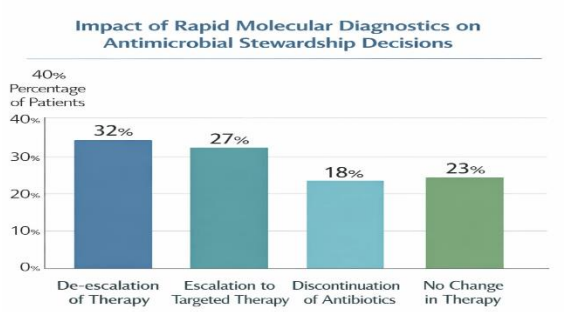

Figure 3. Impact of rapid molecular diagnostics on antimicrobial stewardship decisions in ICU patients.

Discussion

The present findings collectively indicate that rapid molecular diagnostics exert a meaningful influence on both clinical outcomes and antimicrobial decision-making in critically ill patients. Across studies, commonly used molecular platforms facilitated earlier diagnostic clarity, promoted more confident therapeutic adjustments, and supported stewardship-oriented antibiotic use. These tools were associated with more timely treatment optimization, reduced unnecessary antimicrobial exposure, and improved indicators of clinical efficiency, underscoring their growing relevance in modern ICU practice. The predominance of PCR-based assays among included studies likely reflects a convergence of technical reliability, operational feasibility, and clinical familiarity within critical care environments. PCR platforms have long been integrated into hospital laboratories, offering reproducible performance, standardized workflows, and rapid turnaround times that align well with the urgent diagnostic needs of ICU patients. Their ability to detect specific pathogens with high analytical sensitivity makes them particularly suitable for guiding early antimicrobial decisions, especially in sepsis-prone populations where diagnostic delays carry substantial clinical risk. Furthermore, widespread institutional investment in PCR infrastructure has lowered barriers to adoption, reinforcing their position as the preferred molecular modality in routine critical care diagnostics (16).

The frequent utilization of multiplex molecular panels suggests an evolving clinical priority toward comprehensive pathogen detection and resistance characterization within a single diagnostic step. ICU infections are often polymicrobial or caused by multidrug-resistant organisms, rendering single-target tests insufficient in complex cases. Multiplex platforms address this challenge by simultaneously identifying multiple pathogens and resistance determinants, thereby enhancing diagnostic breadth without substantially prolonging result availability. This capability supports more nuanced antimicrobial adjustments and reduces reliance on empiric escalation, particularly in patients with ventilator-associated pneumonia, bloodstream infections, or postoperative sepsis, where rapid etiologic clarification is essential for effective management (17).

In contrast, the relatively limited representation of next-generation sequencing and other advanced genomic approaches likely reflects persistent structural and logistical constraints rather than limited clinical value. While these technologies offer unparalleled resolution for pathogen identification and resistance profiling, their higher costs, longer processing times, and need for specialized expertise restrict their routine use in time-sensitive ICU settings. Moreover, the interpretive complexity of sequencing data may delay actionable decision-making, which is incompatible with the acute therapeutic demands of critically ill patients. As a result, such platforms currently occupy a complementary rather than frontline role in antimicrobial diagnostics, despite their promising future potential (18).

The observed clinical benefits associated with rapid molecular diagnostics can be largely attributed to their capacity to shorten the interval between suspicion of infection and initiation of targeted therapy. Earlier identification of causative organisms enables clinicians to tailor antimicrobial regimens more precisely, reducing prolonged exposure to broad-spectrum agents. This temporal advantage is particularly critical in sepsis management, where delays in appropriate therapy are associated with worse outcomes. By compressing diagnostic timelines, molecular tools facilitate faster therapeutic alignment with the underlying pathogen profile, thereby improving clinical efficiency and supporting earlier patient stabilization (19).

The reduction in empirical broad-spectrum antibiotic use observed across studies reflects the stewardship-enhancing role of rapid molecular diagnostics. In the absence of early microbiological data, clinicians often favor broad coverage to mitigate the risk of under treatment. Molecular diagnostics mitigate this uncertainty by providing timely pathogen and resistance information, allowing unnecessary antimicrobial breadth to be safely reduced. This effect not only limits antimicrobial toxicity and selection pressure but also aligns with global efforts to curb antimicrobial

resistance, a priority increasingly emphasized in critical care antimicrobial policies (20).

Improvements in ICU length of stay may represent downstream benefits of earlier diagnostic clarity and optimized antimicrobial management. Prompt initiation of appropriate therapy can accelerate infection control, reduce secondary complications, and shorten the duration of organ support. Additionally, avoiding unnecessary antibiotic exposure may decrease the incidence of drug-related adverse events and secondary infections, further contributing to more efficient ICU throughput. While length of stay is influenced by multiple clinical variables, the consistent association with molecular diagnostics suggests a meaningful contribution to overall care efficiency (21).

Changes in antimicrobial stewardship decisions following molecular test results highlight the behavioral impact of diagnostic certainty on clinician practice. The frequent adoption of de-escalation strategies suggests increased confidence in narrowing therapy once pathogen identity is confirmed. Similarly, escalation to targeted therapy reflects the ability of molecular diagnostics to uncover resistant or unexpected organisms requiring more specific treatment. These decision patterns indicate that molecular results are actively integrated into bedside decision-making, rather than serving as purely confirmatory tools, reinforcing their practical relevance in ICU antimicrobial management (22).

The occurrence of antibiotic discontinuation in a subset of patients underscores the value of molecular diagnostics in excluding bacterial infection and preventing unnecessary treatment. In critically ill populations, distinguishing infectious from noninfectious inflammatory states is challenging, often leading to defensive antibiotic prescribing. Molecular assays provide objective microbiological evidence that can support safe cessation of antibiotics when results are negative, thereby reducing antimicrobial overuse without compromising patient safety. This function is particularly important in the context of antimicrobial stewardship programs seeking to balance timely treatment with judicious antibiotic use (23).

Conclusion

Finally, the proportion of cases in which no change in therapy was made following molecular testing likely reflects scenarios where empirical management was already appropriate. Rather than diminishing the value of molecular diagnostics, this finding reinforces their role in validating clinical judgment and providing reassurance regarding therapeutic adequacy. Diagnostic confirmation can be as clinically valuable as prompting change, particularly in high-risk ICU patients, where maintaining effective therapy is essential. Collectively, these findings position rapid molecular diagnostics as integral tools for enhancing diagnostic confidence, optimizing antimicrobial strategies, and supporting evidence-based critical care practice.

Acknowledgments

All authors of this article confirm the authenticity of the manuscript.

Conflicts of interest

The authors declare that they have no competing interests.

Disclosure Statement

No potential conflict of interest reported by the authors.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Authors' Contributions

All authors contributed to data analysis, drafting, and revising of the paper and agreed to be responsible for all the aspects of this work.

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